

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549**

**FORM 10-K**

**ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the fiscal year ended December 31, 2021

or

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15 (d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file Number 001-37853

**FIRST WAVE BIOPHARMA, INC.**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of incorporation or organization)

46-4993860  
(I.R.S. Employer Identification No.)

777 Yamato Road, Suite 502  
Boca Raton, Florida 33431  
(Address of principal executive offices)

(561) 589-7020  
(Registrant's telephone number, including area code)

**Securities registered pursuant to Section 12(b) of the Act:**

<u>Title of each class</u>	<u>Trading Symbol</u>	<u>Name of each exchange on which registered</u>
Common stock, par value \$0.0001 per share	FWBI	Nasdaq Capital Market

**Securities registered under Section 12(g) of the Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes  No

The aggregate market value of common stock held by non-affiliates of the registrant, based on the closing price of a share of the registrant's common stock on June 30, 2021, which is the last business day of the registrant's most recently completed second fiscal quarter, as reported by the Nasdaq Capital Market on such date, was approximately \$67.1 million.

There were 16,700,640 shares of the registrant's common stock, par value \$0.0001 per share (the "Common Stock"), outstanding as of March 28, 2022.

FIRST WAVE BIOPHARMA, INC.  
ANNUAL REPORT ON FORM 10-K  
YEAR ENDED DECEMBER 31, 2021

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (“*Annual Report*”) contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this Annual Report other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate”, “believe”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “target”, “potential”, “will”, “would”, “could”, “should”, “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- our ability to regain and maintain compliance with the continued listing requirements of the Nasdaq Capital Market;
- our ability to satisfy our payment obligations under the First Wave Acquisition (as defined below);
- statements regarding the impact of the COVID-19 pandemic and other geopolitical events, including the war in Ukraine and their effects on our operations, access to capital, research and development and clinical trials and potential disruption in the operations and business of third-party vendors, contract research organizations (“CROs”), contract development and manufacturing organizations (“CDMOs”), other service providers, and collaborators with whom we conduct business;
- the availability of capital to satisfy our working capital requirements;
- our current and future capital requirements and our ability to raise additional funds to satisfy our capital needs;
- the integration and effects of our acquisitions, including the First Wave Acquisition, and other strategic transactions;
- the accuracy of our estimates regarding expense, future revenue and capital requirements;
- our ability to continue operating as a going concern;
- our plans to develop and commercialize our product candidates, including niclosamide and the biologic adrulipase (formerly MS1819);
- our ability to initiate and complete our clinical trials and to advance our principal product candidates into additional clinical trials, including pivotal clinical trials, and successfully complete such clinical trials;
- regulatory developments in the U.S. and foreign countries;
- the performance of our third-party vendor(s), CROs, CDMOs and other third-party non-clinical and clinical development collaborators and regulatory service providers;
- our ability to obtain and maintain intellectual property protection for our core assets;
- the size of the potential markets for our product candidates and our ability to serve those markets;

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- the rate and degree of market acceptance of our product candidates for any indication once approved;
- the success of competing products and product candidates in development by others that are or become available for the indications that we are pursuing;
- the loss of key scientific, clinical and nonclinical development, and/or management personnel, internally or from one of our third-party collaborators; and
- other risks and uncertainties, including those listed under Part I, Item 1A., “*Risk Factors*” of this Annual Report.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A, “*Risk Factors*,” herein and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs and consumer products, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources and we have not independently verified the data from third party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to “*First Wave*,” the “*Company*,” “*we*,” “*us*,” “*our*” and similar references are to First Wave BioPharma, Inc. and its subsidiaries on a consolidated basis. References to “*First Wave BioPharma*” refer to First Wave BioPharma, Inc. on an unconsolidated basis. References to “*AzurRx SAS*” refer to AzurRx SAS, First Wave BioPharma’s wholly-owned subsidiary through which we conduct our European operations. References to “*FWB*” refer to First Wave Bio, Inc., First Wave BioPharma’s wholly-owned subsidiary.

**PART I**

**ITEM 1. BUSINESS**

**Overview**

We are engaged in the research and development of targeted, non-systemic therapies for the treatment of patients with gastrointestinal (“GI”) diseases. Non-systemic therapies are drugs that act locally, i.e. in the intestinal lumen, skin or mucosa, without reaching an individual’s systemic circulation.

We are currently focused on developing our pipeline of gut-restricted GI clinical product candidates, including niclosamide, an oral small molecule with anti-viral and anti-inflammatory properties, and the biologic adrulipase (formerly MS1819), a recombinant lipase enzyme designed to enable the digestion of fats and other nutrients.

Our niclosamide programs leverage proprietary oral and topical formulations to address multiple GI conditions, including inflammatory bowel diseases (“IBD”) indications and viral diseases. We are currently advancing two separate clinical programs of our niclosamide formulations, both of which are currently in Phase 2 clinical trials including FW-COV for Severe Acute Respiratory Syndrome Coronavirus 2 (“COVID-19”) GI infections, and FW-UP for ulcerative proctitis (“UP”) and ulcerative proctosigmoiditis (“UPS”).

We are further developing FW-ICI-AC for Immune Checkpoint Inhibitor-associated colitis (“ICI-AC”) and diarrhea in advanced stage oncology patients, which received U.S. Food and Drug Administration (“FDA”) clearance for the investigational new drug (“IND”) application filed in September 2021, and two pre-IND programs of our niclosamide therapies for additional IBD indications, including FW-UC for ulcerative colitis (“UC”) and FW-CD for Crohn’s disease (“CD”).

Our adrulipase programs are focused on the development of an oral, non-systemic, biologic capsule for the treatment of exocrine pancreatic insufficiency (“EPI”) in patients with cystic fibrosis (“CF”) and chronic pancreatitis (“CP”). Our goal is to provide CF and CP patients with a safe and effective therapy to control EPI that is non-animal derived and offers the potential to dramatically reduce their daily pill burden.

We are developing our product candidates for a host of GI diseases where there are significant unmet clinical needs and limited therapeutic options, resulting in painful, life threatening and discomforting consequences for patients. Our mission is to help protect the health and restore quality of life for the millions of people afflicted by these GI diseases.

Each drug candidate and clinical program is described below.

*Niclosamide*

Niclosamide, a pro-inflammatory pathway inhibitor, is a prescription small molecule drug that has been safely used on millions of patients. Niclosamide is listed as an essential medicine by the World Health Organization (WHO). In the U.S., niclosamide was approved by the United States Food and Drug Administration (“FDA”) in 1982 for the treatment of intestinal tapeworm infections. Niclosamide’s activity as an anthelmintic results from direct action in the intestinal lumen where it disrupts a parasitic metabolic function called oxidative phosphorylation, killing parasites. Niclosamide has been commercially available worldwide for more than 50 years as 500mg single-dose tablets intended for use in pediatric and adult populations, at a dose rate of 2g per adult or child over six years of age. No safety issues have ever been identified. In addition to its anthelmintic activity, niclosamide has demonstrated novel anti-inflammatory and anti-viral properties.

We believe niclosamide, and more specifically our proprietary and patent-pending micronized niclosamide formulation, has the potential to be an ideal therapeutic to treat multiple GI indications due to the following favorable properties

- (i) it has a reduced particle size (D(90) between 5 and 9  $\mu\text{M}$ ) as compared to regular non-micronized niclosamide (approximately D(90)  $\geq 60\mu\text{M}$ ) with greater surface to solvent ratio;
- (ii) low oral bio-availability with minimal systemic absorption / exposure;

- (iii) improved dissolution with broader distribution allowing for higher local GI concentrations (up to approximately 200 times based on preclinical study results); and
- (iv) it exhibits anti-inflammatory effects while avoiding steroid-related complications and adverse events.

*Scientific Background*

Recent discoveries in immune cell metabolism suggest that it may be possible to selectively target disease-causing immune cells to treat inflammatory diseases without unwanted side effects associated with broad-based immunosuppression. Research indicates that IBD, including ulcerative colitis, ulcerative proctitis/proctosigmoiditis and Crohn's disease, is driven by pathogenic Th17 cells, which release a cascade of local cytokines that in turn cause inflammation in bowel wall tissues.

Th17 cells rely on a cellular process called oxidative phosphorylation to survive. Niclosamide is known to disrupt the oxidative phosphorylation in the mitochondria of pathogenic Th17 cells in a manner that selectively induces apoptosis of pathogenic Th17 cells, overcoming their inherent resistance to cell death. This effect is mild enough that it does not interfere with normal cells. By killing Th17 cells, niclosamide may reduce inflammation and calm the gut, selectively killing pathogenic, inflammatory cells while leaving healthy cells untouched.

Niclosamide has demonstrated beneficial effects in numerous cell culture studies using cells obtained by biopsy of inflamed bowel tissues from IBD patients, and also in animal models of IBD.

Our suite of proprietary, gut-restricted niclosamide product candidates are designed to target the metabolism of disease-causing Th17 cells to potentially halt or delay the progression of disease, stop flare-ups, and address patient needs at all stages of IBD, from mild to severe, and for cancer patients with ICI-AC.

*Inflammatory Bowel Disease Background*

IBD is an umbrella term used to describe disorders that involve chronic inflammation of the digestive track. IBD affects approximately 3 million people in the U.S. annually. IBD is divided into two main classes of gastrointestinal inflammatory diseases: (i) ulcerative colitis (UC), including ulcerative proctitis (UP) and ulcerative proctosigmoiditis (UPS), and (ii) Crohn's Disease (CD). There are similarities between UC and CD, such as immunopathology, and equal distribution between males and females. However, there are also notable differences. UC is generally limited to the colon, while CD may occur anywhere in the small or large intestine. UC usually affects continuous mucosal surfaces, while CD is patchier, with areas of normal bowel mucosa separating the inflammatory patches. Importantly, CD often involves deep bowel tissues and can lead to fistulas into the abdominal cavity or out to the skin surface. CD requires surgical intervention more often than UC. While medical treatments for UC and CD are generally similar, CD is much less responsive.

*FW-COV Program for COVID-19 GI infections*

The COVID-19 pandemic is a global public health emergency caused by the SARS-CoV-2 virus. An increasing volume of convergent evidence indicates that GI infection and fecal-oral transmission of SARS-CoV-2 are important factors in the clinical presentation, virology and epidemiology of COVID-19. There is currently no etiological treatment for COVID-19 GI effects. As a result, we believe there is an unmet therapeutic need for safe and effective treatment of these effects.

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A study published in July 2020 in *Antimicrobial Agents and Chemotherapy*, an American Society for Microbiology journal (Jeon *et. Al*, 2020) examined a small set (n=49) of FDA-approved drugs that were selected based on either having known activity against SARS-CoV or being recommended by infectious disease experts for activity against the SARS-CoV-2 virus. Results from this study indicated that niclosamide was the most potent of all agents tested in a Vero cell cytopathic assay with an IC50 value of 0.28 µM. For comparison, in terms of potency, niclosamide outperformed reference compounds chloroquine, lopinavir, and remdesivir with IC50 values of 7.28, 9.12, and 11.41 µM, respectively. IC50 is a quantitative measure that indicates how much of a particular inhibitory substance (e.g. a drug) is needed to inhibit, *in vitro*, a given biological process or biological component by fifty percent. Thus, niclosamide is approximately 40-fold more potent *in vitro* than VEKLURY® (remdesivir), an antiviral drug marketed by Gilead Sciences Inc. that received FDA approval in October 2020 for use in adult and pediatric patients for the treatment of COVID-19 requiring hospitalization.

Following oral administration, niclosamide is poorly absorbed, which results in a majority of the administered dose remaining in the GI tract. We believe this basic property of niclosamide, when combined with micronized niclosamide in the drug product to accelerate dissolution, will enable this drug product to achieve pharmacologically effective concentrations of niclosamide in the GI tract while having almost no bioavailability, potentially enhancing efficacy and safety. We believe these properties make our micronized niclosamide formulation a potential differentiated therapeutic for treating COVID-19 infections and GI symptoms.

There are multiple other late-stage clinical trials evaluating the standard (non-micronized) formulation of niclosamide in COVID-19. We believe this further indicates that available data on niclosamide's antiviral properties against SARS-CoV-2 is considered by others to be sufficient to proceed with clinical testing.

Based on evidence of niclosamide's antiviral properties we believe that it is reasonable to expect a clinical pharmacodynamic response against viral replication and clinical benefit, justifying the proposed clinical study in COVID-19 patients and favorable benefit-risk assessment.

We are developing FW-COV, a small molecule micronized niclosamide in an oral immediate release tablet formulation as a potential treatment for SARS-CoV-2 intestinal infection. The formulation to be used has been milled (micronized) to allow superior dissolution in the gut fluids which we believe should allow local niclosamide concentrations to reach anti-viral levels. Thus, FW-COV has the potential to benefit COVID-19 patients by decreasing viral load in the GI tract, treating infection symptoms and preventing transmission of the virus through fecal spread. We believe that evidence of niclosamide's antiviral properties is sufficient to expect a clinical pharmacodynamic response against viral replication and clinical benefit, which we believe justifies the proposed clinical study in COVID-19 patients and favorable benefit-risk assessment

An IND for FW-COV micronized niclosamide for COVID-19 GI infections was cleared by the FDA in September 2020. In April 2021, we initiated our Phase 2 RESERVOIR clinical trial for the treatment of COVID-19 related GI infections. The Phase 2 RESERVOIR clinical trial is a two-part, two-arm, randomized, placebo-controlled study examining the safety and efficacy of micronized oral niclosamide tablets in patients with COVID-19 GI infection. The two primary objectives of the RESERVOIR trial are to confirm the safety of niclosamide in the treatment of patients with COVID-19 GI infection and to demonstrate efficacy in clearing the SARS-CoV-2 virus from the GI tract.

Part 1 of the trial studied 9 patients with COVID-19 and diarrhea. Patients were randomized (2:1 niclosamide: placebo), treated for 14 days and observed closely for any signs of safety issues. In September 2021, we announced positive results from an independent Data Monitoring Committee review of the interim safety data. The Data Monitoring Committee also approved initiating patient enrollment in Part 2.

Part 2 of the trial studied approximately 150 patients in the U.S., Ukraine and India with mild or moderate COVID-19. Patients were randomized to either niclosamide, 400 mg tablets, three times a day, or placebo tablets three times a day. After 14 days of treatment, patients are taken off study drugs and remain on study observation for up to 6 months. Our trial samples from the clinical trial site in Ukraine have been completed and transported out of Ukraine.

The primary efficacy measure of the RESERVOIR trial is the rate of fecal SARS-CoV-2 virus clearance (rectal swab or stool sample) assessed by RT-PCR, comparing the niclosamide arm to the placebo arm for up to six months. These long-term observation data could indicate that niclosamide treatment has the potential to improve 'long haul' COVID-19 symptoms by decreasing viral load in the GI tract. There is evidence to support that the GI tract may be a possible reservoir for persistence and fecal spread of COVID-19 because ACE-2, the entry receptor for COVID-19, is highly expressed on GI cells.

In January 2022, we announced completion of patient enrollment for Part 2 of the RESERVOIR trial. No drug-related serious adverse events (SAEs) have been reported from the trial participants. We expect to report topline data in the first half of 2022.

*FW-UC for Ulcerative Colitis (UC)*

UC is an IBD that causes inflammation and ulcers (sores) in the digestive tract. UC generally affects the innermost lining of the large intestine (colon). UC affects approximately 830,000 patients in the U.S. annually and approximately 84% or 700,000 have mild to moderate disease. The immunopathology of UC is complex and is generally considered to be caused by a dysregulated immune system. There is evidence that a hereditary trait is involved. While the cause is not known, many researchers believe that invasive bacteria or virus in the bowel wall sets off an abnormal response by local T lymphocytes. Normally, a subgroup of lymphocytes called Th17 cells protect the bowel wall from microbial invaders. However, in patients with UC, these Th17 cells become pathogenic and release a cascade of local cytokines, which in turn cause inflammation in bowel wall tissues. This persistent inflammation causes tissue damage, and clinical symptoms. Clinical symptoms include abdominal pain, diarrhea, which is sometimes bloody, intermittent fever, anemia, and weight loss, and symptoms usually develop over time, rather than suddenly.

Severity of UC is generally classified as mild, moderate or severe. Mild disease is treated by sulfasalazine and 5-ASA's, most commonly mesalamine. These may be given orally or rectally and are modestly potent anti-inflammatory agents. While inexpensive and well tolerated, only about 50% of UC patients will maintain a clinical response to these agents. Non-responders or relapsers will progress to moderate or even severe disease.

Patients failing on 5-ASA's are usually placed onto steroid therapy, such as budesonide or prednisone, risking the well-known side effects of steroids. Failing, or not tolerating steroids leads to treatment with much more potent and expensive immunosuppressive agents such as anti-TNFs, or newer agents such as Entyvio® or Xeljanz®. We believe there is an unmet medical need for a well-tolerated, effective therapeutic for patients who fail first line treatment with 5-ASAs.

Our initial clinical trial in UC involves patients with ulcerative proctitis (UP) and ulcerative proctosigmoiditis (UPS), who are being treated with a topical rectal formulation, which is currently in a Phase 1b/2a clinical trial.

We intend to commence the clinical development of FW-UC, employing an oral tablet formulation in a Phase 1 clinical trial for subjects with UC in 2023, subject to successful results from Stage 2 of the FW-UP Phase 1b/2a clinical trial.

*FW-UP Program for Ulcerative Proctitis (UP) and Ulcerative Proctosigmoiditis (UPS)*

UP and UPS are two types of UC, a chronic inflammatory bowel disease consisting of fine ulcerations in the inner mucosal lining of the large intestine that do not penetrate the bowel muscle wall. UPS causes inflammation in the colon and rectum, while UP is confined only to the rectum. Symptoms include weight loss, fatigue, abdominal pain and cramps, rectal pain and bleeding, and diarrhea, although constipation can also develop as the body struggles to maintain normal bowel function. UP and UPS affect approximately 200,000 patients in the U.S. annually.

UP and UPS can occur at any point throughout life, with a high occurrence in young children and then again around 40-50 years of age. Progression of this disease to ulcerative colitis, extending farther up the bowel to involve the sigmoid colon, occurs in about 30-50% of patients. UP and UPS allow convenient clinical management and observation by local sigmoidoscopy. Although there is a range of treatments to help ease symptoms and induce remission, there is no cure.

We are developing FW-UP, a niclosamide-based, small molecule anti-inflammatory inhibitor therapy in enema formulation for the potential treatment of UP and UPS. FW-UP is currently being investigated in a three-stage Phase 1b/2a clinical trial in Europe studying the safety and potential efficacy of niclosamide in patients with UP and UPS.

Stage 1 of the trial studied 17 subjects with UP who had failed first line therapy with 5-ASAs. They were treated for six weeks with low dose FW-UP niclosamide rectal enemas twice a day. Preliminary results demonstrated that FW-UP niclosamide enemas were well tolerated, with a durable therapeutic effect. The efficacy endpoint was to achieve a clinical remission, defined as a Modified Mayo Score of 2 or less. A clinical remission rate of 59% was achieved, which is higher than currently approved second line therapy with budesonide (38% to 44%).



Stage 2 of the trial is designed to study a higher dose of niclosamide enema twice daily for six-weeks. Stage 2 enrollment was initiated in September 2021 and will enroll 28 patients in a placebo-controlled study to compare FW-UP, administered as an enema twice daily at a dose of 450 mg, to placebo enemas twice daily. We expect to complete enrollment in the second half of 2022 and expect to report topline data by the end of 2022.

Upon completion of Stage 2, we will assess overall dose response, efficacy and tolerability. Stage 3 of the trial will be an adaptively designed stage based upon the results obtained from Stage 2. We cannot provide an anticipated timeline for Stage 3 at this time.

#### *FW-ICI-AC for Immune Checkpoint Inhibitor Colitis (ICI-AC)*

Immune checkpoint inhibitors ("ICIs") are monoclonal antibodies that target down-regulators of the anti-cancer immune response and have significantly affected the treatment of a variety of malignancies. However, many immune-related adverse events, especially diarrhea and colitis, limit their use. A 2019 study titled, "Immune checkpoint inhibitor-induced colitis: A comprehensive review," published in *World Journal of Clinical Cases* (Sol *et.al*, 2019) estimated the incidence of IMC ranges from 1% to 25% depending on the type of ICI and whether they are used in combination. A 2017 study titled "Incidence of immune checkpoint inhibitor-related colitis in solid tumor patients: a systematic review and meta-analysis" published in *Oncoimmunology* (Wang *et.al*, 2017) estimated that approximately 44%, or 260,000 patients with advanced and metastatic tumors were eligible to receive ICIs. Further, approximately 30% of ICI patients develop diarrhea, which can progress to colitis. The onset of diarrhea in ICI-AC patients occurs within six to seven weeks and progressively worsens, and the progression to colitis is rapid and unpredictable.

In patients taking Yervoy® (ipilimumab), between 25% to 30% developed diarrhea and approximately 8% to 12% developed colitis, as reported in a peer-reviewed article, "Immune-checkpoint inhibitor-induced diarrhea and colitis in patients with advanced malignancies: retrospective review at MD Anderson" published in the *Journal for ImmunoTherapy of Cancer* (Wang *et. al.*, 2018). Moreover, there is a treatment trend towards the use of combination ICI therapies (for example combining Yervoy® and Opdivo®), which is believed to lead to a concomitant increase in both diarrhea and colitis.

We believe there currently is no approved treatment for Grade 1 colitis. The recommended treatment for Grade 2 or more severe colitis is administration of corticosteroids, or treatment with certain immunosuppressive biologics, while withholding ICI therapy (National Cancer Institute, 2020). The impact of this colitis complication and treatment may reduce the goal of progression-free cancer survival. We believe there is an unmet medical need and an oral, non-absorbed therapeutic, such as our FW-ICI-AC niclosamide, for Grade-1 colitis (diarrhea) which may prevent progression to Grade 2 or more severe disease.

In October 2021, we received FDA IND clearance to commence our Phase 1b/2a PASSPORT ICI-AC clinical trial using an oral immediate-release tablet formulation of niclosamide for Grade 1 and Grade 2 colitis and diarrhea in oncology patients receiving treatment with ICIs.

The Phase 2a PASSPORT clinical trial is designed as a double-blind, placebo-controlled study to determine the safety, tolerability, and preliminary efficacy of FW-ICI-AC in the treatment of immune checkpoint inhibitor-associated colitis (ICI-AC) and diarrhea in advanced cancer patients. 60 patients are planned to be enrolled in the trial and divided into two arms (30 patients per arm). One arm will receive FW-ICI-AC three times daily for two weeks, while the other arm will receive placebo three times daily for two weeks. Following treatment, each patient will enter a four-week evaluation period. The primary endpoint of the trial is safety and tolerability of FW-ICI-AC. Additional endpoints will measure early signals of efficacy, including resolution of the patient's diarrhea, sparing of steroids, and prevention of disease progression.

We plan to initiate the PASSPORT trial in the U.S. upon securing sufficient financial resources.

#### *FW-CD for Crohn's Disease (CD)*

While the immunopathology of CD resembles that of UC, the location of disease, the response to treatment and the overall morbidity are different, as CD is more difficult to manage. Patient response to standard therapy is more variable than in UC, thus making clinical management more challenging. In UC, a reasonably clear course of disease from mild to moderate severity can be predicted based upon response to first line treatment. In CD, first line treatment often includes more immunosuppressive agents, such as steroids, immunomodulators, and anti-TNF agents as compared to the 5-ASAs used for first line in UC.

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CD affects approximately 660,000 patients in the U.S. annually and approximately 76% or 500,000 have mild to moderate disease. We believe FW-CD, an oral niclosamide-based small molecule anti-inflammatory inhibitor therapy can be an important therapeutic in the treatment of mild to moderate CD, with the goal of reducing steroid and immunomodulators treatments.

We intend to commence clinical development of FW-CD in a Phase 2a clinical trial as early as 2025, subject to the successful completion of a FW-UC Phase 1 clinical trial.

*Adrulipase*

Adrulipase is the active pharmaceutical ingredient ("API"), derived from *Yarrowia lipolytica*, an aerobic yeast naturally found in various foods such as cheese and olive oil that is widely used as a biocatalyst in several industrial processes. Adrulipase is a secreted lipase naturally produced by *Yarrowia lipolytica*, known as LIP2, that we are developing through recombinant DNA technology for the treatment of EPI associated with CF and CP. Lipases are enzymes that help with the digestion of lipids and fat.

We previously held the exclusive right to commercialize adrulipase in the U.S., Canada, South America (excluding Brazil), Asia (excluding China and Japan), Australia, New Zealand and Israel pursuant to a sublicense from Laboratories Mayoly Spindler SAS ("*Mayoly*") under the JDLA (as defined below), which also granted us joint commercialization rights for Brazil, Italy, China and Japan. In March 2019, we purchased all rights, title and interest in and to adrulipase from Mayoly pursuant to the Mayoly APA (as defined below), *provided, however*, Mayoly retained exclusive commercial rights in France and Russia.

*Background*

The pancreas is both an endocrine gland that produces several important hormones, including insulin, glucagon, and pancreatic polypeptide, as well as a digestive organ that secretes pancreatic juice containing digestive enzymes that assist the absorption of nutrients and digestion in the small intestine.

The targeted indication of adrulipase is the compensation of EPI, which is observed when the exocrine functions of the pancreas are below 10% of normal. The symptomatology of EPI is essentially due to the deficiency of pancreatic lipase, an enzyme that hydrolyses triglycerides into monoglycerides and free fatty acids. The pancreatic lipase enzymatic activity is hardly compensated by extra-pancreatic mechanisms, because gastric lipase has nearly no lipolytic activity in the pH range of the intestine. On the other hand, when they are impaired, the pancreatic amylase and protease (enzymes that break up carbohydrates (starches) and proteins, respectively) activities can be compensated by the salivary amylase, the intestinal glycosidase, the gastric pepsin, and the intestinal peptidases, all of which are components of the gastric juice secreted by the stomach walls. Lipid maldigestion due to lipase deficiency is responsible for weight loss, steatorrhea featured by greasy diarrhea, and fat-soluble vitamin deficiencies (i.e. A, D, E and K vitamins).

CP, the most common cause of EPI, is a long-standing inflammation of the pancreas that alters its normal structure and functions. In the U.S., its prevalence rate is of 42 cases per 100,000 inhabitants, resulting in approximately 132,000 cases. Approximately 60% of patients affected with CP display EPI, resulting in approximately 90,000 patients requiring substitution therapy in the U.S. In Western societies, CP is caused by chronic alcoholic consumption in approximately 55-80% of cases. Other relatively frequent etiologies include the genetic form of the disease that is inherited as an autosomal dominant condition with variable penetrance, pancreatic trauma and idiopathic causes.

CF, another dominant etiology of EPI, is a severe genetic disease associated with chronic morbidity and life-span decrease of most affected individuals. In most Caucasian populations, CF prevalence is of 7-8 cases per 100,000 inhabitants, but is less common in other populations, resulting in more than 30,000 affected individuals in the U.S. and more than 70,000 affected individuals worldwide. CF is inherited as monogenic autosomal recessive disease due to the defect at a single gene locus that encodes the Cystic Fibrosis Transmembrane Regulator protein, or CFTR, a regulated chloride channel. Mutation of both alleles of this chloride channel gene results in the production of thick mucus, which causes a multisystem disease of the upper and lower respiratory tracts, digestive system, and the reproductive tract. The progressive destruction of the pancreas results in EPI that is responsible for malnutrition and contributes to significant morbidity and mortality. About 80-90% of patients with CF develop EPI, resulting in approximately 25,000-27,000 patients in the U.S. that require substitution therapy.

Current treatments for EPI stemming from CP and CF rely on porcine (pig derived) PERTs, which have been on the market since the late 1800s. PERTs are typically comprised of three digestive enzymes; lipases, proteases, and amylases. The PERT market is well established with estimated sales of approximately \$1.4 billion in 2019 in the U.S. and has been growing for the past five years at a compound annual growth rate of approximately 20%. In spite of their long-term use, however, PERTs suffer from poor stability, formulation problems, possible transmission of conventional and non-conventional infectious agents due to their animal origins, and possible adverse events at high doses in patients with CF and limited effectiveness.

#### *Pre-Clinical Program*

The efficacy of adrulipase has been investigated in normal minipigs, which are generally considered as a relevant model for digestive drug development when considering their physiological similarities with humans and their omnivore diet. Experimental pancreatitis was induced by pancreatic duct ligation, resulting in severe EPI with baseline CFA around 60% post-ligature. CFA is a measurement obtained by quantifying the amount of fat ingested orally over a defined time period and subtracting the amount eliminated in the stool to ascertain the amount of fat absorbed by the body. Pigs were treated with either adrulipase or enteric-coated PERTs, both administered as a single-daily dose.

At doses ranging from 10.5 to 211 mg, adrulipase increased the CFA by +25 to +29% in comparison to baseline ( $p < 0.05$  at all doses), whereas the 2.5 mg dose had milder activity. Similar efficacy was observed in pigs receiving 100,000 U lipase of enteric-coated porcine pancreatic extract. These findings demonstrate the *in vivo* activity of adrulipase in a relevant *in vivo* model at a level similar to the PERTs at dosages of 10.5mg or greater.

To date, two non-clinical toxicology studies have been conducted. Both show that adrulipase lipase is clinically well tolerated at levels up to 1000mg/kg in rats and 250 mg/kg in minipigs up to 13 weeks. adrulipase is therefore considered non-toxic in both rodent and non-rodent species up to a maximum feasible dose of 1,000 mg/kg/day in the rats over six months of administration.

#### *Clinical Program*

We believe that there are two principal therapeutic indications for EPI compensation by adrulipase: (i) children and adults affected by CF, and (ii) adult patients with CP. We have determined to initially pursue the indication for adults first in CF.

#### *Chronic Pancreatitis*

During 2010 and 2011, a phase 1/2a clinical trial of adrulipase was conducted in conjunction with Mayoly in a single center in France. The study was an exploratory study mainly designed to investigate the safety of adrulipase and was a randomized, double blind, placebo controlled, parallel clinical trial in 12 patients affected with CP or pancreatectomy and severe EPI. The primary efficacy endpoint of the study was defined as the relative change in steatorrhea (an established surrogate biomarker of EPI correction) in comparison to baseline. The study found that adrulipase was well tolerated with no serious adverse events. Only two adverse events were observed: constipation (two patients out of eight with adrulipase) and hypoglycemia (two patients out of eight with adrulipase, and one patient out of four with placebo). A non-statistically significant difference of the primary endpoint, possibly due to the small group size, was found between the two groups both in intention-to-treat, a group that included three patients who received the in-patient facility study diet but did not fulfill the protocol's inclusion criteria, and per-protocol analysis. This study was not designed, nor did it aim, to demonstrate statistically significant changes of CFA or steatorrhea under adrulipase.

We received regulatory approval in Australia and New Zealand in 2016, with the addition of a 2018 regulatory approval in France, to conduct a Phase 2 multi-center dose escalation study of adrulipase in CP and pancreatotomy. The primary endpoint of this study was to evaluate the safety of escalating doses of adrulipase in 11 CP patients. The secondary endpoint was to investigate the efficacy of adrulipase in these patients by analysis of the CFA and its change from baseline. In September 2018, we announced that in pre-planned analyses, both the study's primary and secondary endpoints were reached with a statistically significant ( $p=0.002$ ) improvement in the CFA of 21.8%, in a per protocol analysis, with the highest evaluated dose of 2,240 mg/day of adrulipase. Statistical significance of the trial results is typically based on widely used, conventional statistical methods that establishes the p-value of the results. A p-value of 0.05 or less is required to demonstrate statistical significance. As such, these CFA levels are considered to be statistically significant.

#### *Cystic Fibrosis Monotherapy*

In October 2018, the FDA cleared our IND application for adrulipase in patients with EPI due to CF. In December 2018, we initiated the Phase 2 OPTION Bridging Dose Study to investigate adrulipase in CF patients with EPI and in February 2019, we dosed the first patients. The Phase 2 OPTION Bridging Dose Study investigated the safety, tolerability and efficacy of adrulipase in a head-to-head comparison against the current PERT standard of care. The OPTION Bridging Dose Study employed a six-week non-inferiority CFA primary efficacy endpoint comparing adrulipase to PERTs.

In September 2019, we announced positive results from the OPTION Bridging Dose Study. Results showed that the primary efficacy endpoint of CFA was comparable to the CFA in a prior Phase 2 study in patients with CP, while using the same dosage of adrulipase. The dosage used in the OPTION Bridging Dose Study was 2.2 grams per day, which was determined in agreement with the FDA as a bridging dose from the highest safe dose used in the Phase 2 CP dose escalation study. Although the study was not powered for statistical significance, the data demonstrated meaningful efficacy results, with approximately 50% of the patients showing CFAs high enough to reach non-inferiority with standard PERTs. Additionally, the CNA was comparable between the adrulipase and PERT arms, 93% vs. 97%, respectively, in the OPTION Bridging Dose Study. This important finding confirms that protease supplementation is not likely to be required with adrulipase treatment. A total of 32 patients, ages 18 or older, completed the OPTION Bridging Dose Study.

In October 2019, the CFF DSMB completed its review of our final results of the OPTION Bridging Dose Study and found no safety concerns for adrulipase and supported our plan to proceed to the Phase 2b OPTION 2 Trial. In December 2019, we submitted the clinical trial protocol to the existing IND at the FDA. In April 2020, we received approval to conduct the OPTION 2 Trial in Therapeutics Development Network clinical sites in the U.S.

The OPTION 2 Trial was designed to investigate the safety, tolerability and efficacy of adrulipase (2.2 gram and 4.4 gram doses in enteric capsules) head-to-head versus the current standard of care, PERT pills. The OPTION 2 Trial was an open-label, crossover study, conducted in 15 sites in the U.S. and Europe. Enrollment included a total of 30 CF patients 18 years or older. Adrulipase was administered in enteric capsules to provide gastric protection and test for optimal delivery of enzyme to the duodenum. Patients will first be randomized into two cohorts: to either the adrulipase arm, where they receive a 2.2 gram daily oral dose of adrulipase for three weeks; or to the PERT arm, where they receive their pre-study dose of PERT pills for three weeks. After three weeks, stools will be collected for analysis of CFA. Patients will then be crossed over for another three weeks of the alternative treatment. After three weeks of cross-over therapy, stools will again be collected for analysis of CFA. A parallel group of patients will be randomized and studied in the same fashion, using a 4.4 gram daily dose of adrulipase. All patients will be followed for an additional two weeks after completing both crossover treatments for post study safety observation. Patients will be assessed using descriptive methods for efficacy, comparing CFA between adrulipase and PERT arms, and for safety.

In January 2021, we announced an additional study arm in OPTION 2 Trial using an immediate release adrulipase capsules in order to identify the optimal dose and delivery method of adrulipase. This extension phase tested patients 18 years or older, who have already completed the crossover phase, at higher doses relative to the previously conducted OPTION Bridging Dose Study. This allowed us to compare data from the existing crossover arm using enteric (delayed release) capsules with data from the new immediate release extension arm.

In March 2021 we announced topline OPTION 2 data. The trial demonstrated that adrulipase was safe and well-tolerated and data from OPTION 2, and the other adrulipase Phase 2 clinical trials, demonstrated drug activity. However, OPTION 2 did not consistently meet the primary efficacy endpoint. Some patients were able to achieve CFA at levels beyond what is required to demonstrate non-inferiority with PERT therapies, but the majority did not.

We believe that the underlying cause of the drug's uneven efficacy performance in the OPTION 2 trial was the enteric capsule formulation. While the enteric coating protected the capsule from breaking down in the stomach acid, it also appeared to dissolve too slowly in the small intestine to release the lipase enzyme in time to aid with proper digestion and nutrient absorption.

In August 2021 we announced that we would begin development of a new enteric microgranule formulation of adrulipase. The new formulation is planned to be administered with food as an oral capsule that dissolves in the stomach and disperses acid-resistant micro-granules that thoroughly mix with food during the digestion process. The resultant mixture then passes to the small intestine where the lipase enzyme breaks up fat molecules so that they can be absorbed. We expect to complete the formulation work in the first half of 2022 and to initiate a Phase 2b pilot monotherapy trial during the second half of 2022.

#### *Combination Therapy*

We launched the Phase 2 Combination Trial in Hungary in July 2019 to investigate adrulipase, in combination with PERT, in CF patients who suffer from severe EPI but continue to experience clinical symptoms of fat malabsorption despite taking the maximum daily dose of PERTs. The Combination Trial is designed to investigate the safety, tolerability and efficacy of escalating doses of adrulipase (700 mg, 1120 mg and 2240 mg per day, respectively), in conjunction with a stable dose of PERTs, in order to increase CFA and relieve abdominal symptoms. In October 2020, we opened a total of five clinical sites in Turkey and dosed the first patients in November 2020. In March 2021, we reached targeted minimum enrollment of 18 patients.

We announced positive interim data on the first five patients in the Combination Trial in August 2020. The primary efficacy endpoint was met, with CFAs greater than 80% for all patients across all visits. For secondary efficacy endpoints, we observed that stool weight decreased, the number of stools per day decreased, steatorrhea improved, and body weight increased. Additionally, no serious adverse events were reported.

In August 2021, we announced topline data collected from the 20 patients enrolled in the study. The data indicated that adrulipase in combination with PERT led to clinically meaningful improvements in CFA, the primary efficacy endpoint. Patients showed an average gain of more than six percentage points from baseline, compared to the five-point improvement in CFA cited by the clinical literature as clinically significant. The study also demonstrated positive improvements in weight gain and other secondary endpoints.

We believe a combination therapy of PERT and adrulipase has the potential to: (i) correct macronutrient and micronutrient maldigestion; (ii) eliminate abdominal symptoms attributable to maldigestion; and (iii) sustain optimal nutritional status on a normal diet in CF patients with severe EPI. We are focused on developing a new enteric microgranule formulation, which we anticipate bringing to the clinic in the second half of 2022 in a pilot monotherapy trial. Depending on the results of this trial, we may elect to conduct further combination therapy trials using the new formulation.

#### **Recent Developments**

##### *Nasdaq Deficiency Notice*

On November 26, 2021, we received a letter from the Listing Qualifications Department of The Nasdaq Stock Market LLC ("*Nasdaq*") indicating that we were not in compliance with the minimum stockholders' equity requirement for continued listing on the Nasdaq Capital Market, under Listing Rule 5550(b)(1), because our stockholders' equity of \$(6,969,988) as reported in our Quarterly Report on Form 10-Q for the period ended September 30, 2021 was below the required minimum of \$2.5 million, and because, as of November 24, 2021, we did not meet the alternative compliance standards, relating to the market value of listed securities of \$35 million or net income from continuing operations of \$500,000 in the most recently completed fiscal year or in two of the last three most recently completed fiscal years.

On January 10, 2022, we submitted to Nasdaq a plan to regain compliance with Listing Rule 5550(b)(1). On February 15, 2022, Nasdaq notified us that they have granted us an extension of up to 180 calendar days from November 26, 2021, or through May 25, 2022, to regain compliance. If we fail to evidence compliance upon filing our periodic report for the quarter ending June 30, 2022, we may be subject to delisting. If Nasdaq determines to delist our common stock, we will have the right to appeal to a Nasdaq hearings panel.

*Waiver Agreements with Certain Holders of Series B Convertible Preferred Stock*

Between February 1 and February 7, 2022, we entered into waiver agreements (the “*Waiver*”) with certain holders of the Company’s Series B Convertible Preferred Stock, par value \$0.0001 per share (the “*Series B Preferred Stock*”), pursuant to which we agreed to pay a cash waiver fee equal to ten percent of the stated value of the shares of Series B Preferred Stock held by such holder (other than holders who are insiders of the Company who did not receive a cash waiver fee) and such holder agreed to irrevocably waive its Series B Exchange Right (as defined below) with respect to any Subsequent Financing (as defined below) that occurs from and after the date of the Waiver until December 31, 2022.

Pursuant to the Series B Preferred Stock Certificate of Designations (the “*Series B Certificate of Designations*”), in the event of any issuance by the Company or any of its subsidiaries of its common stock, par value \$0.0001, or common stock equivalents for cash consideration or a combination of units thereof (a “*Subsequent Financing*”), each holder of the Company’s Series B Preferred Stock has the right, subject to certain exceptions set forth in the Certificate of Designations, at its option, to exchange (in lieu of cash subscription payments) all or some of the Series B Preferred Stock then held (with a value per share of Series B Preferred Stock equal to the stated value of each share of Series B Preferred Stock, or \$7,700.00, plus accrued and unpaid dividends thereon, of the Series B Preferred Stock) for any securities or units issued in a Subsequent Financing on a dollar-for-dollar basis (the “*Series B Exchange Right*”).

We entered into Waivers with holders of approximately \$2.88 million of stated value of our Series B Preferred Stock. We also entered into Waivers with Company insiders holding approximately \$474,000 of stated value of our Series B Preferred Stock for which we did not pay a waiver fee.

*Amendment to Charter and Increase in Authorized Shares*

On January 14, 2022, at the Annual Meeting of Stockholders (“*Annual Meeting*”), our stockholders approved an amendment to the Amended and Restated Certificate of Incorporation (the “*Charter*”) to increase the number of authorized shares of Common Stock by 25,000,000 shares to 50,000,000 shares.

We filed a Certificate of Amendment to the Charter with the Secretary of State of the State of Delaware on January 14, 2022, to increase the number of authorized shares of Common Stock to 50,000,000 shares.

*March 2022 Registered Direct Offering*

On February 27, 2022, we entered into a securities purchase agreement with a single institutional investor (the “*March 2022 Purchase Agreement*”) pursuant to which we agreed to sell, in a registered direct offering (the “*March 2022 Registered Direct Offering*”) priced at market under Nasdaq rules, an aggregate of (i) 1,650,000 shares of Common Stock, (ii) pre-funded warrants (the “*March 2022 Pre-Funded Warrants*”) exercisable for an aggregate of up to 4,848,195 shares of Common Stock, and (iii) Series C warrants (the “*Series C Warrants*”) exercisable for an aggregate of up to 6,498,195 shares of Common Stock. The public offering price for each share of Common Stock and accompanying Series C Warrant to purchase one share of Common Stock was \$1.385, and the public offering price for each March 2022 Pre-Funded Warrant and accompanying Series C Warrant to purchase one share of Common Stock was \$1.375. The March 2022 Registered Direct Offering closed on March 2, 2022.

The net proceeds of the March 2022 Registered Direct Offering, after deducting the placement agent’s fees and expenses and other estimated offering expenses payable by us and excluding the net proceeds, if any, from the exercise of the Series C Warrants, were approximately \$8.1 million. We intend to use the net proceeds from the March 2022 Registered Direct Offering to pay a portion of the cash purchase price for its acquisition of First Wave Bio, Inc. and for other general corporate purposes, which may include product manufacturing, clinical development and/or increases in working capital.

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In the March 2022 Purchase Agreement, we agreed not to issue, enter into any agreement to issue or announce the issuance or proposed issuance of, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or file any registration statement or prospectus, or any amendment or supplement thereto for 60 days after the closing date of the March 2022 Registered Direct Offering. In addition, we agreed not to effect or enter into an agreement to effect any issuance of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock involving a variable rate transaction (as defined in the March 2022 Purchase Agreement) until the one-year anniversary of the date of the March 2022 Purchase Agreement, subject to certain exceptions.

*Series B Most Favored Nations (MFN) Exchanges*

Under the Series B Certificate of Designations, in the event we effect any issuance of Common Stock or Common Stock equivalents for cash consideration, or a combination of units thereof (a "Subsequent Financing"), each holder of Series B Preferred Stock, has the right to exchange the Exchange Amount of the Series B Preferred Stock for any securities issued in the Subsequent Financing, in lieu of any cash subscription payments therefor (the "Series B Exchange Right").

We entered into the March 2022 Purchase Agreement as part of the March 2022 Registered Direct Offering, and the holders of the Series B Preferred Stock became entitled to exercise their Series B Exchange Right to exchange into shares of Common Stock and related Series C Warrants. As of March 28, 2022, holders of approximately 17.05 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$145,000 had previously elected to exercise their Series B Exchange Rights into 104,735 shares of Common Stock, and additional Series C Warrants exercisable for up to an aggregate of 104,735 shares of Common Stock.

*Issuance of Stock Options*

On January 3, 2022, we issued employees ten-year stock options to purchase 161,000 shares of Common Stock with a strike price of \$1.45 per share, subject to service-based milestone vesting over three years under the 2020 Plan as payment for services rendered. Such issuance was exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act").

**Corporate History**

We were incorporated on January 30, 2014 in the State of Delaware. In May 2014, we entered into a stock purchase agreement with Protea Biosciences Group, Inc. ("Protea Group") and its wholly-owned subsidiary, Protea Biosciences, Inc. ("Protea Sub" and, together with Protea Group, "Protea"), to acquire 100% of the outstanding capital stock of AzurRx SAS (formerly ProteaBio Europe SAS), a wholly-owned subsidiary of Protea Sub, which was completed in June 2014. In October 2016, we completed an initial public offering, which allowed us to list our shares of Common Stock on the Nasdaq Capital Market.

On September 13, 2021, we completed the acquisition of First Wave Bio, Inc. ("FWB"), in accordance with the terms of an Agreement and Plan of Merger dated as of September 13, 2021 (the "Merger Agreement") by and among the Company, Alpha Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of the Company ("Merger Sub"), and FWB. On September 13, 2021, pursuant to the Merger Agreement, Merger Sub was merged with and into FWB (the "Merger" or "First Wave Acquisition"), with FWB being the surviving corporation and becoming a wholly-owned subsidiary of the Company. In connection with the Merger, AzurRx BioPharma, Inc. changed its name to First Wave BioPharma, Inc.

**Agreements and Collaborations**

*License Agreement with First Wave Bio, Inc.*

On December 31, 2020, we entered into a license agreement with FWB (the "FWB License Agreement"), pursuant to which FWB granted us a worldwide, exclusive right to develop, manufacture, and commercialize FWB's proprietary immediate release and enema formulations of nicosamide for the fields of treating ICI-AC and COVID-19 in humans (the "Nicosamide Product").

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In consideration of the license and other rights granted by FWB, we agreed to pay FWB a \$9.0 million upfront cash payment due within 10 days and were obligated to make an additional payment of \$1.25 million due on June 30, 2021. In addition, we were obligated to pay potential milestone payments to FWB totaling up to \$37.0 million for each indication, based upon the achievement of specified development and regulatory milestones. Under the FWB License Agreement we were obligated to pay FWB royalties as a mid-single digit percentage of net sales of the Niclosamide Product, subject to specified reductions. We were also obligated to issue to FWB junior convertible preferred stock, initially convertible into \$3.0 million worth of Common Stock, based upon the volume weighted average price of the Common Stock for the five-day period immediately preceding the date of the FWB License Agreement, or \$9.118 per share.

In addition, on January 8, 2021, pursuant to the First Wave License Agreement we entered into a securities purchase agreement with FWB (the "*FWB Purchase Agreement*") pursuant to which we issued to FWB 3,290,196 shares of Series C Preferred Stock, initially convertible into an aggregate of 329,019 shares of Common Stock, at an initial stated value of \$750.00 per share and a conversion price of \$7.50 per share, which was the equivalent of \$3.0 million at \$9.118 per share. The preferred stock automatically converted into Common Stock upon the stockholder approval.

Upon consummation of the Merger on September 13, 2021, the FWB License Agreement was effectively canceled.

*Protea Stock Purchase Agreement and Asset Sale and Purchase Agreement*

In May 2014, we entered into a stock purchase agreement (the "*Protea SPA*") with Protea to acquire 100% of the outstanding capital stock of ProteaBio Europe SAS (the "*Protea Acquisition*"). In June 2014, we completed the Protea Acquisition in exchange for the payment to Protea of \$600,000 and the issuance of shares of our Series A Preferred convertible into 33% of our outstanding Common Stock. Pursuant to the Protea SPA, Protea Sub assigned (i) to Protea Europe all of its rights, assets, know-how and intellectual property rights in connection with the adrulipase (formerly MS1819) program and those granted under that certain Joint Research and Development Agreement (the "*JDLA*"), by and among Protea Sub, Protea Europe and Mayoly, dated March 22, 2010; and (ii) to us all amounts, together with any right of reimbursement, due to Protea Sub in connection with outstanding stockholder loans.

Pursuant to the Protea SPA, we were obligated to pay certain other contingent consideration upon the satisfaction of certain events, including (a) a one-time milestone payment of \$2.0 million due within ten days of receipt of the first approval by the FDA of a New Drug Application ("*NDA*") or Biological License Application ("*BLA*") for a Business Product (as such term is defined in the Protea SPA); (b) royalty payments equal to 2.5% of net sales of Business Product up to \$100.0 million and 1.5% of net sales of Business Product in excess of \$100.0 million; and (c) 10% of the transaction value (as defined in the Protea SPA) received in connection with a sale or transfer of the pharmaceutical development business of Protea Europe.

In December 2018, we entered into a purchase agreement (the "*Protea Purchase Agreement*") with Protea Biosciences Group, Inc. and Protea, its wholly owned subsidiary, pursuant to which we agreed to purchase the rights to any milestone payments, royalty payments, and transaction value consideration due from us to Protea now or in the future, arising from the Protea SPA (the "*Purchased Assets*"). In accordance with the terms of the Protea Purchase Agreement, we purchased the Purchased Assets from Protea for an aggregate purchase price of approximately \$1.6 million. We paid approximately \$0.3 million of the purchase price in cash, and the remaining approximately \$1.3 million was paid by the issuance of shares of Common Stock to Protea.

*Mayoly JDLA and Subsequent Asset Purchase Agreement*

In March 2010, Protea and AzurRx SAS entered into the JDLA with Mayoly pursuant to which Mayoly sublicensed certain of its exclusive rights to a genetically engineered yeast strain cell line on which our adrulipase is based that derive from a Usage and Cross-Licensing Agreement dated February 2, 2006 between Mayoly and INRA, in charge of patent management acting for and on behalf of CNRS and INRA.



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In January 2014, Protea entered into an amended and restated JDLA with Mayoly (the "*Mayoly Agreement*"), pursuant to which Protea acquired the exclusive right to Mayoly patents and technology, with the right to sublicense, develop, manufacture and commercialize human pharmaceuticals based on the adrulipase lipase within the following territories: U.S. and Canada, South America (excluding Brazil), Asia (excluding China and Japan), Australia, New Zealand and Israel. The JDLA further provided Mayoly the exclusive right to Protea's patents and technology, with the right to sublicense, develop, manufacture and commercialize human pharmaceuticals based on the adrulipase lipase within the following territories: Mexico, Europe (excluding Italy, Portugal and Spain) and any other country not granted to us alone, or jointly with Mayoly. Prior to the execution of the Mayoly APA, rights to the following territories were held jointly with Mayoly: Brazil, Italy, Portugal, Spain, China and Japan. In addition, the Mayoly Agreement required Protea to pay 70% of all development costs and required each of the parties to use reasonable efforts to:

- devote sufficient personnel and facilities required for the performance of its assigned tasks;
- make available appropriately qualified personnel to supervise, analyze and report on the results obtained in the furtherance of the development program; and
- deploy such scientific, technical, financial and other resources as is necessary to conduct the development program.

*Asset Purchase Agreement with Mayoly*

In March 2019, the Company and Mayoly entered into an Asset Purchase Agreement and associated Assignment Agreement and Delegation and Set-off Agreement (together, the "*Mayoly APA*"), pursuant to which we purchased all remaining rights, title and interest in and to adrulipase. Upon execution of the Mayoly APA, the JDLA previously executed by AzurRx SAS and Mayoly was assigned to us. In addition, the Company executed a Patent License Agreement with Mayoly pursuant to which we granted to Mayoly an exclusive, royalty-bearing right to revenue received from commercialization of adrulipase within France and Russia. We have exclusive rights to adrulipase in all other global territories.

In accordance with the Mayoly APA and related transaction documents, we provided to Mayoly the following consideration:

- (i) we assumed certain of Mayoly's liabilities with respect to adrulipase;
- (ii) we assumed all amounts currently owed to AzurRx SAS by Mayoly under the JDLA;
- (iii) we agreed to pay, within 30 days after the execution of the Mayoly APA, all amounts incurred by Mayoly for the maintenance of patents related to adrulipase from January 1, 2019 through the date of the Mayoly APA;
- (iv) we made an initial payment to Mayoly of €800,000, which amount was paid by the issuance of 40,048 shares of Common Stock at a price of \$22.90 per share (the "*Closing Payment Shares*"); and
- (v) we agreed to pay to Mayoly an additional €1,500,000, payable in a mix of cash and shares of Common Stock as follows (the "*Milestone Payments*"): (i) on December 31, 2019, a cash payment of €400,000 and 20,024 shares of Common Stock (the "*2019 Escrow Shares*") and (ii) on December 31, 2020, a cash payment of €350,000 and 17,521 shares of Common Stock (the "*2020 Escrow Shares*" and, together with the 2019 Escrow Shares, the "*Escrow Shares*").

The Closing Payment Shares and the Escrow Shares were all issued upon execution of the Mayoly APA; *provided, however*, per the terms of the Mayoly APA, the Escrow Shares will be held in escrow until the applicable milestone payment date, at which time the respective Escrow Shares will be vested and released to Mayoly (See Note 14).

## Intellectual Property

Our goal is to obtain, maintain and enforce patent protection for our product candidates, formulations, processes, methods and any other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. However, patent protection may not afford us with complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management and research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently rely and will in the future rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

### Niclosamide

Our FW-ICI-AC, FW-UP, FW-UC and FW-CD niclosamide programs are protected by patent filings that include the following :

- US10,912,746; US10,905,666; US10,292,951; US10,772,854; US10,744,103; US10,799,468; US10,849,867; and related continuation applications as well as corresponding worldwide patent filings all entitled "Methods and Compositions for Treating Conditions Associated with an Abnormal Inflammatory Process." The expiration date of the issued patents is September 1, 2036; and
- A PCT International application filed in 2020 and corresponding U.S. and foreign patent applications directed to compositions and methods for treating conditions characterized by an abnormal inflammatory response such as an autoimmune disorder, colitis, autoimmune colitis, an inflammatory bowel disease, Crohn's disease and ulcerative colitis. Any national designated patent application from this filing upon issuance will have an expected expiration in 2040.

Our FW-COV niclosamide programs are protected by patent filings that include the following:

- US10,980,756 and corresponding PCT International and foreign patent applications directed to the use of niclosamide for the treatment of COVID-19 gastrointestinal infections. The expiration of the issued patent is March 31, 2040.
- In addition, a PCT International application and a corresponding U.S. application was filed in 2022 directed to methods of treating Long Covid with niclosamide. Any patents issuing from these filings will have an expected expiration in 2042.

### Adrulipase

The adrulipase program is protected by the following issued patents that we have licensed under the Mayoly Agreement:

- PCT/FR2006/001352 patent family (including the patent EP2035556 and patent US8,334,130 and US8,834,867) "Method for producing lipase, transformed *Yarrowia lipolytica* cell capable of producing said lipase and their uses" describes a method for producing *Yarrowia lipolytica* acid-resistant recombinant lipase utilizing a culture medium without any products of animal origin or non-characterized mixtures such as tryptone, peptone or lactoserum, in addition to its uses. The European patents expire June 15, 2026, U.S. patent 8,334,130 expires September 11, 2028, and U.S. patent 8,834,867 expires September 15, 2026.

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In addition, a PCT International application was filed in 2021 directed to our proprietary formulation of FW-EPI. Any national designated patent application from this filing upon issuance will have an expected expiration in 2041.

A U.S. Provisional Application was filed in 2021 directed to stable lipase formulations and methods of treatment. Any patents issuing from this filing will have an expected expiration in 2042.

**Manufacturing**

We currently outsource all manufacturing, and we intend to use our collaborators and contract development and manufacturing organizations (“*CDMOs*”) for the foreseeable future.

*Niclosamide*

Niclosamide API is obtained by chemical synthesis and is currently manufactured by Olon SpA at a facility in Murcia, Spain. Niclosamide drug product is currently manufactured at a contract facility located in Milan, Italy owned by Monteresearch s.r.l. and at a contract facility located in Tianjin, China owned by Asymchem Inc. We believe there are multiple alternative contract manufacturers capable of producing the product we need for clinical trials; however, there is no guarantee that the processes are easily reproducible and transferrable.

*Adrulipase*

Adrulipase API is obtained by fermentation in bioreactors using our engineered and proprietary *Yarrowia lipolytica* strain. The proprietary yeast cell line from which the API is derived is kept at a storage facility maintained by Charles River Laboratories Inc. Adrulipase drug substance is currently manufactured at a contract facility located in Capua, Italy owned by Olon SpA. Adrulipase drug product is currently manufactured at a contract facilities located in Reims, France and Craigavon, United Kingdom owned by Delpharm SAS and Almac Pharma Services Ltd. We believe there are multiple alternative contract manufacturers capable of producing the product we need for clinical trials. We are in the process of establishing alternative manufacturers and manufacturing sites for the product; however, there is no guarantee that the processes are easily reproducible and transferrable. In December 2020, we entered into a master service agreement with Asymchem Inc. to initiate the transfer of the manufacturing process for API, drug substance and drug product.

**Competition**

The pharmaceutical and biotechnology industries are characterized by rapidly evolving technology and intense competition. Many companies of all sizes, including major pharmaceutical companies and specialized biotechnology companies, are engaged in the development and commercialization of therapeutic agents designed for the treatment of the same diseases and disorders that we target. Many of our competitors have substantially greater financial and other resources, larger research and development staff and more experience in the regulatory approval process. Moreover, potential competitors have or may have patents or other rights that conflict with patents covering our technologies.

*Niclosamide*

With respect to FW-COV, our oral micronized formulation of niclosamide for COVID-19 GI infections, if approved, would compete with currently approved antivirals, including Pfizer’s Inc.’s PAXLOVID™, Merck & Co. Inc. and Ridgeback Biotherapeutics’ molnupiravir, VEKLURY® (remdesivir) marketed by Gilead Sciences, Inc. and vaccines, including those marketed by Pfizer Inc. and BioNTech SE, Moderna, Inc. Johnson & Johnson and AstraZeneca plc. There are also several therapeutic and vaccine candidates in various stages of development that may obtain regulatory approval for the treatment or prevention of COVID-19 infections. Additionally, there are currently ongoing clinical studies using niclosamide by ANA Therapeutics (acquired by NeuroBo Pharmaceuticals, Inc.), Daewoong Pharmaceuticals Co Ltd, and Union Therapeutics A/S, among others at various stages of development. We believe our approach to target COVID-19 GI infections is differentiated. We believe our ability to compete in this market, if we are successful in developing and obtaining regulatory approval to market FW-COV, will depend on our ability (or that of future corporate partners) to convince patients, their physicians, healthcare agencies and payors and the medical community of the benefits of using FW-COV to treat patients with COVID-19 infections with GI symptoms.

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With respect to FW-ICI-AC, our oral micronized formulation and niclosamide for ICI-AC, if approved, would compete with both oral and intravenous administered steroids as well as hospital-based infusions of biologics, including infliximab and vedolizumab. We believe our ability to compete in this market, if we are successful in developing and obtaining regulatory approval to market FW- ICI-AC, will depend on our ability (or that of future corporate partners) to convince patients, their physicians, healthcare agencies and payors and the medical community of the benefits of using a non-steroidal, non-biologic therapeutic option for the treatment of ICI-AC.

With respect to FW-UP and FW-UC, our topical formulation of niclosamide for UP, if approved, would compete with sulfasalazines and 5-ASAs, for the treatment of mild disease, steroids, including budesonide and prednisone, azathioprine, 6-mercaptopurine, and methotrexate for the treatment of moderate disease, and Anti-TNFs, Entyvio® (vedolizumab), Xeljanz® (Tofacitinib); Stelara® (Ustekinumab) for the treatment of severe disease. We believe our ability to compete in this market, if we are successful in developing and obtaining regulatory approval to market FW-UP and FW-UC, will depend on our ability (or that of future corporate partners) to convince patients, their physicians, healthcare agencies and payors and the medical community of the benefits of using a non-steroidal, non-biologic therapeutic option to prevent the advancement disease requiring more toxic immunosuppressive therapeutic option for the treatment of mild and moderate UP and UC.

*Adrulipase*

With respect to adrulipase, if approved, we would compete with PERTs (pancrelipase), a well-established market that is currently dominated by a few large pharmaceutical companies, including CREON® marketed by AbbVie Inc., ZENPEP® sold to Nestlé S.A. by Allergan plc. in January 2020, PANCREAZE® marketed by VIVUS, Inc. and PERTZYE® marketed by Chiesi Farmaceutici S.p.A. There are currently six PERT products that have been approved by the FDA for sale in the U.S. We believe our ability to compete in this market, if we are successful in developing and obtaining regulatory approval to market adrulipase, will depend on our ability (or that of a future corporate partner) to convince patients, their physicians, healthcare payors and the medical community of the benefits of using a non-animal-based product to treat EPI, as well as by addressing other shortcomings associated with PERTs, including a large pill burden.

**Government Regulation and Product Approval**

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. To date, our internal research and development efforts have been conducted in France. We expect to conduct late-stage development work, including clinical trials for niclosamide and adrulipase in both the United States and Europe, as North America is our principal target market for our product candidates that we may successfully develop.

**U.S. Government Regulation**

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA and the Public Health Service Act, or PHS Act, and its implementing regulations. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, placement on Import Alerts, debarment of personnel, employees or officers, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies, and toxicity data, all performed in accordance with the good laboratory practices, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin;
- approval by an independent IRB or ethics committee representing each clinical site before each clinical study may be initiated;
- performance of adequate and well-controlled human clinical studies to establish the safety and efficacy, or in the case of a biologic, the safety, purity and potency, of the drug candidate for each proposed indication;
- preparation of and submission to the FDA of a new drug application, or NDA, or biologics license application, or BLA, which must include data from required pre-clinical studies and all pivotal clinical studies and information showing that the product can be manufactured in a controlled manner;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- Review of the product application by an FDA advisory committee, where appropriate and if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the drug candidate is produced to assess compliance with cGMP; and
- FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the drug or biologic in the United States.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical studies may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical studies. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical studies can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical studies to commence.

#### *Clinical Studies*

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, and the parameters to be used in monitoring safety and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical study site's IRB before the studies may be initiated, and the IRB must monitor the study until completed. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries, such as [ClinicalTrials.gov](#).

The clinical investigation of a drug or biologic is generally divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- *Phase 1.* The drug or biologic is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- *Phase 2.* The drug or biologic is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks and preliminarily evaluate efficacy.
- *Phase 3.* The drug or biologic is administered to an expanded patient population, generally at geographically dispersed clinical study sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational product and to provide an adequate basis for product approval.
- *Phase 4.* In some cases, the FDA may condition approval of an NDA or BLA for a drug candidate on the sponsor's agreement to conduct additional clinical studies after approval. In other cases, a sponsor may commit to conducting or voluntarily conduct additional clinical studies after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical studies.

A confirmatory or pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are Phase 3 studies, but the FDA may accept results from Phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need and the results are sufficiently robust. In such cases, FDA may require post-market studies for safety and efficacy to be conducted for the drug candidate. The FDA may withdraw the approval if the results indicate that the approved drug is not safe or effective.

The FDA, the IRB or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

#### *Chemistry, Manufacturing and Control Information*

Companies seeking FDA approval of drugs must also develop data and information about the physical characteristics of the components of a product as well as finalize processes for manufacturing the components in commercial quantities in accordance with GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the components of a product candidate do not undergo unacceptable deterioration over their shelf life.

#### *Submission of an NDA or BLA to the FDA*

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs and BLAs is subject to a substantial application user fee. Applications for orphan drug products are exempted from the NDA and BLA application user fees.

An NDA or BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational product to the satisfaction of the FDA.

Once an NDA or BLA has been submitted, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA is required to refer an application for an investigational drug or biologic to an advisory committee or explain why such referral was not made. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the investigational product application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions and typically follows such recommendations.

*The FDA's Decision on an NDA or BLA*

After the FDA evaluates the NDA or BLA and conducts inspections of manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical study(ies), and/or other significant, expensive and time-consuming requirements related to clinical studies, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA could also approve the NDA or BLA with a REMS to mitigate risks, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications or a commitment to conduct one or more post-market studies or clinical studies. Such post-market testing may include Phase 4 clinical studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. The FDA may have the authority to withdraw its approval if post-market testing fails to verify the approved drug's clinical benefit, if the applicant does not perform the required testing with due diligence, or if the any other evidence demonstrates the approved drug is not safe or effective, among other reasons. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

*Expedited Review and Accelerated Approval Programs*

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, regenerative medicine advanced therapy and priority review, that are intended to expedite the development and approval of new drugs and biologics that address unmet medical needs in the treatment of serious or life-threatening diseases and conditions. To be eligible for a fast-track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA may review sections of the NDA for a fast-track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current. These six and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast-track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the FDA Safety and Innovation Act passed in July 2012, a sponsor can request designation of a drug candidate as a “breakthrough therapy.” A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for the other expedited review and approval programs, including accelerated approval, priority review, regenerative medicine advanced therapy, and fast-track designation. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

In addition, the 21st Century Cures Act in 2016 made the Regenerative Medicine Advanced Therapy, or RMAT, designation available for investigational drugs that are intended to treat, modify, reverse, or cure a serious condition, with preliminary clinical evidence indicating that the drug has the potential for addressing unmet medical needs for such condition. The RMAT designation is available for cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products that use such therapies or products. The advantages of RMAT designation include those of breakthrough and fast track designations, such as early interactions with FDA and rolling review of applications, and the drug candidate with the RMAT designation may be eligible for accelerated approval. Requests for RMAT designations should be made with the IND application (if preliminary clinical evidence is available), but no later than the end-of-phase-2 meeting.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

#### *Post-Approval Requirements*

Drugs and biologics marketed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements.

Manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA’s policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things.



- restrictions on the marketing or manufacturing of the product;
- complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of product licenses or approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

#### *Orphan Designation and Exclusivity*

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA or NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product marketing exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same use or indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA or NDA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

#### *Biosimilars and Exclusivity*

The Affordable Care Act, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, only a handful of biosimilars have been licensed under the BPCIA, although numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, human PK and PD studies, clinical immunogenicity assessments, animal studies and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical studies to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

#### *Hatch-Waxman Amendments and Exclusivity*

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug or a method of using the drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

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Upon submission of an ANDA or a 505(b)(2) NDA, an applicant must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must send notice of the Paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve.

The FDA also cannot approve an ANDA or 505(b)(2) application until all applicable non-patent exclusivities listed in the Orange Book for the branded reference drug have expired. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a new chemical entity, or NCE, which is a drug containing an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule responsible for the drug substance's physiological or pharmacologic action. During that five-year exclusivity period, the FDA cannot accept for filing (and therefore cannot approve) any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA that relies on the FDA's approval of the drug, provided that that the FDA may accept an ANDA four years into the NCE exclusivity period if the ANDA applicant also files a Paragraph IV certification.

A drug, including one approved under Section 505(b)(2), may obtain a three-year period of exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

*Other Healthcare Laws and Compliance Requirements*

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, exclusion from participation in federal and state healthcare programs and individual imprisonment.

*Coverage and Reimbursement*

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales. Even after FDA approves a product, failure to have the product covered by third-party payors may have material adverse effect on sales. Federal and state governments continue to promulgate new policies and regulations; such policies and regulations may have material adverse effect on sales. These laws and regulations may restrict, prohibit, or preventing us from implementing a wide range of pricing, discounting, marketing, promotion, sales commission, incentive programs, and other business activities. No uniform policy of coverage and reimbursement among third-party payors exists in the United States. Such payors often rely upon Medicare coverage policy establishing their coverage and reimbursement policies. However, each payor makes independent and separate decisions regarding the extent of coverage and amount of reimbursement to be provided.

*Legislative and Regulatory Changes, Including Health Care Reform*

The laws and regulation that affect our business are subject to change from time to time, and entirely new laws and regulations are sometimes adopted. In particular, healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. On September 9, 2021, the Biden administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The Department of Health and Human Services, or HHS, plan includes, among other reform measures, proposals to lower prescription drug prices, including by allowing Medicare to negotiate prices and disincentivizing price increases, and to support market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase price transparency. Many similar proposals, including the plans to give Medicare Part D authority to negotiate drug prices, require drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation, and cap out-of-pocket costs, have already been included in policy statements and legislation currently being considered by Congress. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, proposing to encourage importation from other countries and bulk purchasing. It is unclear to what extent these and other statutory, regulatory, and administrative initiatives will be enacted and implemented.

*Foreign Corrupt Practices Act*

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

### **European Union Drug Development**

In the European Union, our product candidates may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union, national regulations and international standards for good clinical practice, or GCP.

Clinical trials are currently governed by EU Clinical Trials Directive 2001/20/EC that set out common rules for the control and authorization of clinical trials in the European Union.

To improve the current system, Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use was adopted in 2014. The Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency, notably via a clinical trial information system set up by the EMA. The new Regulation expressly provides that it will not be applied before six months after the publication of a notice delivered by the European Commission on the European Union clinical trial portal and database. As such notice requires a successful (partial) audit of the database and as that database is still under development, there is no scheduled application date yet. Pursuant to the transitory provisions of the new regulation, the Clinical Trials Directive 2001/20/EC will still apply for three years after the implementation of the European Union clinical trial portal and database. Thus, the sponsor has the possibility to choose between the requirements of the directive and the regulation for a period of three years from the entry into force of the regulation.

### **European Union Drug Review and Approval**

In the EEA (which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. MAs may be granted either centrally (Community MA) or nationally (National MA).

The Community MA is issued centrally by the European Commission through the Centralized Procedure, based on the opinion of the CHMP of the EMA and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products such as orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of neurodegenerative disorders. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs are issued nationally by the competent authorities of the Member States of the EEA and only cover their respective territory. National MAs are available for products not falling within the mandatory scope of the Centralized Procedure. We do not foresee that any of our current product candidates will be suitable for a National MA as they fall within the mandatory criteria for the Centralized Procedure. Therefore, our product candidates will be approved through Community MAs.

Under the above-described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The pediatric use marketing authorization, or PUMA, is a dedicated marketing authorization for medicinal products indicated exclusively for use in the pediatric population, with, if necessary, an age-appropriate formulation. Pursuant to Regulation (EC) No. 1901/2006 (The "*Pediatric Regulation*"), all PUMA applications for marketing authorization for new medicines must include to be valid, in addition to the particulars and documents referred to in Directive 2001/83/EC, the results of all studies performed and details of all information collected in compliance with a pediatric investigation plan agreed between regulatory authorities and the applicant, unless the medicine is exempt because of a deferral or waiver of the EMA.

Before the EMA is able to begin its assessment of a Community MA application, it will validate that the applicant has complied with the agreed pediatric investigation plan. The applicant and the EMA may, where such a step is adequately justified, agree to modify a pediatric investigation plan to assist validation. Modifications are not always possible; may take longer to agree than the period of validation permits; and may still require the applicant to withdraw its marketing authorization application and to conduct additional non-clinical and clinical studies. Products that are granted a MA on the basis of the pediatric clinical trials conducted in accordance with the Pediatric Investigation Plan, or PIP, are eligible for a six-month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

#### *Orphan Drugs*

In the European Union, Regulation (EC) No 141/2000 of the European Parliament and of the Council of December 16, 1999 on orphan medicinal products, as amended, states that a drug shall be designated as an orphan drug if its sponsor can establish that the three following cumulative conditions are met:

- the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition;
- the prevalence of the conditions is not more than five in ten thousand persons in the European Union when the application is made, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment; and
- that there is no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Pursuant to Regulation (EC) No. 847/2000 of April 27, 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts "similar medicinal product" and "clinical superiority", an application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug before filing of a MA application.

The European Union offers incentives to encourage the development of designated orphan medicines (protocol assistance, fee reductions, etc.) and provides opportunities for market exclusivity. Pursuant to abovementioned Regulation (EC) No. 141/2000, products receiving orphan designation in the European Union can obtain market exclusivity for a certain number of years in the European Union following the marketing approval.

If a Community MA in respect of an orphan drug is granted, regulatory authorities will not, for a period of usually ten years, accept another application for a MA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a similar drug. This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the drug concerned, that the above-mentioned criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Pursuant to Regulation No. 1901/2006, for orphan medicinal products, instead of an extension of the supplementary protection certificate, the ten-year period of orphan market exclusivity should be extended to 12 years if the requirement for data on use in the pediatric population is fully met (i.e. when the request contains the results of all studies carried out under the approved PIP and when the declaration attesting the conformity of the request to this PIP is included in the MA).

Notwithstanding the foregoing, a MA may be granted, for the same therapeutic indication, to a similar drug if:

- the holder of the MA for the original orphan drug has given its consent to the second applicant;
- the holder of the MA for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

The abovementioned Regulation (EC) No. 141/2000 provides for other incentives regarding orphan medicinal products.

#### *Post-Approval Controls*

The holder of a MA must comply with EU requirements applicable to manufacturing, marketing, promotion and sale of medicinal products. In particular, the holder of the MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system and who will reside and operate in the EU. Key obligations include safety expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAs must include a risk management plan, or RMP, to submit to the EMA, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

#### *Reimbursement*

The European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A Member State may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines covered by national health insurance is negotiated with the Economic Committee for Health Products, or CEPS. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

## **Other European Regulatory Matters**

### *French Regulatory Framework for Clinical Development*

In France, Directive No. 2001/20/EC has been implemented in French national law, establishing a system of prior authorization and requiring a prior favorable opinion from an ethics committee.

Parties to a clinical trial agreement, or CTA, must use a CTA template ("unique agreement" or "convention unique") to organize the conduct of interventional clinical trials with commercial purpose, as well as specific template exhibits to this agreement. Once concluded, the CTA is communicated for information by the sponsor to the French national board of physicians (Ordre national des médecins) without delay.

The processing of personal data collected during clinical trials has to comply with the Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 and Law No 2018-493 of June 20, 2018 on the protection of personal data, implementing the Regulation (EU) 2016/679 requirements. Regarding automatic processing operations for the purpose of research or clinical studies, formalities have to be completed before the French data protection authority, the Commission Nationale de l'Informatique et des Libertés, or CNIL, so as to obtain the authorization to process personal data. However, there are simplified standards.

Law No. 2011-2012 of December 29, 2011, or Loi Bertrand, aimed at strengthening the health safety of medicinal and health products, as amended (and its implementing decrees), introduced into French law provisions regarding transparency of fees received by some healthcare professionals from health product industries, i.e. companies manufacturing or marketing health products (Article L.1453-1 of the French Public Health Code). These provisions have been recently extended and redefined by Decree No. 2016-1939 of December 28, 2016, which clarified French "Sunshine" regulations. The decree notably provides that companies manufacturing or marketing health care products (medicinal products, medical devices, etc.) in France shall publicly disclose (mainly on a specific public website available at: <https://www.entreprises-transparence.sante.gouv.fr>) the advantages and fees paid to healthcare professionals amounting to €10 or above, as well as the agreements concluded with the latter, along with detailed information about each agreement (the precise subject matter of the agreement, the date of signature of the agreement, its end date, the total amount paid to the healthcare professional, etc.). Another declaration must also be filed to the competent healthcare professional body. Law No. 2011-2012 also reinforced the French anti-gift rules and Order No. 2017-49 of January 19, 2017 amended the law and expanded the scope of the general prohibition of payments from pharmaceutical and device manufacturers to healthcare professionals to broadly cover any company manufacturing or marketing health products, regardless of whether or not payment for the products is reimbursed under the French social security system (new Articles L. 1453-3 et seq. of the French Public Health Code). It also changed the procedure related to the prior submission to the national or departmental board of the relevant healthcare professional body. Moreover, the penalties incurred for non-compliance with the requirements of the Anti-Gift Law will be doubled to a fine of up to €750,000. The changes of the anti-gift rules will only enter into force after the publication of implementing measures.

### **Employees**

As of December 31, 2021, we had 17 full-time employees, of whom one was employed by AzurRx SAS and located in France and 16 were employed by us and located in our offices in the United States.

### **Available Information**

As a public company, we are required to file our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements on Schedule 14A and other information (including any amendments) with the Securities and Exchange Commission (the "SEC"). The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. You can find our SEC filings at the SEC's website at [www.sec.gov](http://www.sec.gov).

Our Internet address is [www.firstwavebio.com](http://www.firstwavebio.com). Information contained on our website is not part of this Annual Report. Our SEC filings (including any amendments) will be made available free of charge on [www.firstwavebio.com](http://www.firstwavebio.com), as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.



## ITEM 1A. RISK FACTORS

We are subject to various risks that could have a material adverse effect on our business, our financial condition and our results of operations. These risks could cause actual operating results to differ from those expressed in certain "forward looking statements" contained in this Annual Report as well as in other communications.

### Summary of Risk Factors

- We have never generated any product revenues.
- We expect to incur significant losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding, and certain terms included in our financing transactions may restrict our ability to raise such capital at the times and in the manner we may require.
- To date, most of our development activities have been focused on our niclosamide and adrulipase product candidates, which are still under clinical development, and if niclosamide and adrulipase do not receive regulatory approval or is not successfully commercialized, our business will be harmed.
- The COVID-19 pandemic and other geopolitical events, including the war in Ukraine could adversely impact our business, including our clinical trials.
- We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our product candidates.
- Clinical trials are very expensive, time-consuming, difficult to design and implement and involve an uncertain outcome.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of our product candidates.
- We intend to rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.
- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.
- We do not currently intend to pay dividends on our Common Stock in the foreseeable future, and consequently, any gains from an investment in our Common Stock will likely depend on appreciation in the price of our Common Stock.

### Risks Related to Our Business, Financial Position and Capital Requirements

*We are a clinical stage biopharmaceutical company and have a limited operating history upon which to base an investment decision.*

We are a clinical stage biopharmaceutical company. Since inception, we have engaged primarily in research and development activities of niclosamide and adrulipase. We have not generated any revenue from product sales and have incurred significant net losses. We have not demonstrated our ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any of our products will require us to perform a variety of functions, including:

- continuing to undertake pre-clinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products; and
- conducting sales and marketing activities.

Our operations to date have been limited to organizing and staffing, acquiring, developing and securing the proprietary rights for, and undertaking pre-clinical development, manufacturing and clinical trials of adrulipase, and the acquisition of rights to and clinical trials for niclosamide. These operations provide a limited basis for our stockholders and prospective investors to assess our ability to complete development of or commercialize niclosamide and adrulipase or any other product candidates and the advisability of investing in our securities.

We have incurred significant losses and negative cash flows from our operations since inception. As of December 31, 2021, we had accumulated deficit of approximately \$ 153.9 million and negative working capital of approximately \$2.9 million. Based on our historical and anticipated rate of cash expenditures, we do not anticipate our existing working capital will be sufficient to sustain our business through the commercialization of our product candidates. Therefore, we are dependent on obtaining, and are continuing to pursue, the necessary funding from outside sources, including obtaining additional funding from the sale of securities in order to continue our operations. We are actively working to obtain additional funding. We cannot make any assurances that additional financings will be available to us and, if available, completed on a timely basis, on acceptable terms or at all. If we are unable to complete an equity and/or debt offering, or otherwise obtain sufficient financing when and if needed, it would negatively impact our business and operations, which would likely cause the price of our Common Stock to decline or ultimately force us to cease our operations.

***A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or coronavirus, may materially and adversely affect our business and our financial results.***

The spread of COVID-19 has affected segments of the global economy and may affect our operations, including the potential interruption of our clinical trial activities and our supply chain. Beginning in March 2020, the majority of our workforce began working from home. Disruptions caused by the continued spread of COVID-19, including the effects of stay-at-home orders and work-from-home policies, have impacted productivity and may result in further periods of business disruption, including delays in our clinical trials or delays or disruptions in our supply chain. In addition, there could be a potential effect of COVID-19 to the business at FDA or other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates.

The continued spread of COVID-19 globally could adversely affect our clinical trial operations in the United States and Europe and other jurisdictions where we may decide to conduct clinical trials, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. We have already experienced certain delays of our clinical trials and may experience further delays as the pandemic continues. Disruptions in national or international shipments and deliveries could impede our ability to distribute product to trial sites in a timely manner. Any of the foregoing factors could delay our ability to conduct clinical trials or release clinical trial results. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out our clinical trials, which could result in inefficiencies due to reductions in staff and disruptions to work environments.

The spread of COVID-19, or another infectious disease, could also negatively affect the operations at our third-party manufacturers, which could result in delays or disruptions in the supply of our product candidates. In addition, we have taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring all employees to work remotely, suspending all non-essential travel worldwide for our employees, and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business.

We have implemented business continuity plans designed to address and mitigate the impact of the ongoing COVID-19 pandemic on our employees and our business. We continue to operate normally with the exception of enabling all of our employees to work productively at home and abiding by travel restrictions issued by federal, state and local governments. Our current plans to return to the office remain fluid as federal, state and local guidelines, rules and regulations continue to evolve.

We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operation and financial condition.

In addition, the global spread of COVID-19 has created significant volatility and uncertainty in global financial markets and may materially affect us economically and such conditions continue to persist. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. A recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our Common Stock.

***Geopolitical risks associated with Russia's recent invasion of Ukraine could result in increased market volatility and uncertainty, which could negatively impact our business, financial condition, and results of operations.***

The uncertain nature, scope, magnitude, and duration of hostilities stemming from Russia's recent military invasion of Ukraine, including the potential effects of such hostilities as well as sanctions, embargoes, asset freezes, cyber-attacks and other actions taken in response to such hostilities on the world economy and markets, have disrupted global markets and contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic and other factors that affect our business and supply chain. There can be no certainty regarding the impacts stemming from the invasion, including the imposition of additional sanctions, embargoes, asset freezes or other economic or military measures resulting from the invasion. The impact of these developments, and additional events that may occur as a result, is currently unknown and could adversely affect our business, supply chain, suppliers and customers and potential customers. It is not possible to predict the broader consequences of this conflict, which could include further sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, the availability and cost of materials, supplies, labor, currency exchange rates and financial markets, all of which could negatively impact our business, financial condition and results of operations.

***We will face intense competition and may not be able to compete successfully.***

We operate in highly competitive segments of the biotechnology and biopharmaceutical markets. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies, and private and public research institutions. Niclosamide and adrulipase, if successfully developed and approved, will compete with established therapies, as well as new treatments that may be introduced by our competitors. Many of our competitors have significantly greater financial, product development, manufacturing and marketing resources than us. Large pharmaceutical companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. We also may compete with these organizations to recruit management, scientists and clinical development personnel. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. New developments, including the development of other biological and pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. We will also face competition from these third parties in recruiting and retaining qualified personnel, establishing clinical trial sites and patient registration for clinical trials and in identifying and in-licensing new product candidates. In the case of niclosamide, we may also face competition from other companies developing different formulation of niclosamide for the same indications for which we intend to develop niclosamide, or from off-label uses of niclosamide approved for other indications.

***We may incur substantial product liability or indemnification claims relating to the use of our product candidates.***

We face an inherent risk of product liability exposure based on the use of niclosamide and adrulipase in human clinical trials, or, if obtained, following marketing approval and commercialization. Claims could be brought against us if use or misuse of one of our product candidates causes, or merely appears to have caused, personal injury or death. Although we have and intend to maintain product liability insurance relating to our clinical trials, our coverage may not be sufficient to cover claims that may be made against us and we may be unable to maintain such insurance. Any claims against us, regardless of their merit, could severely harm our financial condition, strain our management and other resources or destroy the prospects for commercialization of the product which is the subject of any such claim. We are unable to predict if we will be able to obtain or maintain product liability insurance for any products that may be approved for marketing. Additionally, we have entered into various agreements where we indemnify third parties for certain claims relating to the testing and use of our product candidates. These indemnification obligations may require us to pay significant sums of money for claims that are covered by these indemnifications.

We cannot predict all of the possible harms or side effects that may result from the use of our products and, therefore, the amount of insurance coverage we currently hold, or that we or our collaborators may obtain, may not be adequate to protect us from any claims arising from the use of our products that are beyond the limit of our insurance coverage. If we cannot protect against potential liability claims, we or our collaborators may find it difficult or impossible to commercialize our products, and we may not be able to renew or increase our insurance coverage on reasonable terms, if at all. The marketing, sale and use of our products and our planned future products could lead to the filing of product liability claims against us if someone alleges that our products failed to perform as designed. A product liability or professional liability claim could result in substantial damages and be costly and time-consuming for us to defend.

Any product liability or professional liability claim brought against us, with or without merit, could increase our insurance rates or prevent us from securing insurance coverage. Additionally, any product liability lawsuit could damage our reputation, result in the recall of products, or cause current partners to terminate existing agreements and potential partners to seek other partners, any of which could impact our results of operations.

***We use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.***

We may use hazardous materials, including chemicals and biological agents and compounds, that could be dangerous to human health and safety or the environment. Our operations also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage and our property and casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***We will need to grow the size of our organization, and we may experience difficulties in managing this growth.***

As of December 31, 2021, we had 17 employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, research and development, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA and international regulatory review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including certain aspects of regulatory approval, clinical management and manufacturing. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants and contractors or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

***Significant disruptions of information technology systems or breaches of data security could materially adversely affect our business, results of operations and financial condition.***

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization.

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The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments and cyber-terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged.

In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Clinical Health Act of 2009, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws.

Under the EU regulation and notably the General Data Protection Regulation, or GDPR, No. 2016/679, which entered into force on May 25, 2018 and is applicable personal data that we process in relation to our presence in the EU, the offering of products or services to individuals in the EU or the monitoring of the behavior of individuals in the EU, we have also a legal responsibility to report personal data breaches to the competent supervisory authority. The EU data protection regulation includes a broad definition and a short deadline for the notification of personal data breaches, which may be difficult to implement in practice and requires that we implement robust internal processes. Under this regulation, we have to report personal data breaches to the competent supervisory authority within 72 hours of the time we become aware of a breach "unless the personal data breach is unlikely to result in a risk to the right and freedoms of natural persons" (Article 33 of the GDPR). In addition, the GDPR requires that we communicate the breach to the Data Subject if the breach is "likely to result in a high risk to the rights and freedoms of natural persons" (Article 34 of the GDPR). In order to fulfil these requirements, we have to implement specific internal processes to be followed in case of a personal data breach, which will allow us to (a) contain and recover the breach, (b) assess the risk to the data subjects, (c) notify, and possibly communicate the breach to the data subjects, (d) investigate and respond to the breach. The performance of these processes implies substantial costs in resources and time.

Moreover, as we may rely on third parties that will also process as processor the data for which we are a data controller—for example, in the context of the manufacturing of our product candidates or for the conduct of clinical trials, we must contractually ensure that strict security measures, as well as appropriate obligations including an obligation to report in due delay any security incident are implemented, in order to allow us fulfilling our own regulatory requirements.

We would also be exposed to a risk of loss or litigation and potential liability for any security breach on personal data for which we are data controller. The costs of above-mentioned processes together with legal penalties, possible compensation for damages and any resulting lawsuits arising from a breach may be extensive and may have a negative impact on reputation and materially adversely affect our business, results of operations and financial condition.

In August 2019, management was advised that it was a victim of a cyber-related fraud whereby a hacker impersonated one of our key vendors to redirect payments, totaling approximately \$420,000. Management and our Audit Committee completed our investigation and is reviewing all available avenues of recovery, including from our financial institution to recover the payments. As of December 31, 2021, we have recovered approximately \$50,000 from our financial institution but we are unable to determine the probability of recovering anything further from the cyber-related fraud. As a result of the cyber-related fraud, we have instituted additional controls and procedures and all employees now undergone cybersecurity training.

**Requirements associated with being a public company will increase our costs significantly and will divert significant company resources and management attention.**

Since we are no longer an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, we are no longer able to take advantage of certain exemptions from various reporting requirements that were previously available to us, but which were not available to other public companies that are not emerging growth companies. Accordingly, we will be required to comply with increased disclosure obligations regarding executive compensation in our periodic reports and proxy statements and the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, we will incur greater expenses associated with such reporting requirements. These expenses would further increase if we ceased to be a “smaller reporting company.” In addition, if we are deemed an accelerated filer or large accelerated filer in the future, we expect to incur additional management time and cost to comply with the more stringent reporting requirements applicable to companies that are deemed accelerated filers or large accelerated filers, including complying with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. We have not yet completed the process of compiling the system and processing documentation needed to comply with such requirements. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion when required to do so. In that regard, we currently do not have an internal audit function, and we will need to hire or contract for additional accounting and financial staff with appropriate public company experience and technical accounting knowledge.

Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. We cannot predict or estimate the amount of additional costs we may incur as a result of this.

**Risks Related to Clinical Development, Regulatory Approval and Commercialization**

***Our product candidates are at an early stage of development and may not be successfully developed or commercialized.***

We have no products approved for sale. Niclosamide, which we acquired in 2021, and adrulipase are in the early stages of clinical development. Our product candidates will require substantial capital expenditures, development, testing, and regulatory clearances prior to commercialization. The development and regulatory approval process take several years, and it is not likely that any such products, even if successfully developed and approved by the FDA or any comparable foreign regulatory authority, would be commercially available for a significant period of time. Many promising drug candidates fail at some stage of their clinical development. Accordingly, even if we are able to obtain the requisite financing to fund our development programs, we cannot assure you that our product candidates will be successfully developed, receive required regulatory approvals and successfully commercialized. Our failure to develop, manufacture or receive regulatory approval for or successfully commercialize any of our product candidates, could result in the failure of our business and a loss of all of your investment in our company.

***Any product candidates we advance into and through clinical development are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.***

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable health authorities in foreign markets, including Health Canada’s Therapeutic Products Directorate, or the TPD, and the European Medicines Agency, or the EMA. In the United States, we are not permitted to market our product candidates until we receive approval of an NDA (New Drug Application) or BLA (Biologic License Application) from the FDA. The process of obtaining such approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. In addition to the significant clinical testing requirements, our ability to obtain marketing approval for these product candidates depends on obtaining the final results of required non-clinical testing, including characterization of the manufactured components of our product candidates and validation of our manufacturing processes. The FDA may determine that our product manufacturing processes, testing procedures or facilities are insufficient to justify approval. Approval policies or regulations may change, and the FDA has substantial discretion in the pharmaceutical approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA, the TPD and/or the EMA can delay, limit or deny approval of a product candidate for many reasons, including, but not limited to:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate to their satisfaction that a product candidate is safe and effective for any indication;
- failure to accept clinical data from trials which are conducted outside their jurisdiction;
- the results of clinical trials may not meet the level of statistical significance required for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such agencies may disagree with our interpretation of data from preclinical studies or clinical trials;
- failure to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies; or
- changes in the approval policies or regulations of such agencies may significantly change in a manner rendering our clinical data insufficient for approval.

Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us from commercializing our product candidates.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population;
- the proximity and availability of clinical trial sites for prospective patients;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- The availability of other clinical trials and competition for eligible patients;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.



Our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates. This competition will reduce the number and types of patients and qualified clinical investigators available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors or clinical trial sites may not allow us to conduct our clinical trial at such site if competing trials are already being conducted there. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. We may also encounter difficulties finding a clinical trial site at which to conduct our trials.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our planned clinical trials, which could prevent completion of these clinical trials and adversely affect our ability to advance the development of our product candidates.

***Because the results of preclinical studies and early clinical trials are not necessarily predictive of future results, any product candidate we advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval.***

Pharmaceutical development has inherent risk. We will be required to demonstrate through well-controlled clinical trials that our product candidates are safe and effective with a favorable benefit-risk profile for use in their target indications before we can seek regulatory approvals for their commercial sale. Adrulipase, has only completed three Phase 2 clinical trials in two separate indications (two Phase 2 in CF patients and one Phase 2 in CP patients). Niclosamide has completed a Phase 1b/2a study, conducted by First Wave, in patients with mild-to-moderate ulcerative colitis. Success in pre-clinical studies or early clinical trials does not mean that later clinical trials will be successful, as product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. We also may need to conduct additional clinical trials that are not currently anticipated. Drug developers frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results.

***Any product candidate we advance into and through clinical trials may cause unacceptable adverse events or have other properties that may delay or prevent their regulatory approval or commercialization or limit their commercial potential.***

Unacceptable adverse events caused by niclosamide and adrulipase in clinical trials could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This, in turn, could prevent us from commercializing the affected product candidate and generating revenues from its sale. We have not yet completed testing of any of our product candidates for the treatment of the indications for which we intend to seek product approval in humans, and we currently do not know the extent of adverse events, if any, that will be observed in patients who receive any of our product candidates. If any of our product candidates cause unacceptable adverse events in clinical trials, we may not be able to obtain regulatory approval or commercialize such product or, if such product candidate is approved for marketing, future adverse events could cause us to withdraw such product from the market.

***Delays in the commencement or completion of our clinical trials could result in increased costs and delay our ability to pursue regulatory approval and commercialization of our product candidates.***

Although we commenced the ongoing FW-COV RESEVOIR and the FW-UP clinical trials in 2021, the commencement and completion of clinical trials can be delayed for a variety of reasons, including delays in:

- obtaining regulatory clearance to commence a clinical trial;
- identifying, recruiting and training suitable clinical investigators;
- reaching agreement on acceptable terms with prospective clinical research organizations (“CROs”) and trial sites, the terms of which can be subject to extensive negotiation, may be subject to modification from time to time and may vary significantly among different CROs and trial sites;
- obtaining sufficient quantities of investigational product (“IP”) for our product candidates for use in clinical trials;
- obtaining Institutional Review Board (“IRB”) or ethics committee approval to conduct a clinical trial at a prospective site;
- identifying, recruiting and enrolling patients to participate in a clinical trial, including delays and/or interruptions resulting from geo-political actions, such as the war in Ukraine, disease or public health epidemics, such as the coronavirus, or natural disasters;
- retaining patients who have initiated a clinical trial but may withdraw due to adverse events from the therapy, insufficient efficacy, changing clinical protocols, fatigue with the clinical trial process, or personal issues;
- retaining patients who may not follow the clinical trial protocols due to factors including the coronavirus epidemic; and
- availability of funds.

Any delays in the commencement of our clinical trials will delay our ability to pursue regulatory approval for our product candidates. In addition, many of the factors that cause, or lead to, a delay in the commencement of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including the size and nature of the patient population and the patient eligibility criteria defined in the protocol, competition from competing companies, natural disasters, geo-political events, such as the war in Ukraine or public health epidemics, such as the coronavirus impacting the U.S., Europe and elsewhere.

***We may be required to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive or the trials are not well designed.***

Regulatory agencies, IRBs or data safety monitoring boards may at any time recommend the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. Clinical trials must be conducted in accordance with current cGCPs or other applicable foreign government guidelines governing the design, safety monitoring, quality assurance and ethical considerations associated with clinical studies. Clinical trials are subject to oversight by the FDA, other foreign governmental agencies and IRBs at the study sites where the clinical trials are conducted. In addition, clinical trials must be conducted with product candidates produced in accordance with applicable cGMPs, which are the FDA’s regulations governing the design, monitoring and control of manufacturing processes and facilities. Clinical trials may be suspended by the FDA, other foreign governmental agencies, or us for various reasons, including:

- deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites;
- the product candidate may have unforeseen adverse side effects;
- deficiencies in the trial design necessary to demonstrate efficacy;
- fatalities or other adverse events arising during a clinical trial due to medical problems that may not be related to clinical trial treatments;
- the product candidate may not appear to be more effective than current therapies; or
- the quality or stability of the product candidate may fall below acceptable standards.

If we elect or are forced to suspend or terminate a clinical trial for niclosamide and adrulipase the commercial prospects for that product candidate will be harmed and our ability to generate product revenue from that product candidate may be delayed or eliminated. Furthermore, any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates and impair our ability to generate revenue from the commercialization of these product candidates either by us or by our collaboration partners.

***The approval processes of regulatory authorities are lengthy, time consuming, expensive and inherently unpredictable. If we are unable to obtain approval for our product candidates from applicable regulatory authorities, we will not be able to market and sell those product candidates in those countries or regions and our business will be substantially harmed.***

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. We have not submitted an NDA or similar filing or obtained regulatory approval for any drug candidate in any jurisdiction and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Niclosamide and adrulipase could fail to receive regulatory approval for many reasons, including any one or more of the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA or other submission or to obtain regulatory approval in the United States or elsewhere;

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- the FDA or comparable foreign regulatory authorities may fail to hold to previous agreements or commitments;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve our product candidates;
- invest significant additional cash in each of the above activities; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

The time and expense of the approval process, as well as the unpredictability of clinical trial results and other contributing factors, may result in our failure to obtain regulatory approval to market, in one or more jurisdictions niclosamide, adrulipase or future product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain regulatory approval in one or more jurisdictions, regulatory authorities may approve niclosamide and adrulipase for fewer or more limited indications than we request, may not approve the prices we may propose to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with labeling that does not include the claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing circumstances could materially harm the commercial prospects for niclosamide and adrulipase.

***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of the approved labeling, or result in significant negative consequences following marketing approval, if any.***

Results of current and future clinical trials of niclosamide and adrulipase could reveal a high and/or unacceptable severity and frequency of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Further, any observed drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences could materially harm our business, financial condition and prospects.

Additionally, if niclosamide and adrulipase receive marketing approval, and we or others later identify undesirable side effects caused by our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings in the product's labeling;
- we may be required to create a medication guide for distribution to patients that outlines the risks of such side effects;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product, if approved, and could significantly harm our business, results of operations and prospects

***If we are unable to execute our sales and marketing strategy for our products and are unable to gain market acceptance, we may be unable to generate sufficient revenue to sustain our business.***

We are a clinical-stage biopharmaceutical company and have yet to begin to generate revenue from niclosamide and adrulipase. Our product candidates are in an early stage of clinical development, and, if we obtain marketing approval for any of products in the future, which we anticipate would not occur for several years, if at all.

We may never gain significant market acceptance for our product candidates and therefore may never generate substantial revenue or profits for us. We will need to establish a market for any of our product candidates that receive regulatory approval through physician education, sales and marketing efforts, awareness programs and the publication of clinical data. Gaining acceptance in medical communities requires, among other things, publication in leading peer-reviewed journals of results from our studies. The process of publication in leading medical journals is subject to a peer review process and peer reviewers may not consider the results of our studies sufficiently novel or worthy of publication. Failure to have our studies published in peer-reviewed journals could limit the adoption of niclosamide and adrulipase. Our ability to successfully market our product candidates that we may develop will depend on numerous factors, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- the efficacy and safety as demonstrated in clinical trials;
- the clinical indications for which the product is approved;
- the inability to demonstrate effectively that the clinical and other benefits of a product candidate outweigh any safety or other perceived risks;
- the inability to demonstrate effectively that the efficacy of a product candidate is superior to a competing treatment;
- conducting clinical utility studies of our product candidates to demonstrate economic usefulness to providers and payers;
- relative convenience and ease of administration;
- whether our current or future partners, support our offerings;
- the success of the sales force and marketing effort;
- unfavorable publicity relating to the product;
- whether healthcare providers believe our product candidates provide clinical utility relative to their cost; and
- whether private health insurers, government health programs and other third-party payers will cover our product candidates.

***We currently have no commercial organization. If we are unable to establish satisfactory sales and marketing capabilities or secure a sales and marketing partner, we may not successfully commercialize any of our product candidates.***

We have no commercial infrastructure. In order to commercialize products that are approved for marketing, we must either establish our own sales and marketing infrastructure or collaborate with third parties that have such commercial infrastructure.

We may not be able to enter into collaboration agreements on terms acceptable to us or at all. In addition, even if we enter into such relationships, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. If we elect to establish a sales and marketing infrastructure, we may not realize a positive return on this investment. In addition, we will have to compete with established and well-funded pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. Factors that may inhibit our efforts to commercialize our product candidates without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe our future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, or if we do not successfully enter into appropriate collaboration arrangements, we will have difficulty successfully commercializing our product candidates and any we may develop or acquire, which would adversely affect our business, operating results and financial condition. Outside the United States, we may commercialize our product candidates by entering into collaboration agreements with pharmaceutical partners. We may not be able to enter into such agreements on terms acceptable to us or at all. In addition, even if we enter into such relationships, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

***We may form or seek strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.***

From time to time, we may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to niclosamide and adrulipase and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. These relationships also may result in a delay in the development of niclosamide and adrulipase if we become dependent upon the other party and such other party does not prioritize the development of our product candidates relative to its other development activities. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. We rely completely on third parties to manufacture our preclinical and clinical pharmaceutical supplies and expect to continue to rely on third parties to produce commercial supplies of our product candidates, and our dependence on third party suppliers could adversely impact our business.

***We rely completely on third parties to manufacture our preclinical and clinical pharmaceutical supplies and expect to continue to rely on third parties to produce commercial supplies of any approved product candidate, and our dependence on third party suppliers could adversely impact our business.***

We rely on third parties to manufacture our product candidates, including niclosamide and adrulipase. The proprietary yeast cell line from which the adrulipase API is derived is kept at a storage facility maintained by Charles River Laboratories Inc. Adrulipase drug substance and drug product are currently manufactured at a contract facility located in Tianjin, China owned by Asymchem Life Science Co., Ltd. We believe there are multiple alternative contract manufacturers capable of producing the adrulipase product we need for clinical trials. There is no guarantee that the processes are easily reproducible and transferrable.

Niclosamide API is obtained by chemical synthesis and is currently manufactured by Olon SpA at a facility in Murcia, Spain. The drug product manufacturing for niclosamide is currently conducted at a contract facility located in Milan, Italy and Tianjin, China owned by Monteresearch s.r.l. and Asymchem Life Science Co., Ltd, respectively.

We are completely dependent on these third parties for product supply and our niclosamide and adrulipase development programs would be adversely affected by a significant interruption in our ability to receive such materials. We have not yet entered into long-term manufacturing or supply agreements with any third parties. Furthermore, our third-party suppliers will be required to maintain compliance with cGMPs and will be subject to inspections by the FDA or comparable regulatory authorities in other jurisdictions to confirm such compliance. In the event that the FDA or such other authorities determine that our third-party suppliers have not complied with cGMP, our clinical trials could be terminated or subjected to a clinical hold until such time as we are able to obtain appropriate replacement material. Any delay, interruption or other issues that arise in the manufacture, packaging, or storage of our products as a result of a failure of the facilities or operations of our third-party suppliers to pass any regulatory agency inspection could significantly impair our ability to develop and commercialize our products.

We do not expect to have the resources or capacity to commercially manufacture any of our proposed products, if approved, and will likely continue to be dependent upon third party manufacturers. Our dependence on third parties to manufacture and supply us with clinical trial materials and any approved products may adversely affect our ability to develop and commercialize our products on a timely basis or at all.

***We rely on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.***

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We use contract research organizations (CROs) to conduct our clinical trials and will rely upon such CROs, as well as medical institutions, clinical investigators and consultants, to conduct our trials in accordance with our clinical protocols. Our CROs, investigators and other third parties will play a significant role in the conduct of these trials and the subsequent collection and analysis of data from the clinical trials.

There is no guarantee that any CROs, investigators and other third parties upon which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, fail to adhere to our clinical protocols or otherwise perform in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminate for any reason, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical trial site may be jeopardized.

***We intend to rely on market exclusivity periods that may not be or remain available to us.***

We intend to rely on our ability to obtain and maintain a regulatory period of market exclusivity for any of our product candidates, including niclosamide and adrulipase that are successfully developed and approved for commercialization. Although this period in the United States is currently 12 years from the date of marketing approval, reductions to this period have been proposed. This exclusivity period in Europe is currently 10 years from the date of marketing approval by the EMA. Once any regulatory period of exclusivity expires, depending on the status of our patent coverage and the nature of the product, we may not be able to prevent others from marketing products that are biosimilar to or interchangeable with our products, which would materially adversely affect us.

Because niclosamide is a small molecule it would be subject either to three or five year exclusivity, depending on the regulatory pathway of any clinical trials. Niclosamide is not entitled to the same 12-year exclusivity as our biologic product candidates.

***Due to the significant resources required for the development of our product candidates, we must prioritize development of certain product candidates and/or certain disease indications. We may expend our limited resources on candidates or indications that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

We intend to develop a pipeline of product candidates to treat GI and other diseases. Due to the significant resources required for the development of product candidates, we must focus our attention and resources on specific diseases and/or indications and decide which product candidates to pursue and the amount of resources to allocate to each. We are currently focusing our resources on the development of our product candidates, niclosamide and adrulipase.

Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, any decision to delay, terminate or collaborate with third parties in respect of certain programs or product candidates may subsequently prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the GI, CF, CP, COVID-19, ICI-AC or biotechnology industry, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and indications that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain development and commercialization rights.

***If we fail to attract and retain key management and clinical development personnel, we may be unable to successfully develop or commercialize our product candidates.***

We are dependent on our management team and clinical development personnel and our success will depend on their continued service, as well as our ability to attract and retain highly qualified personnel. In particular, the continued development of our senior management team which now includes James Sapirstein, our President and Chief Executive Officer, Sarah Romano, our Chief Financial Officer, and James Pennington, our Chief Medical Officer, is critical to our success. The market for the services of qualified personnel in the biotechnology and pharmaceutical industries are highly competitive. The loss of service of any member of our senior management team or key personnel could prevent, impair or delay the implementation of our business plan, the successful conduct and completion of our planned clinical trials and the commercialization of any product candidates that we may successfully develop. We do not carry key man insurance for any member of our senior management team.

***Healthcare reform and restrictions on reimbursements may limit our financial returns.***

Our ability or the ability of our collaborators to commercialize any of our product candidates that we successfully develop may depend, in part, on the extent to which government health administration authorities, private health insurers and other organizations will reimburse consumers for the cost of these products. These third parties are increasingly challenging both the need for and the price of new drug products. Significant uncertainty exists as to the reimbursement status of newly approved therapeutics. Adequate third-party reimbursement may not be available for our product candidates to enable us or our collaborators to maintain price levels sufficient to realize an appropriate return on their and our investments in research and product development.



**Changes in healthcare law and implementing regulations, including government restrictions on pricing and reimbursement, as well as healthcare policy and other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues.**

The potential pricing and reimbursement environment for niclosamide, adrulipase and any future drug products may change in the future and become more challenging due to, among other reasons, policies advanced by the current or any new presidential administration, federal agencies, healthcare legislation passed by Congress, or fiscal challenges faced by all levels of government health administration authorities.

**If we or any of our independent contractors, consultants, collaborators, manufacturers, vendors or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions, which could result in penalties and affect our ability to develop, market and sell our product candidates and may harm our reputation.**

We are subject to federal, state, and foreign healthcare laws and regulations pertaining to fraud and abuse and patients' rights. These laws and regulations include:

- the U.S. federal healthcare program anti-kickback law, which prohibits, among other things, persons and entities from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;
- the U.S. federal false claims and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government funded programs such as Medicare or Medicaid that are false or fraudulent, and which may apply to us by virtue of statements and representations made to customers or third parties;
- the U.S. federal Health Insurance Portability and Accountability Act ("HIPAA"), which prohibits, among other things, executing a scheme to defraud healthcare programs;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, imposes requirements relating to the privacy, security, and transmission of individually identifiable health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members, which is published in a searchable form on an annual basis; and
- state laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws that may be broader in scope and also apply to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to patient data privacy and security.

If our operations are found to be in violation of any such health care laws and regulations, we may be subject to penalties, including administrative, civil and criminal penalties, monetary damages, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

***Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.***

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA, EMA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; healthcare fraud and abuse, data privacy laws and other similar laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in governmental healthcare programs, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

#### **Risks Related to our Intellectual Property**

***Our success will depend upon intellectual property, proprietary technologies and regulatory market exclusivity periods, and we may be unable to protect our intellectual property.***

Our success will depend, in large part, on obtaining and maintaining patent protection and trade secret protection for niclosamide and adrulipase and their formulations and uses, as well as successfully defending these patents against third-party challenges. If we or our licensors fail to appropriately prosecute and maintain patent protection for our product candidates, our ability to develop and commercialize these product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. This failure to properly protect the intellectual property rights relating to these product candidates could have a material adverse effect on our financial condition and results of operations.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or our partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or otherwise may not provide any competitive advantage;
- our competitors, many of which have substantially greater resources than we or our partners and many of which have made significant investments in competing technologies, may seek, or may already have obtained, patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential products;

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- there may be significant pressure on the United States government and other international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop, and market competing products; and
- we may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

In addition to patents, we and our partners also rely on trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, third parties may still obtain this information or come upon this same or similar information independently. We may become subject to claims that we or consultants, advisors or independent contractors that we may engage to assist us in developing niclosamide and adrulipase have wrongfully or inadvertently disclosed to us or used trade secrets or other proprietary information of their former employers or their other clients.

***If we or our partners are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.***

Our success also depends upon our ability and the ability of any of our future collaborators to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing products, some of which may be directed at claims that overlap with the subject matter of our intellectual property. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe. Similarly, there may be issued patents relevant to our product candidates of which we are not aware.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third-party claims that we or any of our licensors, suppliers or collaborators infringe the third party's intellectual property rights, we may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- abandon an infringing product candidate or redesign our products or processes to avoid infringement;
- pay substantial damages, including the possibility of treble damages and attorneys' fees, if a court decides that the product or proprietary technology at issue infringes on or violates the third party's rights;
- pay substantial royalties, fees and/or grant cross licenses to our technology; and/or
- defend litigation or administrative proceedings which may be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

***Our ability to compete may decline if we do not adequately protect our proprietary rights.***

Our success depends on obtaining and maintaining proprietary rights to our product candidates for the treatment of age-related diseases, as well as successfully defending these rights against third-party challenges. We will only be able to protect our product candidates, and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Our ability to obtain patent protection for our product candidates is uncertain due to a number of factors, including:

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- we may not have been the first to make the inventions covered by pending patent applications or issued patent
- we may not have been the first to file patent applications for our product candidates or the compositions we developed or for their uses;
- others may independently develop identical, similar or alternative products or compositions and uses thereof;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications may not result in issued patents;

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- we may not seek or obtain patent protection in countries that may eventually provide us a significant business opportunity;
- any patents issued to us may not provide a basis for commercially viable products, may not provide any competitive advantages, or may be successfully challenged by third parties;
- our compositions and methods may not be patentable;
- others may design around our patent claims to produce competitive products which fall outside of the scope of our patents;
- others may identify prior art or other bases which could invalidate our patents.

Even if we have or obtain patents covering our product candidates or compositions, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering compositions or products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to chemical compounds and therapeutic products, and some of these relate to compounds we intend to commercialize. These could materially affect our ability to develop our product candidates or sell our products if approved. Because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our product candidates or compositions may infringe. These patent applications may have priority over patent applications filed by us.

Obtaining and maintaining a patent portfolio entails significant expense and resources. Part of the expense includes periodic maintenance fees, renewal fees, annuity fees, various other governmental fees on patents and/or applications due in several stages over the lifetime of patents and/or applications, as well as the cost associated with complying with numerous procedural provisions during the patent application process. We may or may not choose to pursue or maintain protection for particular inventions. In addition, there are situations in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we choose to forgo patent protection or allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer.

Legal actions to enforce our proprietary rights (including patents and trademarks) can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation of our patents or trademarks or a finding that they are unenforceable. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents or trademarks, or used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

## **Risks Related to our Securities**

### ***Our failure to maintain compliance with Nasdaq's continued listing requirements could result in the delisting of our Common Stock.***

Our common stock is currently listed for trading on the Nasdaq Capital Market. We must satisfy Nasdaq Capital Market's continued listing requirements, including, among other things, a minimum stockholders' equity of \$2.5 million or risk delisting, which would have a material adverse effect on our business. A delisting of our common stock from the Nasdaq Capital Market could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities.

On November 26, 2021, we received notice from the Listing Qualifications Staff of Nasdaq indicating that we were not in compliance with the minimum stockholders' equity requirement for continued listing on the Nasdaq Capital Market, under Listing Rule 5550(b)(1) because our stockholders' equity of \$(6,969,988) as reported in our Quarterly Report on Form 10-Q for the period ended September 30, 2021 was below the required minimum of \$2.5 million, and because, as of November 24, 2021, we did not meet the alternative compliance standards, relating to the market value of listed securities of \$35 million or net income from continuing operations of \$500,000 in the most recently completed fiscal year or in two of the last three most recently completed fiscal years.

On January 10, 2022, we submitted to Nasdaq a plan to regain compliance with Listing Rule 5550(b)(1). On February 15, 2022, Nasdaq notified us that they have granted us an extension of up to 180 calendar days from November 26, 2021, or through May 25, 2022, to regain compliance. If we fail to evidence compliance upon filing our periodic report for the quarter ending June 30, 2022 with the SEC, we may be subject to delisting. If Nasdaq determines to delist our common stock, we will have the right to appeal to a Nasdaq hearings panel.

If our common stock were delisted from Nasdaq, trading of our common stock would most likely take place on an over-the-counter market established for unlisted securities, such as the OTCQB or the Pink Market maintained by OTC Markets Group Inc. An investor would likely find it less convenient to sell, or to obtain accurate quotations in seeking to buy, our common stock on an over-the-counter market, and many investors would likely not buy or sell our common stock due to difficulty in accessing over-the-counter markets, policies preventing them from trading in securities not listed on a national exchange or other reasons. In addition, as a delisted security, our common stock would be subject to SEC rules as a "penny stock," which impose additional disclosure requirements on broker-dealers. The regulations relating to penny stocks, coupled with the typically higher cost per trade to the investor of penny stocks due to factors such as broker commissions generally representing a higher percentage of the price of a penny stock than of a higher-priced stock, would further limit the ability of investors to trade in our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities. For these reasons and others, delisting would adversely affect the liquidity, trading volume and price of our common stock, causing the value of an investment in us to decrease and having an adverse effect on our business, financial condition and results of operations, including our ability to attract and retain qualified employees and to raise capital.

### ***The limited public market for our securities may adversely affect an investor's ability to liquidate an investment in us.***

Although our Common Stock is currently listed on the Nasdaq Capital Market, there is limited trading activity. We can give no assurance that an active market will develop, or if developed, that it will be sustained. If an investor acquires shares of our Common Stock, the investor may not be able to liquidate our shares should there be a need or desire to do so.

**The market price of our Common Stock may be volatile which could subject us to securities class action litigation and prevent you from being able to sell your shares at or above the offering price.**

The market price for our Common Stock has been and may continue to be volatile and subject to wide fluctuations in response to factors including the following:

- sales or potential sales of substantial amounts of our Common Stock, including sales required for us to regain and maintain compliance with Nasdaq's continued listing requirements;
- delay or failure in initiating or completing pre-clinical or clinical trials or unsatisfactory results of these trials;
- announcements about us or about our competitors, including clinical trial results, regulatory approvals or new product introductions;
- developments concerning our licensors or product manufacturers;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the pharmaceutical or biotechnology industries;
- governmental regulation and legislation;
- variations in our anticipated or actual operating results;
- change in securities analysts' estimates of our performance, or our failure to meet analysts' expectations; foreign currency values and fluctuations; and
- overall economic conditions.

Many of these factors are beyond our control. The stock markets in general, and the market for pharmaceutical and biotechnological companies in particular, have historically experienced extreme price and volume fluctuations. These fluctuations often have been unrelated or disproportionate to the operating performance of these companies. These broad market and industry factors could reduce the market price of our Common Stock, regardless of our actual operating performance.

**We have never paid and do not intend to pay cash dividends on our Common Stock. As a result, capital appreciation, if any, will be your sole source of gain.**

We have never paid cash dividends on any of our capital stock and we currently intend to retain future earnings, if any, to fund the development and growth of our business. Our Series B Preferred Stock carries a dividend rate of 9.0% per year, which is cumulative and continues to accrue on a daily basis whether or not declared and whether or not we have assets legally available therefor. We may pay such dividends at our option either in cash or in kind in additional shares of preferred stock. We do not expect to pay any dividends in cash and have paid accrued dividends in kind in additional shares of preferred stock to date. In addition, the terms of future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our Common Stock will be your sole source of gain for the foreseeable future.

**Provisions in our Charter, our amended and restated by-laws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our Common Stock.**

Provisions of our Charter, our amended and restated by-laws and Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interests. These provisions include:

- the inability of stockholders to call special meetings;
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could include the right to approve an acquisition or other change in our control or could be used to institute a rights plan, also known as a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors;
- advance notice required for any nomination or other business to be properly brought before an annual meeting of stockholders which requires notice to be delivered to our secretary not later than the close of business on the 90th day, nor earlier than the close of business on the 120th day prior to the first anniversary of the preceding year's annual meeting, subject to certain exceptions;
- any vacancies on our board of directors that results from the death, disability, resignation, disqualification or removal of any director or from any other cause shall be filled solely by the affirmative vote of a majority of the total number of directors then in office, even if less than a quorum, or by a sole remaining director and shall not be filled by the stockholders; provided that a vacancy created by the removal of a director by the stockholders may be filled by the stockholders; and
- forum selection provisions that state that unless we consent in writing to the selection of an alternative forum, (A) (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any current or former director, officer, other employee or stockholder of the Company to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware ("DGCL"), the Charter or the by-laws as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (iv) any action asserting a claim governed by the internal affairs doctrine of the law of the State of Delaware shall, to the fullest extent permitted by law, be exclusively brought in the Court of Chancery of the State of Delaware or, if such court does not have subject matter jurisdiction thereof, the federal district court of the State of Delaware; and (B) the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended.

In addition, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years, has owned 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our Common Stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your Common Stock in an acquisition.

***If securities or industry analysts do not publish research or reports about our business, if they adversely change their recommendations regarding our shares or if our results of operations do not meet their expectations, our share price and trading volume could decline.***



The trading market for our shares is influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over these analysts. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our share price or trading volume to decline. Moreover, if one or more of the analysts who cover us downgrade our stock, or if our results of operations do not meet their expectations, our share price could decline.

**We currently have Series B Preferred Stock outstanding and may be required to issue additional shares of our Series C Preferred Stock upon the exercise of the Series B Exchange Right. Our certificate of incorporation authorizes our Board to create new series of preferred stock without further approval by our stockholders, which could adversely affect the rights of the holders of our Common Stock.**

Our Board has the authority to fix and determine the relative rights and preferences of preferred stock. Our Board also has the authority to issue preferred stock without further stockholder approval.

We currently have approximately 645.20 shares of Series B Preferred Stock outstanding with a stated value of \$7,700 per share, which are currently convertible at the holder's option at any time, together with any accrued but unpaid dividends thereon, into shares of Common Stock at a conversion price of \$7.70, subject to certain adjustments.

Our Series B Preferred Stock gives its holders the preferred right to our assets upon liquidation and the right to receive dividend payments at 9.00% per annum before dividends are distributed to the holders of Common Stock, among other things. In addition, in the event we effect any issuance of Common Stock or Common Stock equivalents for cash consideration, or a combination of units thereof, the holders of the Series B Preferred Stock have the right, subject to certain exceptions, at their option, to exchange (in lieu of cash subscription payments) all or some of the Series B Preferred Stock then held (with a value per share of the Series B Preferred Stock equal to the Series B stated value per share of \$7,700 plus accrued and unpaid dividends thereon) for any securities or units issued in such issuance on a dollar-for-dollar basis. The holders of the Series B Preferred Stock, voting as a separate class, also have customary consent rights with respect to certain corporate actions, including the issuance of an increased number of shares of Series B Preferred Stock, the establishment of any capital stock ranking senior to or on parity the Series B Preferred Stock as to dividends or upon liquidation, the incurrence of indebtedness, and certain changes to our Charter or Bylaws including other actions.

Our Board created a series of preferred stock designated as Series C Preferred Stock ("Series C Preferred Stock"), of which 57,000 shares are authorized for issuance, none of which are currently outstanding. Pursuant to the Series B Exchange Right, we may be required to issue shares of Series C Preferred Stock in certain circumstances.

Our obligations to the holders of the Series B Preferred Stock and any future holders of any additional series of preferred stock we may issue could limit our ability to obtain additional financing or increase our borrowing costs, which could have an adverse effect on our financial condition and hinder the accomplishment of our corporate goals.

In addition to the Series B Preferred Stock and Series C Preferred Stock, our Board could authorize the issuance of additional series of preferred stock with such rights preferential to the rights of our Common Stock, including the issuance of a series of preferred stock that has greater voting power than our Common Stock or that is convertible into our Common Stock, which could decrease the relative voting power of our Common Stock or result in dilution to our existing stockholders.

**As a result of the "most favored nation" in the Certificate of Designations, Powers, Preferences and Rights of the Series B Preferred Stock (the "Series B Certificate of Designations"), we may be required to issue additional securities to the investors who purchased shares of our Series B Preferred Stock and related warrants to purchase shares of our Common Stock in a private placement in July 2020.**

On July 16, 2020, we consummated a private placement offering (the "Series B Private Placement") in which we issued an aggregate of approximately 2,912.58 shares of Series B Preferred Stock, at a price of \$7,700.00 per share, initially convertible into an aggregate of 2,912,576 shares of Common Stock at \$7.70 per share, together with warrants to purchase an aggregate of 1,456,283 shares of Common Stock at an exercise price of \$8.50 per share. The Series B Preferred Stock carries a cumulative dividend at a rate of 9.0% per annum, payable at our option either in cash or in kind in additional shares of Series B Preferred Stock.

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As a result of previous conversions and exchanges, as of March 28, 2022, 645.20 shares of Series B Preferred Stock were outstanding, with an aggregate stated value of approximately \$5,100,000, plus accrued and unpaid dividends through such date of approximately \$519,000, and a conversion price of \$7.70 per share.

Under the Series B Certificate of Designations, in the event we effect any issuance of Common Stock or Common Stock equivalents for cash consideration, or a combination of units thereof (a "Subsequent Financing"), each holder of the Series B Preferred Stock has the right to exchange the stated value, plus accrued and unpaid dividends, of the Series B Preferred Stock for any securities issued in the Subsequent Financing, in lieu of any cash subscription payments therefor (the "Series B Exchange Right"). As a result of our registered direct offering and private placement consummated in January 2021, as of March 28, 2022, we may be required to issue in the aggregate up to 7,047.48 additional shares of Series C Preferred Stock that would be convertible into up to 704,750 underlying shares of common stock, together with warrants to purchase up to an additional 704,750 shares of our common stock, to any holders of Series B Preferred Stock who elect to exercise their Series B Exchange Right in connection with that offering. Alternatively, as a result of sales of additional shares of common stock made on November 30, 2021, at a price of \$2.1657 per share, pursuant to our At The Market Agreement dated May 26, 2021 (the "ATM Agreement") (such price being the lowest price per share sold under the ATM Agreement to date), as of March 28, 2022, we may be required to issue in aggregate up to 2,020,785 shares of common stock, with no warrants, to any holders of Series B Preferred Stock who elect to exercise their Series B Exchange Right into shares of common stock. In any event, we anticipate that we would convert any shares of Series C Preferred Stock to be issued pursuant to the Series B Exchange Right into underlying shares of common stock immediately upon issuance.

In February 2022, we entered into Waivers with certain holders of Series B Preferred Stock, pursuant to which we agreed to pay a cash waiver fee equal to ten percent of the stated value of the shares of Series B Preferred Stock held by such holder (other than holders who are insiders of our company), and such holder agreed to irrevocably waive its Series B Exchange Right with respect to any Subsequent Financing that occurs from and after the date of the Waiver until December 31, 2022. However, as of February 18, 2022, holders of Series B Preferred Stock holding approximately \$2.21 million of stated value of the shares of Series B Preferred Stock outstanding did not enter into a Waiver with us. Accordingly, such non-waiving holders may exercise their Series B Exchange Right in connection with the offerings of the Company through December 31, 2022. However, as of March 28, 2022, holders of Series B Preferred Stock holding approximately \$2.1 million of stated value of the shares of Series B Preferred Stock outstanding did not enter into a Waiver with us. Accordingly, such non-waiving holders may exercise their Series B Exchange Right in connection with the March 2022 Offering. If the holders of Series B Preferred Stock who did not enter into Waivers with us elect to exchange into the March 2022 Offering, up to 1,482,153 additional shares of Common Stock may be issued pursuant to the Series B Exchange Right in excess of amounts currently underlying the Series B Preferred Stock and up to 1,671,395 shares of Common Stock issuable upon exercise of the warrants.

If the holders of our Series B Preferred Stock exercise their Series B Exchange Rights, it will result in certain dilution to our stockholders, and would afford our stockholders a smaller percentage interest in our voting power, liquidation value and aggregate book value. The sale or resale of the Common Stock issued upon conversion of the preferred stock could cause the market price of our Common Stock to decline. In addition, the issuance of Common Stock upon the exercise of the Investor Warrants will result in similar dilution to our stockholders. This dilution, or the possibility that it may occur, may make it more difficult for us to sell equity securities in the future at a time and a price that we deem appropriate.

To raise additional capital, we may in the future offer additional shares of common stock or other securities convertible into or exchangeable for our common stock at prices and other terms that may be more favorable to investors than the terms of our prior offerings that may have been previously approved by our stockholders. As a result, holders of Series B Preferred Stock may become entitled to exercise their Series B Exchange Right in connection with that future offering. This may result in certain dilution to our stockholders and could afford our stockholders a smaller percentage interest in our voting power, liquidation value and aggregate book value. The existence of the Series B Exchange Right may make it more difficult for us to consummate future offerings of our securities at a time and a price that we deem appropriate and may trigger the obligation for the Company to obtain stockholder approval in connection with our future offerings under certain Nasdaq Listing Rules and related guidance.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

**ITEM 2. PROPERTIES**

**Facilities**

We lease the space for our principal executive offices at 777 Yamato Road, Suite 502, Boca Raton, FL 334315 and an administrative office at 760 Parkside Avenue, Downstate Biotechnology Incubator, Suite 217, Brooklyn, NY 11226 on a month-to-month basis. Our U.S. clinical operations office is located in approximately 1,990 square feet of office space at 22320 Foothill Boulevard, Suite 200, Hayward, CA 94541 that we occupy under a lease expiring on May 31, 2022. The operations of AzurRx SAS are conducted at office space located at 290 chemin de Saint Dionisy, Jardin des Entreprises, 30980 Langlade, France, that we occupy under a short-term lease. We believe that our facilities are adequate to meet our current needs.

**ITEM 3. LEGAL PROCEEDINGS**

As of the date hereof, we know of no material, existing or pending legal proceedings against us, nor are we the plaintiff in any material proceedings or pending litigation. There are no proceedings in which any of our directors, executive officers or affiliates, or any registered or beneficial stockholder, is an adverse party to us or has a material interest adverse to our interest. From time to time, we may be subject to various claims, legal actions and regulatory proceedings arising in the ordinary course of business.

**ITEM 4. MINE SAFETY DISCLOSURES**

None.

**PART II**

**ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

Our Common Stock is listed on the Nasdaq Capital Market, or Nasdaq, under the symbol "FWBI".

**Holders of Record**

At March 28, 2022, there were 16,700,640 shares of our Common Stock issued and outstanding and approximately 161 stockholders of record.

**Dividends**

We did not declare any dividends on our Common Stock for the years ended December 31, 2021 and 2020, respectively. Our board of directors does not intend to distribute dividends in the future. Instead, we plan to retain any earnings to finance the development of our product candidates and expansion of our business. The declaration, payment and amount of any future dividends will be made at the discretion of the board of directors, and will depend upon, among other things, the results of our operations, cash flows and financial condition, operating and capital requirements, and other factors as the board of directors considers relevant. There is no assurance that future dividends will be paid, and if dividends are paid, there is no assurance with respect to the amount of any such dividend.

Future cash dividends, if any, will be at the discretion of our board of directors and will depend upon our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors as our board of directors may deem relevant. We can pay dividends only out of our profits or other distributable reserves and dividends or distribution will only be paid or made if we are able to pay our debts as they fall due in the ordinary course of business.

Cumulative dividends on the shares of Series B Preferred Stock accrue at the rate of 9% of the Stated Value per annum, payable semi-annually on June 30 and December 31 of each year, commencing on December 31, 2020. Dividends are payable in additional shares of Series B Preferred Stock valued at the Stated Value or in cash at our sole option.

**Unregistered Sales of Equity Securities**

In August 2021, we issued an employee, stock options to purchase 7,500 shares of Common Stock with a strike price of \$5.80 per share, subject to time-based vesting, under the 2020 Plan. Such issuance was exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended.

In September 2021, we issued an employee, stock options to purchase 250 shares of Common Stock with a strike price of \$6.40 per share, subject to time-based vesting, under the 2020 Plan. Such issuance was exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended.

In September 2021, we issued consultants an aggregate of 18,000 shares of Common Stock for investor relations services. Such issuances were exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended.

In September 2021, we issued Terry Coelho, a non-executive member of our Board, stock options to purchase an aggregate of 10,310 shares of Common Stock with a strike price of \$0.64 per share, subject to time-based vesting, under the 2020 Plan as payment for services provided to the Board. Such issuance was exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended.

In December 2021, we issued a consultant 25,000 shares of Common Stock for investor relations services. Such issuance was exempt from registration under 4(a)(2) of the Securities Act of 1933, as amended.

During the year ended December 31, 2021, there were no other sales of our securities that were not reported in a Current Report on Form 8-K or our Quarterly Report on Form 10-Q.

**ITEM 6. RESERVED**

**ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*You should read the following discussion and analysis in conjunction with our consolidated financial statements, including the notes thereto contained in this Annual Report. This discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of a variety of certain factors, including those set forth under "Risk Factors Associated with Our Business" and elsewhere in this Annual Report.*

**Overview**

We are engaged in the research and development of targeted, non-systemic therapies for the treatment of patients with gastrointestinal ("GI") diseases. Non-systemic therapies are non-absorbable drugs that act locally, i.e. in the intestinal lumen, skin or mucosa, without reaching an individual's systemic circulation.

We are currently focused on developing our pipeline of gut-restricted GI clinical product candidates, including nicosamide, an oral small molecule which we believe has anti-viral and anti-inflammatory properties, and the biologic adrulipase (formerly MS1819), a recombinant lipase enzyme designed to potentially enable the digestion of fats and other nutrients.

Our nicosamide programs leverage proprietary oral and topical formulations to potentially address multiple GI conditions, including inflammatory bowel diseases ("IBD") indications and viral diseases. We are currently advancing two separate clinical programs of our nicosamide formulations, which are currently in Phase 2 clinical trials; FW-COV for Severe Acute Respiratory Syndrome Coronavirus 2 ("COVID-19") GI infections, and FW-UP for ulcerative proctitis ("UP") and ulcerative proctosigmoiditis ("UPS").

We are further developing FW-ICI-AC for Immune Checkpoint Inhibitor-associated colitis ("ICI-AC") and diarrhea in advanced stage oncology patients, for which the U.S. Food and Drug Administration ("FDA") cleared our investigational new drug ("IND") application filed in September 2021, and two pre-IND programs of our nicosamide therapies for potential additional IBD indications, including FW-UC for ulcerative colitis ("UC") and FW-CD for Crohn's disease ("CD").

Our adrulipase programs are focused on the development of an oral, non-systemic, biologic capsule for the potential treatment of exocrine pancreatic insufficiency ("EPI") in patients with cystic fibrosis ("CF") and chronic pancreatitis ("CP"). Our goal is to provide CF and CP patients with a safe and effective therapy to control EPI that is non-animal derived and offers the potential to dramatically reduce their daily pill burden.

We are developing our product candidates for a host of GI diseases where we believe there are significant unmet clinical needs and limited therapeutic options, resulting in painful, life threatening and discomforting consequences for patients. Our mission is to help protect the health and restore quality of life for the millions of people afflicted by these GI diseases.

**COVID-19 Update**

In March 2020, the WHO declared the novel coronavirus disease, or COVID-19, outbreak a global pandemic. To limit the spread of COVID-19, governments have taken various actions including the issuance of stay-at-home orders and physical distancing guidelines. Accordingly, businesses have adjusted, reduced or suspended operating activities. Beginning in March 2020, the majority of our workforce began working from home. Disruptions caused by the COVID-19 pandemic, including the effects of the stay-at-home orders and work-from-home policies, have impacted productivity, including delayed enrollment of new patients at certain of our clinical trial sites, and may further disrupt our business and delay our development programs and regulatory timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct business in the ordinary course. As a result, our expenses may vary significantly if there is an increased impact from COVID-19 on the costs and timing associated with the conduct of our clinical trials and other related business activities.

We have implemented business continuity plans designed to address and mitigate the impact of the ongoing COVID-19 pandemic on our employees and our business. We continue to operate normally with the exception of enabling all of our employees to work productively at home and abiding by travel restrictions issued by federal, state and local governments. Our current plans to return to the office remain fluid as federal, state and local guidelines, rules and regulations continue to evolve.

## **Financial Operations Overview**

### **Revenue**

To date, we have not generated any revenue from the sale of our product candidates or otherwise. In the future, we expect that we will seek to generate revenue primarily from product sales, but we may also generate non-product revenue from sources including, but not limited to, research funding, development and milestone payments, and royalties on future product sales in connection with any out-license or other strategic relationships and/or government grants we may establish. Our product candidates are at an early stage of development and may never be successfully developed or commercialized.

### **Research and Development Expense**

Conducting research and development is central to our business. Historically, the majority of our research and development expenses have been focused on the development of adrulipase and the acquisition and development of niclosamide.

Research and development expenses consist primarily of internal and external costs incurred for our development activities, which include, among other things:

- personnel-related costs, which include salaries, benefits, and stock-based compensation expense;
- fees paid to third parties for services directly related to our drug development and regulatory efforts;
- Expenses incurred under agreements with clinical research organizations ("CROs"), investigative sites and consultants and contractors that conduct or provide other services relating to our clinical trials and research activities;
- the cost of acquiring drug product, drug supply and clinical trial materials from contract development and manufacturing organization ("CDMOs") and third-party contractors;
- costs associated with preclinical and non-clinical activities;
- payments and other costs in connection with the acquisition of our product candidates under licensing agreements; and
- amortization of intangible assets, including patents, in-process research and development and license agreements.

Costs incurred in connection with research and development activities are expensed as incurred.

We expect our research and development expenses to increase for the foreseeable future as we focus our efforts on the clinical development of our product candidates, including niclosamide and adrulipase through late-stage clinical trials, as well as chemistry, manufacturing and controls ("CMC") efforts. The process of conducting non-clinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. It is difficult to determine with certainty the duration and costs of any non-clinical study or clinical trial that we may conduct. In addition, if our product development efforts are successful, we expect to incur substantial costs to prepare for potential commercialization of any late-stage product candidates and, in the event any of our product candidates receives regulatory approval, to potentially fund the launch and sales and marketing efforts of the product.

The probability of success for any of our current or future product candidates will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each drug candidate, as well as an assessment of each drug candidate's commercial potential.

We do not record or maintain information regarding costs incurred in research and development on a program or project specific basis. Our research and development staff, outside consultants, contractors, CROs, and CDMOs are deployed across several programs and/or indications. Additionally, many of our costs are not attributable to individual programs and/or indications. Therefore, we believe that allocating costs on the basis of time incurred by our personnel does not accurately reflect the actual costs of a project.

#### **General and Administrative Expense**

General and administrative expenses consist primarily of personnel-related expenses, including salaries, benefits and stock-based compensation, related to our executive, finance, business development and support functions, legal fees relating to both intellectual property and corporate matters, insurance, costs associated with operating as a public company, including corporate communications and investor relations expense, information technology, professional fees for accounting, auditing and other professional services, and facility-related costs.

We anticipate our general and administrative expenses to increase for the foreseeable future to support of our expanded research and development activities, intellectual property, patent and corporate legal expense, insurance, and costs associated with operating as a public company, including corporate communications and investor relations expense. Additional increases in general and administrative expenses are expected in connection with increased business development efforts, including potential partnership and/or collaboration agreements and financing activities, expanding infrastructure, including information technology administration, and the hiring of additional personnel and consultants, among other expenses.

#### **Liquidity and Capital Resources**

To date, we have not generated any revenues and have experienced net losses and negative cash flows from our activities.

As of December 31, 2021, we had cash and cash equivalents of approximately \$8.2 million, negative working capital of approximately \$2.9 million, and had sustained cumulative losses attributable to common stockholders of approximately \$153.9 million. Subsequent to December 31, 2021, we have raised aggregate gross proceeds of approximately \$9.0 million from the sale of Common Stock and warrants in a public offering. We have not yet achieved profitability and anticipate that we will continue to incur net losses for the foreseeable future. We expect that our expenses will continue to grow and, as a result, we will need to generate significant product revenues to achieve profitability. We may never achieve profitability. As such, we are dependent on obtaining, and are continuing to pursue, the necessary funding from outside sources, including obtaining additional funding from the sale of securities in order to continue our operations. Without adequate funding, we may not be able to meet our obligations. We believe these conditions may raise substantial doubt about our ability to continue as a going concern.

Our primary sources of liquidity come from capital raises through additional equity and/or debt financings. This may be impacted by the COVID-19 pandemic and other geopolitical events, including war in Ukraine, which are evolving and could negatively impact our ability to raise additional capital in the future.

We have funded our operations to date primarily through the issuance of debt, convertible debt securities, preferred stock, as well as the issuance of Common Stock in various public offerings and private placement transactions. We expect to incur substantial expenditures in the foreseeable future for the development of nicosamide and adrulipase. We will require additional financing to develop our product candidates, run clinical trials, prepare regulatory filings and obtain regulatory approvals, fund operating losses, and, if deemed appropriate, establish manufacturing, sales and marketing capabilities. Our current financial condition raises substantial doubt about our ability to continue as a going concern. Our failure to raise capital as and when needed would have a material adverse impact on our financial condition, our ability to meet our obligations, and our ability to pursue our business strategies. We will seek funds through additional equity and/or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing.

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Although, we are primarily focused on the development of our product candidates, including niclosamide and adrulipase, we are also opportunistically focused on expanding our product pipeline of clinical assets through collaborations, and also through acquisitions of products and companies. We are continually evaluating potential asset acquisitions business combinations, and other partnership opportunities. To finance such acquisitions, we might raise additional equity capital, incur additional debt, or both.

We are able to sell securities on a shelf registration statement pursuant to the ATM Agreement with H.C. Wainwright & Co., LLC. Under current Securities and Exchange Commission regulations, if at any time our public float is less than \$75.0 million, and for so long as our public float remains less than \$75.0 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is limited to an aggregate of one-third of our public float, which is referred to as the baby shelf rules. As of March 31, 2022, our calculated public float is below \$75.0 million and we will be subject to baby shelf rules for any offerings conducted on our shelf registration statement. As such, we will be restricted from selling more than an aggregate of one-third of our public float pursuant to a shelf registration statement in any twelve-month period, so long as the aggregate market value of our Common Stock held by non-affiliates is less than \$75.0 million.

Our ability to issue securities is subject to market conditions. Each issuance under the shelf registration statements will require the filing of a prospectus supplement identifying the amount and terms of the securities to be issued.

On September 13, 2021, we entered into the Merger Agreement with FWB. At the effective time of the Merger, the former FWB stockholders received an applicable pro rata share of (i) \$3.0 million in cash and (ii) 624,025 shares of the Common Stock. The remaining non-contingent purchase price was payable to the former FWB stockholders on a pro rata basis upon our payment of (i) \$8.0 million in cash, payable within 45 days of the Merger and, (iii) \$7.0 million in cash, payable by March 31, 2022.

On October 29, 2021, Fortis Advisors LLC, the hired representative (in such capacity, the "*Representative*") of the former stockholders of FWB, in connection with the Merger Agreement filed a complaint against us in the Court of Chancery of the State of Delaware, seeking to enforce rights to payment of \$8.0 million due October 28, 2021, pursuant to the Merger Agreement and the \$2 million milestone payment for initiation of the FW-UP Part 2 trial. On November 15, 2021, we reached an agreement with the Representative to settle the litigation, under terms that, among other things, involve a substantial reduction in immediate payment obligations and deferrals of certain remaining milestone and other payment obligations over time, with an immediate payment of \$2.0 million for the milestone and periodic installments of \$500,000 per month payable from January 2022 through August 2022 and \$1.0 million per month payable from September 2022 through July 2023 until an aggregate of \$17.0 million is received.



**Consolidated Results of Operations for the Years Ended December 31, 2021 and 2020**

The following table summarizes our consolidated results of operations for the periods indicated:

	<b>Years Ended December 31,</b>		<b>Increase (decrease)</b>
	<b>2021</b>	<b>2020</b>	
Operating expenses:			
Research and development expenses	\$ 16,994,828	\$ 5,888,004	\$ 11,106,824
Research and development expenses - Intellectual property acquired	21,325,527	13,250,000	8,075,527
General and administrative expenses	18,384,545	7,294,764	11,089,781
Intangible asset impairment	2,351,988	-	2,351,988
Total operating expenses	59,056,888	26,432,768	32,624,120
Other expenses (income)	(519,039)	6,238,698	(6,757,737)
Net loss	<u>\$ 58,537,849</u>	<u>\$ 32,671,466</u>	<u>\$ 25,866,383</u>

*Revenues*

We have not yet achieved revenue-generating status from any of our product candidates. Since inception, we have devoted substantially all of our time and efforts to acquiring and developing our product candidates, including niclosamide and adrulipase. As a result, we did not have any revenue during the years ended December 31, 2021 and 2020, respectively.

*Research and Development Expenses*

Total research and development expenses for the year ended December 31, 2021 totaled approximately \$38.3 million, an increase of approximately \$19.2 million, or 200% over the approximately \$19.1 million recorded for the year ended December 31, 2020. Excluding research and development expenses for intellectual property acquired in connection with the acquisition of FWB, research and development expenses for the year ended December 31, 2021 totaled approximately \$17.0 million, an increase of approximately \$11.1 million, or 289% over the approximately \$5.9 million recorded for the year ended December 31, 2020.

The increase in research and development expenses, excluding expenses related to the acquired intellectual property, was primarily attributable to increases of approximately \$4.4 million in clinical trial related expenses in connection with the FW-COV and FW-UP niclosamide studies and completion of the OPTION 2 and Combination studies for adrulipase, approximately \$3.0 million in milestone payments to FWB related to the development of niclosamide, approximately \$1.3 million in CMC related costs, approximately \$1.1 million in clinical and regulatory related costs, and approximately \$0.6 million in other expenses.

The increase in research and development expenses for acquired intellectual property was primarily attributable to \$8.1 million of additional expense related to the acquisition of our niclosamide drug candidates through the Merger entered into on September 13, 2021, as compared to the license agreement entered into on December 31, 2020,

*General and Administrative Expense*

General and administrative expenses for the year ended December 31, 2021 totaled approximately \$18.4 million, an increase of approximately \$11.5 million, or 158% over the approximately \$7.3 million recorded for the year ended December 31, 2020.

The increase in total general and administrative expenses was due primarily to increases in costs associated with being a publicly reporting company, including investor relations expenses of approximately \$5.8 million, legal expenses of approximately \$1.8 million, personnel costs of approximately \$0.6 million, directors and officer's insurance of approximately \$0.4 million, directors fees of approximately \$0.4 million, audit and accounting fees of approximately \$0.3 million, and business development related expense of approximately \$0.2 million

**Impairment of Intangible Assets**

We reviewed our definite-lived intangible assets for impairment as there were indicators that their carrying value of our patents might not be recoverable in December 2021. We used a qualitative approach to compare their carrying value to their fair value, and because this evaluation indicated that the carrying value of our definite-lived intangible assets was not recoverable, we performed an impairment test of these assets. Based on these analyses, we recognized an impairment charge of approximately \$2.4 million for the year ended December 31, 2021 to reduce the carrying amounts of our patents to their fair value.

**Other Expense (Income)**

Other expenses (income) for the year ended December 31, 2021 totaled approximately \$(0.5) million, a decrease in expenses of approximately \$6.8 million over the approximately \$6.3 million recorded for the year ended December 31, 2020. Interest expense was approximately \$0 million and \$5.8 million for the year ended December 31, 2021 and 2020, respectively. The decreased interest expense is due to amortization of debt discount and accrued interest related to the convertible debt outstanding during the year ended December 31, 2020, that was not outstanding during the year ended December 31, 2021.

**Net Loss**

As a result of the factors above, our net loss for the year ended December 31, 2021 totaled approximately \$56.2 million, an increase of approximately \$23.5 million, or 72% over the approximately \$32.7 million recorded for the year ended December 31, 2020.

**Cash Flows for the Years Ended December 31, 2021 and 2020**

The following table summarizes our cash flows for the periods indicated:

	Years Ended December 31,	
	2021	2020
Net cash provided by (used in):		
Operating activities	\$ (32,288,218)	\$ (11,221,538)
Investing activities	(10,319,488)	87,350
Financing activities	44,763,493	17,046,121
Net increase in cash and cash equivalents	\$ 2,155,787	\$ 5,911,933

**Operating Activities**

Net cash used in operating activities during the year ended December 31, 2021 of approximately \$32.3 million was primarily attributable to our net loss of approximately \$58.5 million adjusted for addbacks of non-cash expenses of approximately \$9.7 million, mostly related to common stock issued for intellectual property acquired of approximately \$4.0 million, intangible asset impairment of approximately \$2.4 million, Common Stock granted to consultants of approximately \$1.6 million, stock-based compensation of approximately \$1.4 million, change in fair value of liability of \$0.5 million, and depreciation and amortization of approximately \$0.5 million, partially offset by a change in asset and liability balances of approximately \$17.1 million.

Net cash used in operating activities during the year ended December 31, 2020 of approximately \$11.2 million was primarily attributable to our net loss of approximately \$32.7 million adjusted for addbacks of non-cash expenses of approximately \$7.3 million, which includes accretion of debt discount of approximately \$4.6 million, loss on debt extinguishment of approximately \$0.6 million, amortization of approximately \$0.5 million, and stock-based compensation of approximately \$0.5 million and a net increase of working capital of approximately \$14.2 million.

### **Investing Activities**

Net cash used in investing activities during the year ended December 31, 2021 was approximately \$10.3 million, consisting of approximately \$10.3 million in cash payments related to the FWB License Agreement and approximately \$71,000 related to the purchase of office furniture and equipment

Net cash provided by investing activities during the year ended December 31, 2020 of approximately \$87,000 was primarily attributable to the sale of equipment related to the closure of our laboratory in France.

### **Financing Activities**

Net cash provided by financing activities of approximately \$44.8 million for the year ended December 31, 2021 was primarily due to: (i) the sale of an aggregate of 5,333,345 shares of common stock under our ATM Agreement for net proceeds of approximately \$18.5 million; (ii) the sale of an aggregate of 10,666,666 shares of our Series C Preferred Stock and warrants to purchase up to an aggregate of 1,066,667 shares of Common Stock in a concurrent registered direct offering and private placement in January 2021 for net proceeds of approximately \$6.8 million; (iii) the sale of 580,000 shares of Common Stock, pre-funded warrants to purchase up to 205,854 shares of Common Stock and warrants to purchase an aggregate of 392,927 shares of Common Stock in a registered direct offering in March 2021 for net proceeds of approximately \$9.1 million; (iv) the sale of 1,045,454 shares of Common Stock in an underwritten offering in July 2021 for net proceeds of approximately \$5.1 million; and (v) cash proceeds from warrant exercises of approximately \$4.9 million.

Net cash provided by financing activities of approximately \$17.0 million for the year ended December 31, 2020 was primarily due to the net proceeds from the issuance of convertible debt of approximately \$3.2 million in January 2020 and the issuance of the preferred stock of approximately \$13.2 million in the Series B Private Placement in July 2020 offset by repayments of approximately \$0.5 million related to the ADEC Notes and approximately \$0.7 million related to the note payable.

### **Critical Accounting Policies and Significant Judgements and Estimates**

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and related disclosures during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 of the notes to our consolidated financial statements appearing elsewhere in this document, management has identified the following as "Critical Accounting Policies and Estimates": Stock-Based Compensation, Debt and Equity Instruments, Intangible Assets and Goodwill. We believe that the estimates and assumptions involved in these accounting policies may have the greatest potential impact on our financial statements.

### **Stock-Based Compensation**

We account for share-based payment awards issued to employees and members of our Board by measuring the fair value of the award on the date of grant and recognizing this fair value as stock-based compensation using a straight-line basis over the requisite service period, generally the vesting period. For awards issued to non-employees, the measurement date is the date when the performance is complete or when the award vests, whichever is the earliest. Accordingly, non-employee awards are remeasured at each reporting period until the final measurement date. The fair value of the award is recognized as stock-based compensation over the requisite service period, generally the vesting period.

### **Debt and Equity Instruments**

We analyze debt and equity instruments for various features that would generally require either bifurcation and derivative accounting, or recognition of a debt discount or premium under authoritative guidance.

Detachable warrants issued in conjunction with debt are measured at their relative fair value, if they are determined to be equity instrument, or their fair value, if they are determined to be liability instruments, and recorded as a debt discount.

Conversion features that are in the money at the commitment date constitute a beneficial conversion feature that is measured at its intrinsic value and recognized as debt discount or deemed dividend. Debt discount is amortized as interest expense over the maturity period of the debt using the effective interest method.

### **Intangible Assets**

Our definite-lived intangible assets had a carrying value of approximately \$0 and \$2.9 million at December 31, 2021, and 2020, respectively. These assets include patents, in-process research and development and license agreements. These intangible assets were recorded at historical cost and are stated net of accumulated amortization.

The patents, in-process research and development and licenses are amortized over their remaining estimated useful lives, ranging from 5 to 12 years, based on the straight-line method. The estimated useful lives directly impact the amount of amortization expense recorded for these assets on a quarterly and annual basis.

In addition, we test for impairment of definite-lived intangible assets when events or circumstances indicate that the carrying value of the assets may not be recoverable. Judgment is used in determining when these events and circumstances arise. If we determine that the carrying value of the assets may not be recoverable, judgment and estimates are used to assess the fair value of the assets and to determine the amount of any impairment loss. In the year ended December 31, 2020, no events or circumstances arose that indicated that the carrying value of any of our definite-lived intangible assets may not be recoverable.

In testing for impairment of our definite-lived intangible assets, we determined that the carrying value of our patents exceeded their fair value. Based on this analysis, we recognized an impairment charge of approximately \$2.4 million on our patents acquired in the Mayoly APA in the year ended December 31, 2021.

Other than the impairment identified above, in the year ended December 31, 2021, no events or circumstances arose that would indicate that the carrying value of any of our definite-lived intangible assets may not be recoverable.

### **Goodwill**

Goodwill relates to the acquisition of ProteaBio Europe SAS during 2014 and represents the excess of the total purchase consideration over the fair value of acquired assets and assumed liabilities, using the purchase method of accounting. Goodwill is not amortized but is subject to periodic review for impairment. As a result, the amount of goodwill is directly impacted by the estimates of the fair values of the assets acquired and liabilities assumed.

In addition, goodwill will be reviewed annually, and whenever events or changes in circumstances indicate that the carrying amount of the goodwill might not be recoverable. Judgment is used in determining when these events and circumstances arise. We perform our review of goodwill on our one reporting unit. If we determine that the carrying value of the assets may not be recoverable, judgment and estimates are used to assess the fair value of the assets and to determine the amount of any impairment loss.

The carrying value of goodwill was approximately \$1.9 million and \$2.1 million, at December 31, 2021 and 2020, respectively. Goodwill is denominated in a foreign currency and translated to U.S. dollars at period end exchange rates. If actual results are not consistent with our estimates or assumptions, we may be exposed to an impairment charge that could be material.

### **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Not applicable.

**ITEM 8. FINANCIAL STATEMENTS**

The audited consolidated financial statements of First Wave BioPharma, Inc., including the notes thereto, together with the report thereon of Mazars USA LLP, our independent registered public accounting firm, are included in this Annual Report as a separate section beginning on page F-1.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

**ITEM 9A. CONTROLS AND PROCEDURES**

**Evaluation of disclosure controls and procedures.**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended (the "Exchange Act") is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2021, our senior management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Our senior management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2021 our disclosure controls and procedures were effective at the reasonable assurance level.

**Management's Annual Report on Internal Control over Financial Reporting.**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and preparation of our financial statements for external purposes in accordance with generally accepted accounting principles.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect misstatements and, even when determined to be effective, can only provide reasonable, not absolute, assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to risk that controls may become inadequate as a result of changes in conditions or deterioration in the degree of compliance.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") issued in May 2013 and related COSO guidance. Based on our evaluation under this framework, management has concluded that, as of December 31, 2021, our internal control over financial reporting was effective based upon those criteria.

This report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting.

**Changes in Internal Controls over Financial Reporting.**

There were no significant changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the period covered by this Annual Report on Form 10-K that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

**ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS**

Not applicable.

## PART III

## ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

## Directors

The following section sets forth certain information regarding our directors. There are no family relationships between any of the directors and our Named Executive Officers.

Director, Title	Age
James Sapirstein – President, Chief Executive Officer, Chairman and Non-Independent Director	60
Edward J. Borkowski – Lead Independent Director	62
Charles J. Casamento – Independent Director	76
Alastair Riddell, MSc., MBChB., DSc. – Independent Director	72
Gregory Oakes – Independent Director	53
Terry Coelho – Independent Director	60

**James Sapirstein** was appointed to the Board on October 8, 2019 and as our President and Chief Executive Officer effective that same day. Mr. Sapirstein was appointed Chair of the Board effective February 19, 2021. Prior to joining us, Mr. Sapirstein served as Chief Executive Officer and as a director of ContraVir Pharmaceuticals, Inc. (now known as Hepion Pharmaceuticals, Inc.) from March 2014 to October 2018. Previously, Mr. Sapirstein was the Chief Executive Officer of Alliqua Therapeutics from October 2012 to February 2014. He founded and served as Chief Executive Officer of Tobira Therapeutics from October 2006 to April 2011 and served as Executive Vice President, Metabolic and Endocrinology for Sero Laboratories from June 2002 to May 2005. Mr. Sapirstein's earlier career included a number of senior level positions in the area of marketing and commercialization, including as Global Marketing Lead for Viread (tenofovir) while at Gilead Sciences and as Director of International Marketing of the Infectious Disease Division at Bristol Myers Squibb. Mr. Sapirstein is currently the Chair Emeritus of BioNJ, the New Jersey affiliate of the Biotechnology Innovation Organization, and also serves on the Emerging Companies and Health Section Boards of the Biotechnology Innovation Organization. Mr. Sapirstein received his bachelor's degree in pharmacy from Rutgers University and holds an MBA degree in management from Fairleigh Dickinson University.

Mr. Sapirstein's nearly 36 years of pharmaceutical industry experience which spans areas such as drug development and commercialization, including participation in 23 product launches, six of which were global launches led by him makes him a valuable asset to the Board and in his oversight and execution of our business plan.

**Edward J. Borkowski** was appointed to the Board in May 2015, and currently serves as our Lead Independent Director. Mr. Borkowski served as Chair of the Board from 2015 through his resignation effective as of February 19, 2021. Mr. Borkowski is a healthcare executive who currently serves as Executive Vice President for Therapeutics MD. He served as Executive Vice President of MiMedx Group, Inc. (Nasdaq: MDGX) from April 2018 until December 2019. Mr. Borkowski also served as a director for Co-Diagnostics, Inc. (Nasdaq: CODX), from May 2017 until June 2019. Previously, he served as the Chief Financial Officer of Aceto Corporation (Nasdaq: ACET) from February 2018 to April 2018, and has held several executive positions with Concordia International, an international specialty pharmaceutical company, between May 2015 to February 2018. Mr. Borkowski has also served as Chief Financial Officer of Amerigen Pharmaceuticals, a generic pharmaceutical company with a focus on oral, controlled release products and as the Chief Financial Officer and Executive Vice President of Mylan N.V. In addition, Mr. Borkowski previously held the position of Chief Financial Officer with Convatec, a global medical device company focused on wound care and ostomy, and Carefusion, a global medical device company for which he helped lead its spin-out from Cardinal Health into an independent public company. Mr. Borkowski has also served in senior financial positions at Pharmacia and American Home Products (Wyeth). He started his career with Arthur Andersen & Co. after receiving his MBA in accounting from Rutgers University subsequent to having earned his degree in Economics and Political Science from Allegheny College. Mr. Borkowski is currently a Trustee and a member of the Executive Committee of Allegheny College.

Mr. Borkowski's extensive healthcare and financial expertise, together with his public company experience provides the Board and management with valuable insight in the growth of our business plan.

**Charles J. Casamento** was appointed to the Board in March 2017. Since 2007, Mr. Casamento has been executive director and principal of The Sage Group, a health care advisory group. Prior to that, Mr. Casamento was president and Chief Executive Officer of Osteologix, a startup company which he oversaw going public, from October 2004 until April 2007. Mr. Casamento was the founder of Questcor Pharmaceuticals where he was President, Chief Executive Officer and Chair from 1999 through 2004. During his time at Questcor, the company acquired Acthar, a product with sales that would eventually exceed \$1.0 billion. Mr. Casamento also served as President, Chief Executive Officer and Chair of RiboGene Inc. until 1999 when RiboGene was merged another company to form Questcor. He was also the Co-Founder, President and Chief Executive Officer of Indevus (formerly Interneuron Pharmaceuticals) and has held senior management positions at Genzyme Corporation, where he was Senior Vice President, American Hospital Supply, where he was Vice President of Business Development for the Critical Care division, Johnson & Johnson, Hoffmann-LaRoche and Sandoz. He currently serves as Chairman of the Board of Directors of Relmada Therapeutics (OTCQB: RLMD) and also serves on the Board of Directors of Eton Pharmaceuticals (Nasdaq: ETON), and was previously a Director and Vice Chair of the Catholic Medical Missions Board, a large not for profit international organization. Mr. Casamento holds a bachelor's degree in Pharmacy from Fordham University and an MBA from Iona College.

Mr. Casamento's expertise and knowledge of the financial community combined with his experience in the healthcare sector makes him a valued member of the Board.

**Dr. Alastair Riddell** was appointed to the Board in September 2015. Since June 2016, Dr. Riddell has served as Chair of Nemesis Biosciences Ltd and Chair of Feedback plc (LON: FDBK). He has also served as Chair of the South West Academic Health Science network in the UK since January 2016. Since his appointment in December 2015, Dr. Riddell has served as Non-Executive Director of Cristal Therapeutics in The Netherlands. From September 2012 to February 2016, he served as Chair of Defininigen Ltd., and from November 2013 to September 2015 as Chair of Silence Therapeutics Ltd., and from October 2009 to November 2012 as Chair of Procure Therapeutics. Between 2007 to 2009, Dr. Riddell served as the Chief Executive Officer of Stem Cell Sciences plc. and between 2005 to 2007, served at Paradigm Therapeutics Ltd. as the Chief Executive Officer. Between 1998 to 2005, Dr. Riddell also served as the Chief Executive Officer of Pharmagene plc. Dr. Riddell began his career as a doctor in general practice in a variety of hospital specialties and holds a Master of Science and a Bachelor of Medicine and Surgery degrees. He was recently awarded a Doctorate of Science, Honoris Causa by Aston University.

Dr. Riddell's medical background coupled with his expertise in the life sciences industry, directing all phases of clinical trials, before moving to sales, marketing and general management, makes him a well-qualified member of the Board.

**Gregory Oakes** was appointed to the Board on April 13, 2020. Mr. Oakes brings over 25 years of pharmaceutical industry and leadership experience and currently serves as President, North America, Relypsa, Inc, Executive Vice President, Vifor Pharma. Mr. Oakes previously served as Corporate Vice President, Global Integration Lead for Otezla® (apremilast) at Amgen, Inc. where he was responsible for the integration and continued success of the brand with \$2 billion in assets. Prior to Amgen from 2017 - 2019, Mr. Oakes served as Corporate Vice President and U.S. General Manager at Celgene Corp., a global biopharmaceutical company which develops and commercializes medicines for cancer and inflammatory disorders. Mr. Oakes also served as the Global Commercial Integration Lead at Celgene where he helped steer the \$74 billion acquisition by Bristol-Myers Squibb and the \$13.4 billion divestiture of Otezla®. From 2010 to 2017, Mr. Oakes held several positions at Novartis AG, the most recent as Head of Sandoz Biopharmaceuticals, North America. He began his career at Schering-Plough (Merck) where he held executive roles in both the U.S. and Europe. Mr. Oakes holds a bachelor's degree in Marketing and Business Administration from Edinboro University and a M.B.A. from Clemson University. He currently sits on the Board of BioNJ and previously served on various Executive Committees at Celgene, Novartis, and Schering-Plough (Merck).

Mr. Oakes' background of over 25 years of pharmaceutical industry and leadership experience combined with broad experience in pharmaceutical commercialization and acquisitions makes him a qualified member of the Board.



**Terry Coelho** was appointed to the Board on August 11, 2021. Ms. Coelho has served as the Executive Vice President, Chief Financial Officer & Chief Business Development Officer of CinCor Pharma, Inc. (NASDAQ: CINC), a clinical stage cardiorenal therapeutics company, since November 2021. Prior to her current role Ms. Coelho served as Executive Vice President and Chief Financial Officer at BioDelivery Sciences International, Inc. (NASDAQ: BDSI), a commercial-stage specialty pharmaceutical company, since January 2019. Prior to her tenure at BDSI, Ms. Coelho served as Chief Financial Officer and Treasurer at Balchem Corporation (NASDAQ: BCPC) from October 2017 to October 2018. Previous to her role at Balchem she served as Chief Operating Officer for Diversey, Inc., a multi-billion-dollar global private equity carve-out from Sealed Air Corporation. She additionally held senior finance positions at Diversey Care, including that of Division Chief Financial Officer and VP of Global Commercial Excellence, from October 2014 through August 2017. Ms. Coelho has also served in senior finance and operational leadership roles of increasing responsibility with leading global organizations, including Mars, Incorporated, and Novartis Pharmaceuticals from 2007 to 2014, including serving as Global Head of Oncology Development Finance. Ms. Coelho earned an MBA in Finance from IBMEC in Brazil and a Bachelor of Arts degree in both Economics and International Relations, summa cum laude, from The American University School of International Service in Washington, DC. She has led Women's Networking ERGs and is a founding Steering Committee Member of the CFO Leadership Council – Charlotte, North Carolina, chapter.

Ms. Coelho was selected as a director due to her financial background and experience as a senior financial officer of public companies.

#### Executive Officers

The following table sets forth information regarding our current executive officers as appointed by the Board, each to serve in such position until their respective successors have been duly appointed and qualified or until their earlier death, resignation or removal from office. Our executive officers are appointed by and serve at the discretion of the Board, subject to the terms of any employment agreements they may have with us. The following is a brief description of the qualifications and business experience of each of our current executive officers.

Executive Officer	Age	Title
James Sapirstein	60	President, Chief Executive Officer, Chairman and Non-Independent Director
Sarah Romano	42	Chief Financial Officer
James E. Pennington	78	Chief Medical Officer

Our executive officers are appointed by and serve at the discretion of the Board, subject to the terms of any employment agreements they may have with us. The following is a brief description of the qualifications and business experience of each of our current executive officers.

**James Sapirstein.** Please see Mr. Sapirstein's biography under the "Directors" section of this Annual Report.

**Sarah Romano** was appointed to serve as our Chief Financial Officer on March 1, 2022. Ms. Romano previously served as Chief Financial Officer of Kiora Pharmaceuticals, Inc. (NASDAQ: KPRX) (formerly EyeGate Pharmaceuticals, Inc.), a clinical-stage specialty pharmaceutical company developing products for treating ophthalmic diseases, from February 2017 through February 2022 and as its Corporate Controller from August 2016 to January 2017. Prior to joining Kiora, Ms. Romano served as Assistant Controller at TechTarget from June 2015 through August 2016 and Corporate Controller at Bowdoin Group, a healthcare-focused executive recruiting firm, from September 2013 through May 2015. Previously, she held financial reporting positions of increasing responsibility at SoundBite Communications from 2008 until its acquisition by Genesys in 2013, and at Cognex Corporation from 2004 through 2008. Ms. Romano began her career as an auditor in the Boston office of PricewaterhouseCoopers. A licensed CPA in Massachusetts, she holds a Bachelor of Arts in Accounting from College of the Holy Cross and a Master of Accounting from Boston College.

**Dr. James E. Pennington** was appointed as our Chief Medical Officer in May 2018. Prior to joining us, Dr. Pennington served as Senior Clinical Fellow from 2010 to 2018 and as Executive Vice President and Chief Medical Officer from 2007 to 2010 at Anthera Pharmaceuticals, Inc. (Nasdaq: ANTH). From 2004 to 2007, Dr. Pennington served as Executive Vice President and Chief Medical Officer at CoTherix, Inc., and has held various executive positions at a number of pharmaceutical companies, including InterMune Inc., Shaman Pharmaceuticals and Bayer Corporation. He has served on several editorial boards, and has authored numerous original research publications and reviews. Dr. Pennington is currently a Clinical Professor of Medicine with the University of California San Francisco, where he has taught since 1986. Prior to that, he was a professor at Harvard Medical School. Dr. Pennington received a Bachelor of Arts from the University of Oregon and a Doctor of Medicine from the University of Oregon School of Medicine, and is Board Certified in internal medicine and infectious diseases.

## Section 16(a) Beneficial Ownership Reporting Compliance

### *Delinquent Section 16(a) Reports*

Section 16(a) of the Exchange Act, requires our officers, directors, and persons who beneficially own more than 10% of our Common Stock to file reports of ownership and changes in ownership with the SEC. Officers, directors, and greater-than-ten-percent stockholders are also required by the SEC to furnish us with copies of all Section 16(a) forms that they file.

Based solely upon a review of these forms that were furnished to us, we believe that all reports required to be filed by these individuals and persons under Section 16(a) were filed during the year ended December 31, 2021 and that such filings were timely.

### Code of Business Conduct and Ethics

The Board adopted a code of business conduct and ethics (the "Code") that applies to our directors, officers and employees. A copy of this Code is available on our website at [www.firstwavebio.com/investors](http://www.firstwavebio.com/investors). We intend to disclose on our website any amendments to and waivers of the Code that apply to our principal executive officer, principal financial officer, principal accounting officer, controller, or persons performing similar functions.

### Director Nomination Process

The Corporate Governance and Nominating Committee identifies director nominees by first considering those current members of the Board who are willing to continue service. Current members of the Board with skills and experience that are relevant to our business and are willing to continue their service as a director are considered for re-election, balancing the value of continuity of service by existing members of the Board with that of obtaining a new perspective. Nominees for director are selected by a majority of the members of the Board. Although we do not have a formal diversity policy, in considering the suitability of director nominees, the Corporate Governance and Nominating Committee considers such factors as it deems appropriate to develop a Board and its committees that are diverse in nature and comprised of experienced and seasoned advisors. Factors considered by the Corporate Governance and Nominating Committee include sound judgment, knowledge, skill, diversity, integrity, experience with businesses and other organizations of comparable size, including experience in the biopharma industry, clinical studies, FDA compliance, intellectual property, business, finance, administration or public service, the relevance of a candidate's experience to our needs and experience of other Board members, experience with accounting rules and practices, the desire to balance the considerable benefit of continuity with the periodic injection of the fresh perspective provided by new members, and the extent to which a director candidate would be a desirable addition to the Board and its committees.

Nominations of persons for election to the Board may be made at an annual meeting of stockholders only (a) pursuant to our notice of meeting, (b) by or at the direction of the Board or any committee thereof or (c) by any stockholder of the Company who was a stockholder of record of the Company at the time the notice is delivered by such stockholder to the secretary of the Company, who is entitled to vote at the meeting upon such election of directors or upon such other business, as the case may be, and who complies with the notice procedures set forth in our bylaws. For any nominations to be properly brought before an annual meeting by a stockholder, the stockholder must have given timely notice, which must be delivered to the secretary of the Company at our principal executive offices not later than the close of business on the 90th day, nor earlier than the close of business on the 120th day, prior to the first anniversary of the preceding year's annual meeting; provided however, that in the event that the date of the annual meeting is more than 30 days before or more than 70 days after such anniversary date, notice by the stockholder must be so delivered not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90th day prior to such annual meeting or the 10th day following the day on which public announcement of the date of such meeting is first made by the Company. In no event shall the public announcement of an adjournment, postponement or recess of an annual meeting commence a new time period (or extend any time period) for the giving of a stockholder's notice as described above. The number of nominees a stockholder may nominate for election at the annual meeting (or in the case of a stockholder giving the notice on behalf of a beneficial owner, the number of nominees a stockholder may nominate for election at the annual meeting on behalf of such beneficial owner) shall not exceed the number of directors to be elected at such annual meeting.

To be in proper form, such stockholder's notice shall set forth: (a) as to each person whom the stockholder proposes to nominate for election as a director (i) the name, age, business and residence address, and principal occupation or employment of the nominee, (ii) and all other information relating to such nominee that is required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to and in accordance with Section 14(a) of the Exchange Act, and the rules and regulations promulgated thereunder, (iii) a reasonably detailed description of any compensatory, payment or other financial agreement, arrangement or understanding that such nominee has with any other person or entity other than the Company including the amount of any payment or payments received or receivable thereunder, in each case in connection with candidacy or service as a director of the Company, (iv) such person's written consent to being named in the Company's proxy statement and associated proxy card as a nominee of the stockholder and to serving as a director if elected and (v) all information with respect to such nominee that would be required to be set forth in a stockholder's notice if such nominee were the stockholder giving notice hereunder and (b) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made (i) the name and address of such stockholder, as they appear on the Company's books, and of such beneficial owner, (ii) the class or series and number of shares of capital stock of the Company which are, directly or indirectly, owned beneficially (within the meaning of Rule 13d-3 under the Exchange Act) or of record by such stockholder and such beneficial owner (provided, that such stockholder and the beneficial owner, if any, on whose behalf the nomination or proposal is made shall in all events be deemed to beneficially own any shares of any class or series and number of shares of capital stock of the Company as to which such stockholder or beneficial owner, if any, has a right to acquire beneficial ownership at any time in the future), (iii) a description of any agreement, arrangement or understanding with respect to the nomination between or among such stockholder and/or such beneficial owner, any of their respective affiliates or associates, and any others acting in concert with any of the foregoing (including their names), including the nominee, (iv) a description of any agreement, arrangement or understanding (including any derivative or short positions, profit interests, options, warrants, convertible securities, stock appreciation or similar rights, hedging transactions, and borrowed or loaned shares) that has been entered into as of the date of the stockholder's notice by, or on behalf of, such stockholder and such beneficial owners, whether or not such instrument or right shall be subject to settlement in underlying shares of capital stock of the Company, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of, such stockholder or such beneficial owner, with respect to securities of the Company, (v) a representation that the stockholder is a holder of record of stock of the Company entitled to vote at such meeting upon such business or nomination, as the case may be, and intends to appear in person or by proxy at the meeting to propose such business or nomination, (vi) a representation as to whether the stockholder or the beneficial owner, if any, intends or is part of a group which intends (a) to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the Company's outstanding capital stock required to elect the nominee and/or (b) otherwise to solicit proxies or votes from stockholders in support of such nomination, and (vii) any other information relating to such stockholder and beneficial owner, if any, required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the election of directors in an election contest pursuant to and in accordance with Section 14(a) of the Exchange Act and the rules and regulations promulgated thereunder. The Company may require any proposed nominee to furnish such other information as the Company may reasonably require to determine the eligibility of such proposed nominee to serve as a director of the Company. If requested by the Company, the information required on such nominee shall be supplemented by such stockholder and any such beneficial owner not later than 10 days after the record date for the meeting to disclose such information as of the record date. In addition, a stockholder seeking to nominate a director candidate shall promptly provide any other information reasonably requested by the Company.

Provided that stockholders provide the information above required for candidates recommended by stockholders, the Corporate Governance and Nominating Committee will evaluate those candidates by following substantially the same process, and applying substantially the same criteria, as for candidates submitted by members of the Board or other persons, as described above and as set forth in its charter.

## **Board Committees**

The standing committees of the Board consist of the Audit Committee, Compensation Committee, and Corporate Governance and Nominating Committee. Our Board has adopted written charters for each of these committees, copies of which are available on our website at [www.firstwavebio.com/investors](http://www.firstwavebio.com/investors). Our Board may establish other committees as it deems necessary or appropriate from time to time.

### ***Audit Committee***

The duties and responsibilities of the Audit Committee include but are not limited to:

- appointing, compensating, retaining, evaluating, terminating, and overseeing our independent registered public accounting firm;
- discussing with our independent registered public accounting firm the independence of its members from its management;
- reviewing with our independent registered public accounting firm the scope and results of their audit;
- approving all audit and permissible non-audit services to be performed by our independent registered public accounting firm;
- overseeing the financial reporting process and discussing with management and our independent registered public accounting firm the interim and annual financial statements that are filed with the SEC;
- reviewing and monitoring our accounting principles, accounting policies, financial and accounting controls, and compliance with legal and regulatory requirements;
- coordinating oversight of the Code and our disclosure controls and procedures on behalf of the Board;
- establishing procedures for the confidential and/or anonymous submission of concerns regarding accounting, internal controls or auditing matters; and
- reviewing and approving related-person transactions.

The rules of Nasdaq require our Audit Committee to consist of at least three directors, all of whom must be deemed to be independent directors under Nasdaq rules. The Board has affirmatively determined that Ms. Coelho and Messrs. Borkowski and Casamento, each meet the definition of "independent director" for purposes of serving on an Audit Committee under Nasdaq rules. Additionally, the Board has determined that Ms. Coelho and Messrs. Borkowski and Casamento each qualify as an "audit committee financial expert," as such term is defined in Item 407(d)(5) of Regulation S-K.

### ***Compensation Committee***

The duties and responsibilities of the Compensation Committee include but are not limited to:

- reviewing key employee compensation goals, policies, plans and programs;
- reviewing and approving the compensation of our directors and executive officers;
- reviewing and approving employment agreements and other similar arrangements between us and our executive officers; and
- appointing and overseeing any compensation consultants or advisors to the Company.

The rules of Nasdaq require our Compensation Committee to consist entirely of independent directors. The Board has affirmatively determined that Ms. Coelho and Messrs. Riddell and Oakes meet the definition of "independent director" for purposes of serving on the Compensation Committee under Nasdaq rules.

**Corporate Governance and Nominating Committee**

The duties and responsibilities of the Corporate Governance and Nominating Committee include but are not limited to:

- assisting the Board in identifying qualified individuals to become members of the Board;
- determining the composition of the Board and monitoring the activities of the Board to assess overall effectiveness; and
- developing and recommending to our Board corporate governance guidelines applicable to the Company and advising our Board on corporate governance matters.

**ITEM 11. EXECUTIVE COMPENSATION**

**Summary Compensation**

The table set forth below reflects certain information regarding the compensation paid or accrued during the years ended December 31, 2021 and 2020 to our Chief Executive Officer and our executive officers, other than our Chief Executive Officer, who were serving as an executive officer as of December 31, 2021, and whose annual compensation exceeded \$100,000 during such year (collectively the "Named Executive Officers").

**Executive Compensation**

Named Executive Officers	Year	Salary	Bonus	Equity Awards	All Other Compensation	Total
James Sapirstein	2021	\$ 480,000	\$ 186,000	(2) \$ 628,380	(4) \$ -	\$ 1,294,380
President and Chief Executive Officer	2020	\$ 462,500	\$ 159,505	(3) \$ 837,840	(5) \$ -	\$ 1,459,845
James Pennington	2021	\$ 370,000	\$ 49,406	(2) \$ 63,181	(4) \$ -	\$ 482,587
Chief Medical Officer	2020	\$ 260,000	\$ 64,799	(3) \$ 209,460	(5) \$ -	\$ 534,259
Sarah Romano	2021	\$ -	\$ -	(2) \$ -	(4) \$ -	\$ -
Chief Financial Officer	2020	\$ -	\$ -	(3) \$ -	(5) \$ -	\$ -
Daniel Schneiderman (1)	2021	\$ 285,000	\$ 48,592	(2) \$ 199,348	(4) \$ -	\$ 532,940
Chief Financial Officer	2020	\$ 285,000	\$ 71,029	(3) \$ 451,352	(5) \$ -	\$ 807,381

(1) Mr. Schneiderman's employment with us as Chief Financial Officer terminated effective February 28, 2022 due to his resignation.

(2) Represents accrued and unpaid bonuses during 2021, as of December 31, 2021.

(3) Represents accrued and unpaid bonuses during 2020, as of December 31, 2020.

(4) Represents the grant date fair value of restricted stock and stock options issued during the year ended December 31, 2021, calculated in accordance with ASC Topic 718. The assumptions used in the calculation of these amounts are included in Note 14 of the notes to the consolidated financial statements contained in this Annual Report.

(5) Represents the grant date fair value of restricted stock and stock options issued during the year ended December 31, 2020, calculated in accordance with ASC Topic 718. The assumptions used in the calculation of these amounts are included in Note 14 of the notes to the consolidated financial statements contained in the Company's Annual Report, filed with the SEC on March 30, 2020.

## Employment Arrangements and Potential Payments upon Termination or Change of Control

### Current Named Executive Officers

**Sapirstein Employment Agreement.** Effective October 8, 2019, we entered into an employment agreement with Mr. Sapirstein to serve as our President and Chief Executive Officer for a term of three years, subject to further renewal upon agreement of the parties. The employment agreement with Mr. Sapirstein originally provided for a base salary of \$450,000 per year, which was subsequently increased to \$480,000 per year during the year ended December 31, 2020. In addition to the base salary, Mr. Sapirstein is eligible to receive (i) a bonus of up to 40% of his base salary on an annual basis, based on certain milestones that are yet to be determined; (ii) 1% of net fees received by us upon entering into license agreements with any third-party with respect to any product currently in development or upon the sale of all or substantially all of our assets; (iii) a grant of 20,000 restricted shares of our Common Stock which are subject to vesting as follows (a) 10,000 upon the first commercial sale of adrulipase in the U.S., and (b) 10,000 upon our total market capitalization exceeding \$1.0 billion for 20 consecutive trading days; (iv) a grant of 30,000 10-year stock options to purchase shares of our Common Stock which are subject to vesting as follows (a) 5,000 upon us initiating our next Phase 2 clinical trial in the U.S. for adrulipase, (b) 5,000 upon us completing our next or subsequent Phase 2 clinical trial in the U.S. for adrulipase, (c) 10,000 upon us initiating a Phase 2 clinical trial in the U.S. for adrulipase, and (d) 10,000 upon us initiating a Phase 1 clinical trial in the U.S. for any product other than adrulipase. Mr. Sapirstein is entitled to receive 20 days of paid vacation, participate in full employee health benefits and receive reimbursement for all reasonable expenses incurred in connection with his services to us.

In the event that Mr. Sapirstein's employment is terminated by us for Cause, as defined in his employment agreement, or by Mr. Sapirstein voluntarily, then will not be entitled to receive any payments beyond amounts already earned, and any unvested equity awards will terminate. In the event that Mr. Sapirstein's employment is terminated as a result of an Involuntary Termination Other than for Cause, as defined in the Agreement, Mr. Sapirstein will be entitled to receive the following compensation: (i) severance in the form of continuation of his salary (at the Base Salary rate in effect at the time of termination, but prior to any reduction triggering Good Reason) for a period of 12 months following the termination date; (ii) payment of Executive's premiums to cover COBRA for a period of 12 months following the termination date; and (iii) a prorated annual bonus.

**Romano Employment Agreement.** Effective March 1, 2022, we entered into an employment agreement with Ms. Romano to serve as our Chief Financial Officer for a term of three years, subject to further renewal upon agreement of the parties. The employment agreement with Ms. Romano provides for a base salary of \$365,000 per year. In addition to the base salary, Ms. Romano is eligible to receive an annual milestone cash bonus based on certain milestones that will be established by our Board or the Compensation Committee. On March 1, 2022, Ms. Romano was granted stock options to purchase 150,000 shares of Common Stock on March 1, 2022, with an exercise price of \$1.18 per share, which shall vest in over a term of three years pursuant to her employment agreement. Ms. Romano is entitled to receive 20 days of paid vacation, participate in full employee health benefits and receive reimbursement for all reasonable expenses incurred in connection with her service to us. We may terminate Ms. Romano's employment agreement at any time, with or without Cause, as such term is defined in her employment agreement.

In the event that Ms. Romano's employment is terminated by us for Cause, as defined in Ms. Romano's employment agreement, or by Ms. Romano voluntarily, she will not be entitled to receive any payments beyond amounts already earned, and any unvested equity awards will terminate. If we terminate her employment agreement without Cause, not in connection with a Change of Control, as such term is defined in Ms. Romano's employment agreement, she will be entitled to (i) all salary owed through the date of termination; (ii) any unpaid annual milestone bonus; (iii) severance in the form of continuation of her salary for the greater of a period of six months following the termination date or the remaining term of the employment agreement; (iv) payment of premiums to cover COBRA for a period of six months following the termination date; (v) a prorated annual bonus equal to the target annual milestone bonus, if any, for the year of termination multiplied by the formula set forth in the agreement. If we terminate Ms. Romano's employment agreement without Cause, in connection with a Change of Control, she will be entitled to the above and immediate accelerated vesting of any unvested options or other unvested awards.

**Pennington Employment Agreement.** Effective May 28, 2018, we entered into an employment agreement with Mr. Pennington to serve as our Chief Medical Officer. The employment agreement with Dr. Pennington provides for a base annual salary of \$250,000 which was subsequently increased to \$425,000 per year during the year ended December 31, 2021. In addition to his salary, Dr. Pennington is eligible to receive an annual milestone bonus, awarded at the sole discretion of the Board based on his attainment of certain financial, clinical development, and/or business milestones established annually by the Board or Compensation Committee. The employment agreement is terminable by either party at any time. In the event of termination by us other than for cause, Dr. Pennington is entitled to three months' severance payable over such period. In the event of termination by us other than for cause in connection with a Change of Control, Dr. Pennington will receive six months' severance payable over such period.

**Outstanding Equity Incentive Awards at Fiscal Year-End**

The following table sets forth information regarding unexercised options, stock that has not vested and equity incentive awards held by each of the Named Executive Officers outstanding as of December 31, 2021 and 2020:

Name	Grant Date	Number of Securities underlying unexercised options (#) exercisable	Equity incentive plan awards: Number of underlying unexercised unearned options (#)		Option exercise price (\$)	Option expiration date	Number of Shares or units of stock that have not vested (#)	Market value of shares or units of stock that have not vested (\$)	Equity incentive plan awards: Number of Unearned shares, units or other rights that have not vested (#)	Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested (\$)
<i>Named Executive Officers (1)</i>										
James Sapirstein	10/8/2019	20,000	10,000	(2)	\$ 5.60	10/7/2029	-	\$ -	-	\$ -
	10/8/2019	-	-		-	10/7/2029	-	\$ -	20,000	(3) \$ 112,000
	7/16/2020	24,166	5,834	(4)	\$ 8.50	7/15/2030	-	\$ -	-	\$ -
	6/30/2021	20,000	70,000	(4)	\$ 8.50	7/15/2030	-	\$ -	-	\$ -
James Pennington	6/28/2018	7,500	-		\$ 30.40	6/27/2023	-	\$ -	-	\$ -
	6/13/2019	11,000	-		\$ 17.50	6/12/2024	-	\$ -	-	\$ -
	7/16/2020	14,583	15,417	(5)	\$ 8.50	7/15/2030	-	\$ -	-	\$ -
	7/9/2021	1,584	8,416	(6)	\$ 7.50	7/8/2030	-	\$ -	-	\$ -
Daniel Schneiderman	1/2/2020	20,000	10,000	(7)	\$ 10.30	1/1/2030	-	\$ -	-	\$ -
	6/30/2021	12,152	12,848	(8)	\$ 8.50	7/15/2030	-	\$ -	-	\$ -
	6/30/2021	2,332	1,168	(7)	\$ 8.50	7/15/2030	-	\$ -	-	\$ -

(1) Sarah Romano was appointed as Chief Financial Officer subsequent to the year ended December 31, 2021, and therefore is excluded from the table.

- (2) Represents stock options issued to Mr. Sapirstein on October 8, 2019 under the terms of his employment agreement, which options will vest as follows: (i) as to 10,000 shares upon our initiating a Phase 3 clinical trial in the U.S. for adrolipase.
- (3) Represents the restricted stock unit ("RSU") award issued to Mr. Sapirstein on October 8, 2019 under the terms of his employment agreement, which RSU will vest as follows: (i) as to 10,000 shares upon the first commercial sale in the U.S. of adrolipase, and (ii) as to 10,000 shares upon our total market capitalization exceeding \$1.0 billion for 20 consecutive trading days.
- (4) On June 30, 2021, the Board rescinded and cancelled certain stock option awards previously made under the 2014 Plan (the "Prior Sapirstein Awards") to Mr. Sapirstein and issued new stock options awards (the "New Sapirstein Awards") under the 2020 Plan in an equivalent amount and with equivalent exercise price, vesting and expiration terms to the Prior Sapirstein Awards. The terms of the New Sapirstein Awards covering 90,000 shares of the Common Stock at an exercise price of \$8.50 per share comprised of (i) stock options to purchase 30,000 shares of Common Stock that vest over a term of 18 months in 18 equal monthly installments starting with the first monthly installment on February 16, 2022, (ii) stock options to purchase 20,000 shares of Common Stock that vested immediately upon the grant of such stock options, and (iii) stock options to purchase 40,000 shares of Common Stock subject to milestone-based vesting based upon the achievement of certain strategic milestones specified by the Board.

- (5) Represents stock options issued to Mr. Pennington on July 16, 2020, which options will vest over a term of three years, in 36 equal monthly installments on each monthly anniversary of July 16, 2020.
- (6) Represents stock options issued to Mr. Pennington on July 9, 2021, which options will vest over a term of three years, in 36 equal monthly installments on each monthly anniversary of July 9, 2021.
- (7) During the year ended December 31, 2020, the Board approved an amended and restated option grant to Mr. Schneiderman, amending and restating a grant previously made on January 2, 2020, to reduce the amount of shares issuable upon exercise of such option to be the maximum number of shares Mr. Schneiderman was eligible to receive under the 2014 Plan on the original grant date, or 30,000 shares (on a post-split basis), due to the 2014 Plan provisions relating to the Section 162(m) limitations. The Board also approved the issuance of a replacement option covering the balance of shares intended to be issued at that time, or 3,500 shares. The original stock option has an exercise price of \$10.30, the closing sale price of Common Stock on January 2, 2020, which was the date of its original grant, and the replacement stock option has an exercise price of \$8.50, the closing sale price of the Common Stock on its date of grant. Both the original stock option and the replacement stock option vest over a term of three years, in 36 equal monthly installments on each monthly anniversary of January 2, 2020.

On June 30, 2021, the Board rescinded and cancelled certain stock option awards previously made under the 2014 Plan (the "*Prior Schneiderman Awards*") to Mr. Schneiderman and issued new stock options awards (the "*New Schneiderman Awards*") under the 2020 Plan in an equivalent amount and with equivalent exercise price, vesting and expiration terms to the *Prior Schneiderman Awards*. The terms of the *New Schneiderman Awards* covering 28,500 shares of the Common Stock at an exercise price of \$8.50 per share comprised of (i) stock options to purchase 25,000 shares of Common Stock, of which options to purchase 7,986 shares of Common Stock vested immediately upon the grant of such options and the remaining options to purchase 17,014 shares of Common Stock will vest over a term of 2 years and 1 month in 25 equal monthly installments, and (ii) options to purchase 3,500 shares of Common Stock, of which options to purchase 1,750 shares of Common Stock vested immediately upon the grant of such options and the remaining options to purchase 1,750 shares of Common Stock vest over a term of 19 months in 19 equal monthly installments.

- (8) Represents stock options issued to Mr. Schneiderman on July 16, 2021, which options will vest over a term of three years, in 36 equal monthly installments on each monthly anniversary of July 16, 2021.

#### **Non-Executive Director Compensation**

On October 1, 2020, our Board adopted a Non-Executive Director Compensation Policy under which each of our non-executive directors is entitled to receive the following cash compensation for their service on the Board (paid quarterly): (i) an annual retainer of \$35,000; (ii) the chairman of the Board is entitled to receive an additional annual retainer in the amount of \$20,000, (iii) the chair of the Audit Committee is entitled to receive an additional annual retainer in the amount of \$10,000, (iv) each non-chairperson member of the Audit Committee is entitled to receive an additional annual retainer in the amount of \$5,000, (v) the chair of the Compensation Committee is entitled to receive an additional annual retainer in the amount of \$7,500, (vi) each non-chairperson member of the Compensation Committee is entitled to receive an additional annual retainer in the amount of \$3,500, (vii) the chair of the Corporate Governance and Nominating Committee is entitled to receive an additional annual retainer in the amount of \$5,000, and (viii) each non-chairperson member of the Corporate Governance and Nominating Committee is entitled to receive an additional annual retainer in the amount of \$2,500. Additionally, under this policy, each of our non-executive directors is entitled to receive an annual grant of 4,123 stock options for their service on the Board during 2021, which vest in equal quarterly installments.



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Effective September 1, 2021, our Board adopted an updated Non-Executive Director Compensation Policy under which each of our non-executive directors is entitled to receive the following cash compensation for their service on the Board (paid quarterly): (i) an annual retainer of \$60,000; (ii) the chair of the Audit Committee is entitled to receive an additional annual retainer in the amount of \$12,500, (iii) each non-chairperson member of the Audit Committee is entitled to receive an additional annual retainer in the amount of \$5,000, (iv) the chair of the Compensation Committee is entitled to receive an additional annual retainer in the amount of \$10,000, (v) each non-chairperson member of the Compensation Committee is entitled to receive an additional annual retainer in the amount of \$5,000, (vi) the chair of the Corporate Governance and Nominating Committee is entitled to receive an additional annual retainer in the amount of \$10,000, and (viii) each non-chairperson member of the Corporate Governance and Nominating Committee is entitled to receive an additional annual retainer in the amount of \$5,000. Additionally, under this policy, each of our non-executive directors is entitled to receive an annual grant of 34,602 stock options for their service on the Board to purchase \$50,000 of shares of Common Stock at a strike price equal to the closing price of the Common Stock on December 31, 2021, or \$1.445 per share, which vest in equal quarterly installments.

Our Board will review the Non-Executive Director Compensation Policy on an annual basis prior to September 1 of each year.

The following table provides information regarding compensation paid to non-employee directors for the year ended December 31, 2021. Mr. Sapirstein did not receive compensation for his service on the Board as employee director for the year ended December 31, 2021. Information regarding executive compensation paid to Mr. Sapirstein during 2021 is reflected in the Summary Compensation table under "Executive Compensation."

Non-Executive Directors	Fees Earned or Paid in Cash	Stock Award	Option Award <sup>3</sup>	All Other Compensation	Total
Edward J. Bowkowski	\$ 68,125	\$ -	\$ 30,296	\$ -	\$ 98,421
Charles J. Casamento	\$ 54,417	\$ -	\$ 30,296	\$ -	\$ 84,713
Alastair Riddell	\$ 53,167	\$ -	\$ 30,296	\$ -	\$ 83,463
Vern L. Schramm (1)	\$ 54,583	\$ -	\$ 30,296	\$ -	\$ 84,879
Gregory Oakes	\$ 55,833	\$ -	\$ 30,296	\$ -	\$ 86,129
Terry Coelho (2)	\$ 27,626	\$ -	\$ 1,303	\$ -	\$ 28,929

(1) Mr. Schramm resigned from the board effective December 31, 2021.

(2) Ms. Coelho was appointed to the board effective August 11, 2021.

(3) Represents amounts of accrued and unpaid cash compensation for board services through December 31, 2021.

(4) Represents the aggregate grant date fair value of 4,123 stock options issued to each of Messrs. Borkowski, Casamento, Riddell, Oakes and Schramm on January 4, 2021, and 1,031 stock options issued to Ms. Coelho on September 9, 2021, our non-employee directors, calculated in accordance with ASC Topic 718.

**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

**Securities Authorized for Issuance Under Equity Compensation Plans**

The following table provides information as of December 31, 2021 regarding equity compensation plans approved by our security holders and equity compensation plans that have not been approved by our security holders:

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans reflected in column (a) (c)
Equity compensation plans approved by security holders (1) (2)	1,271,550	11.55	823,754
Equity compensation plans not approved by security holders	-	-	-
<b>Total</b>	<b>1,271,550</b>	<b>11.55</b>	<b>823,754</b>

(1) Excludes 38,700 shares of Common Stock reserved under the 2014 Plan as of December 31, 2021, subject to the issuance of restricted stock and RSUs.

(2) Represents outstanding stock options granted to our current or former employees, directors and consultants pursuant to the 2014 Omnibus Equity Incentive Plan (the "2014 Plan" and 2020 Omnibus Equity Incentive Plan (the "2020 Plan").

**Summary of Amended and Restated 2014 Omnibus Equity Incentive Plan**

The Board and stockholders adopted and approved the 2014 Plan, which took effect on May 12, 2014, and the 2020 Plan, which took effect on September 11, 2020. From the effective date of the 2020 Plan, no new awards have been or will be made under the 2014 Plan.

**Stock Options.** The 2014 Plan permitted the grant of "incentive stock options" ("ISOs"), which are intended to meet the requirements for special federal income tax treatment under the Code, and "nonqualified stock options" ("NQSOs") that do not meet the requirements of Section 422 of the Code. No stock option may be transferred other than by will or by the laws of descent and distribution, and during a recipient's lifetime a stock option may be exercised only by the recipient. However, the Compensation Committee may permit the holder of a stock option, SAR or other award to transfer the stock option, right or other award to immediate family members or a family trust for estate planning purposes. The Compensation Committee will determine the extent to which a holder of a stock option may exercise the option following termination of service with us.

**Restricted Stock Awards and Restricted Stock Unit Awards.** A restricted stock award is a grant or sale of Common Stock to the participant, subject to our right to repurchase all or part of the shares at their purchase price (or to require forfeiture of such shares if issued to the participant at no cost) in the event that conditions specified by the Compensation Committee in the award are not satisfied prior to the end of the time period during which the shares subject to the award may be repurchased by or forfeited to us. A restricted stock unit entitles the participant to receive a cash payment equal to the fair market value of a share of Common Stock for each restricted stock unit subject to such restricted stock unit award, if the participant satisfies the applicable vesting requirement. The Compensation Committee will determine the restrictions and conditions applicable to each award of restricted stock award or restricted stock unit award, which may include performance-based conditions.

**Unrestricted Stock Awards.** An unrestricted stock award is a grant or sale of shares of our Common Stock to the participant that is not subject to transfer, forfeiture or other restrictions, in consideration for past services rendered to us or an affiliate or for other valid consideration.

**Change-in-Control Provisions.** In connection with the grant of an award, the Compensation Committee may provide that, in the event of a change in control, such award will become fully vested and immediately exercisable.

#### **Potential Limitation on Company Deductions**

Section 162(m) of the Code generally disallows a tax deduction for compensation in excess of \$1 million paid in a taxable year by a publicly held corporation to its chief executive officer and certain other "covered employees." Effective for taxable years beginning prior to January 1, 2018, an exception to this deduction limit applied to "performance-based compensation" that satisfied certain criteria. Under regulations issued by the Internal Revenue Service under Section 162(m), stock options and stock appreciation rights were treated as performance-based compensation if, among other things, an annual limit was placed on issuing such awards to a single individual. In order to comply with the foregoing exception to the \$1 million deduction limit under Section 162(m), the 2014 Plan previously contained an annual limit on issuing awards of stock options and stock appreciation rights to a single individual, which was intended to allow us to deduct such awards granted as performance-based compensation. Pursuant to the Tax Cut and Jobs Act of 2017, however, the exception for performance-based compensation under Section 162(m) of the Code was repealed. As a result, the annual limit in the 2014 Plan was no longer effective to allow us to claim this deduction. Accordingly, effective July 16, 2020, our Board approved an amendment to the 2014 Plan that removed this annual limit.

#### **Summary of the 2020 Omnibus Equity Incentive Plan**

The Board and stockholders have adopted and approved the 2020 Plan, which is a comprehensive incentive compensation plan under which we can grant equity-based and other incentive awards to our officers, employees, directors, consultants and advisers. The purpose of the 2020 Plan is to help us attract, motivate and retain such persons with awards under the 2020 Plan and thereby enhance stockholder value.

**Administration.** The 2020 Plan is administered by the Compensation Committee of the Board, which consists of three members of the Board, each of whom is a "non-employee director" within the meaning of Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended (the "*Exchange Act*"). The Compensation Committee may grant stock options, stock appreciation rights ("SARs"), performance stock awards, performance unit awards, dividend equivalent right awards, restricted stock awards, restricted stock unit awards, unrestricted stock awards, incentive bonus awards and other cash-based awards and other stock-based awards to our non-employee directors, officers, employees and nonemployee consultants or our affiliates. Among other things, the Compensation Committee has complete discretion, subject to the express limits of the 2020 Plan, to determine the directors, employees and individual consultants to be granted an award, the type of award to be granted, the terms and conditions of the award, the form of payment to be made and/or the number of shares of Common Stock subject to each award, the exercise price of each option and base price of each SAR, the term of each award, the vesting schedule for an award, whether to accelerate vesting, the value of the Common Stock underlying the award, and the required withholding, if any. Except as prohibited by applicable law or stock exchange rules, the Compensation Committee may delegate administrative functions under the 2020 Plan and may authorize a Reporting Person (as defined in the Exchange Act) to make certain awards under the 2020 Plan. Subject to the terms of the Plan, the Compensation Committee shall have the authority to amend the terms of an award in any manner that is not inconsistent with the Plan (including to extend the post-termination exercisability period of options and SARs), provided that no such action (except an action relating to a change of control) shall materially and adversely impair the rights of an award recipient with respect to such an outstanding award without the consent of the award recipient. The Compensation Committee is also authorized to construe the award agreements, and may prescribe rules relating to the 2020 Plan.

**Eligibility.** Employees, directors and individual consultants of the Company or an affiliate as well as prospective employees, directors and individual consultants of the Company or an affiliate are eligible to participate in the 2020 Plan. The 2020 Plan allows for grants to employees, directors and individual consultants of the Company or an affiliate who are non-US persons. Currently, we have nine employees (including one executive director), five non-executive directors and approximately ten non-employee consultants.

**Shares Subject to the 2020 Plan.** The maximum aggregate number of shares of Common Stock that may be issued under the 2020 Plan shall be 1,000,000 shares. The 2020 Plan allows for 1,500,000 shares to be issued as ISOs. In addition, the 2020 Plan contains an "evergreen provision" providing for an annual increase in the number of shares of our Common Stock available for issuance under the 2020 Plan on January 1 of each year for a period of ten years, commencing on January 1, 2021 and ending on (and including) January 1, 2030, in an amount equal to the lesser of (i) ten percent of the total number of shares of Common Stock outstanding on December 31st of the preceding calendar year or (ii) such number of shares determined by the Board.

If any award expires, is cancelled, or terminates unexercised or is forfeited, the number of shares subject thereto is again available for grant under the 2020 Plan. The maximum number of shares of Common Stock that may be subject to awards to outside directors, in the aggregate, during any calendar year is 250,000.

The number of shares authorized for issuance under the 2020 Plan and each of the preceding share limitations are subject to customary adjustments for stock splits, stock dividends, recapitalization, reorganization, merger, combination, exchange or similar transactions.

**Stock Options.** The 2020 Plan provides for either ISOs, which are intended to meet the requirements for special federal income tax treatment under the Code, or NQSOs that do not meet the requirements of Section 422 of the Code. Stock options may be granted on such terms and conditions as the Compensation Committee may determine; *provided, however*, that the per share exercise price under a stock option may not be less than the fair market value of a share of Common Stock on the date of grant and the term of the stock option may not exceed 10 years (110% of such value and five years in the case of an ISO granted to an employee who owns (or is deemed to own) more than 10% of the total combined voting power of all classes of our capital stock or our parent or subsidiary). ISOs may only be granted to employees. In addition, the aggregate fair market value of Common Stock covered by one or more ISOs (determined at the time of grant), which are exercisable for the first time by an employee during any calendar year may not exceed \$100,000. Any excess is treated as a NQSO. Stock options granted under the 2020 Plan will be exercisable at such time or times as the Compensation Committee prescribes at the time of grant and recipients will be permitted to pay the exercise price as set forth by the Compensation Committee in the applicable option agreement. No stock option may be transferred other than by will or by the laws of descent and distribution, and during a recipient's lifetime a stock option may be exercised only by the recipient. However, the Compensation Committee may permit the holder of a stock option, SAR or other award to transfer the stock option, right or other award to immediate family members or a family trust for estate planning purposes. The Compensation Committee will determine the extent to which a holder of a stock option may exercise the option following termination of service with us.

**Stock Appreciation Rights.** A SAR entitles the participant, upon exercise, to receive an amount, in cash or stock or a combination thereof, equal to the increase in the fair market value of the underlying Common Stock between the date of grant and the date of exercise. SARs may be granted in tandem with, or independently of, stock options granted under the 2020 Plan. A SAR granted in tandem with a stock option (i) is exercisable only at such times, and to the extent, that the related stock option is exercisable in accordance with the procedure for exercise of the related stock option; (ii) terminates upon termination or exercise of the related stock option (likewise, the Common Stock option granted in tandem with a SAR terminates upon exercise of the SAR); (iii) is transferable only with the related stock option; and (iv) if the related stock option is an ISO, may be exercised only when the value of the stock subject to the stock option exceeds the exercise price of the stock option. A SAR that is not granted in tandem with a stock option is exercisable at such times as the Compensation Committee may specify. The Compensation Committee will determine the other terms applicable to SARs. The exercise price per share of a SAR will be determined by the Compensation Committee, but will not be less than 100% of the fair market value of a share of our Common Stock on the date of grant, as determined by the Compensation Committee. The maximum term of any SAR granted under the 2020 Plan is ten years from the date of grant. Generally, each SAR will entitle a participant upon exercise to an amount equal to: (i) the excess of the fair market value on the exercise date of one share of our Common Stock over the exercise price, *multiplied by* (ii) the number of shares of Common Stock covered by the SAR. Payment may be made in shares of our Common Stock, in cash, or partly in Common Stock and partly in cash, all as determined by the Compensation Committee.

**Performance Shares and Performance Unit Awards.** Performance share and performance unit awards entitle the participant to receive cash or shares of Common Stock upon the attainment of specified performance goals. In the case of performance units, the right to acquire the units is denominated in cash values. The Compensation Committee will determine the restrictions and conditions applicable to each award of performance shares and performance units.

**Dividend Equivalent Right Awards.** A dividend equivalent right award entitles the participant to receive bookkeeping credits, cash payments and/or Common Stock distributions equal in amount to the distributions that would have been made to the participant had the participant held a specified number of shares of Common Stock during the period the participant held the dividend equivalent right. A dividend equivalent right may be awarded as a component of another award under the 2020 Plan, where, if so awarded, such dividend equivalent right will expire or be forfeited by the participant under the same conditions as under such other award.

**Restricted Stock Awards and Restricted Stock Unit Awards.** A restricted stock award is a grant or sale of Common Stock to the participant, subject to our right to repurchase all or part of the shares at their purchase price (or to require forfeiture of such shares if issued to the participant at no cost) in the event that conditions specified by the Compensation Committee in the award are not satisfied prior to the end of the time period during which the shares subject to the award may be repurchased by or forfeited to us. Restricted stock units entitle the participant to receive a cash payment equal to the fair market value of a share of Common Stock for each restricted stock unit subject to such restricted stock unit award, if the participant satisfies the applicable vesting requirement. The Compensation Committee will determine the restrictions and conditions applicable to each award of restricted stock award or restricted stock unit award, which may include performance-based conditions.

**Unrestricted Stock Awards.** An unrestricted stock award is a grant or sale of shares of our Common Stock to the participant that is not subject to transfer, forfeiture or other restrictions, in consideration for past services rendered to us or an affiliate or for other valid consideration.

**Other Cash-Based Awards and Other Stock-Based Awards.** The Compensation Committee may award other types of cash-based or equity-based awards under the 2020 Plan, including the grant or offer for sale of shares of unrestricted shares and the right to receive one or more cash payments subject to satisfaction of such conditions as the Compensation Committee may impose.

**Incentive Bonus Awards.** Incentive bonus awards may be awarded to the participant based upon the attainment of specified levels of our performance as measured by pre-established, objective performance criteria determined at the discretion of the Compensation Committee.

**Change-of-Control Provisions.** The Compensation Committee may, at the time of the grant of an award, provide for the effect of a change of control (as defined in the 2020 Plan) on an award, including (i) accelerating or extending the time periods for exercising, vesting in, or realizing gain from any award, (ii) eliminating or modifying the performance or other conditions of an award, or (iii) providing for the cash settlement of an award for an equivalent cash value, as determined by the Compensation Committee. The Compensation Committee may, in its discretion and without the need for the consent of any recipient of an award, also take one or more of the following actions contingent upon the occurrence of a change of control: (a) cause any or all outstanding stock options and SARs to become immediately exercisable, in whole or in part; (b) cause any other awards to become non-forfeitable, in whole or in part; (c) cancel any stock option or SAR in exchange for a substitute option; (d) cancel any award of restricted stock, restricted stock units, performance shares or performance units in exchange for a similar award of the capital stock of any successor corporation; (e) redeem any restricted stock, restricted stock unit, performance share or performance unit for cash and/or other substitute consideration with a value equal to the fair market value of an unrestricted share of our Common Stock on the date of the change of control; (f) cancel any stock option or SAR in exchange for cash and/or other substitute consideration based on the value of our Common Stock on the date of the change in control, and cancel any stock option or SAR without any payment if its exercise price exceeds the value of our Common Stock on the date of the change of control; or (g) make such other modifications, adjustments or amendments to outstanding awards as the Compensation Committee deems necessary or appropriate.

**Amendment and Termination.** The Compensation Committee may adopt, amend and rescind rules relating to the administration of the 2020 Plan, and amend, suspend or terminate the 2020 Plan, provided, that (a) to the extent necessary and desirable to comply with any applicable law, regulation, or stock exchange rule, we shall obtain stockholder approval of any 2020 Plan amendment in such a manner and to such a degree as required, and (b) stockholder approval is required for any amendment to the 2020 Plan that (i) increases the number of shares available for issuance under the 2020 Plan, or (ii) changes the persons or class of persons eligible to receive awards.

**Security Ownership of Certain Beneficial Owners and Management**

The following table sets forth information regarding shares of our Common Stock beneficially owned as of March 28, 2022 by:

- each of our officers and directors;
- all officers and directors as a group; and
- each person known by us to beneficially own five percent or more of the outstanding shares of our Common Stock. Percentage of ownership is calculated based on 16,700,640 shares of Common Stock outstanding as of March 28, 2022.

Name and Address of Beneficial Owner (1)	Number of Shares (2)	Percent Ownership of Class (3)
<i>Current Named Executive Officers and Directors</i>		
James Sapirstein, President, Chief Executive Officer and Chairman (4)	192,217	1.1%
Sarah Romano, Chief Financial Officer (5)	-	*
James E. Pennington, Chief Scientific Officer (6)	44,666	*
Edward J. Borkowski, Director (7)	421,776	2.5%
Charles J. Casamento, Director (8)	26,822	*
Alastair Riddell, Director (9)	31,327	*
Terry Coelho, Director (10)	1,031	*
Gregory Oakes, Director (11)	10,123	*
All directors and executive officer as a group (8 persons)	819,734	4.7%

(1) Unless otherwise indicated, the address of such individual is c/o First Wave BioPharma, Inc., 777 Yamato Rd., Suite 502, Boca Raton, FL 33431.

(2) Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. All entries exclude beneficial ownership of shares issuable pursuant to warrants, options or other derivative securities that have not vested or that are not otherwise exercisable as of the date hereof or which will not become vested or exercisable within 60 days.

(3) Percentages are rounded to nearest tenth of a percent. Percentages are based on 16,700,640 shares of Common Stock outstanding. Warrants, options or other derivative securities that are presently exercisable or exercisable within 60 days are deemed to be beneficially owned by the person holding such securities for the purpose of computing the percentage ownership of that person, but are not treated as outstanding for the purpose of computing the percentage of any other person.

(4) Includes (i) 111,250 shares of Common Stock issuable upon exercise of vested options, (ii) 15,032 shares of Common Stock issuable upon conversion of approximately 13.53 shares of Series B Preferred Stock, which includes accrued and unpaid dividends through March 28, 2022, and (iii) 64,935 shares of Common Stock issuable upon exercise of warrants. Excludes (i) 188,750 shares of Common Stock issuable upon exercise of unvested options, and (ii) 20,000 shares of Common Stock issuable upon unvested Restricted Stock Units (RSUs). Pursuant to the Series B Exchange Right, Mr. Sapirstein has the right to exchange the stated value, plus accrued and unpaid dividends, of the shares of Series B Preferred Stock beneficially owned by him for shares of Series C Preferred Stock and Investor Warrants, or shares of Common Stock on a dollar-for-dollar basis.

- (5) Excludes 150,000 shares of Common Stock issuable upon exercise of unvested options.
- (6) Includes 44,666 shares of Common Stock issuable upon exercise of vested options. Excludes 13,834 shares of Common Stock issuable upon exercise of unvested options.
- (7) Includes (i) 40,977 shares of Common Stock; (ii) 307,923 shares of Common Stock issuable upon the exercise of warrants; (iii) 18,123 shares of Common Stock issuable upon exercise of vested options; (iv) 53,385 shares of Common Stock issuable upon conversion of approximately 48,043 shares of Series B Preferred Stock, which includes accrued and unpaid dividends through March 28, 2022, and (v) 1,368 shares of Common Stock held by Mr. Borkowski's spouse. Excludes 4,500 unvested and unissued restricted shares of Common Stock. Pursuant to the Series B Exchange Right, Mr. Borkowski has the right to exchange the stated value, plus accrued and unpaid dividends, of the shares of Series B Preferred Stock beneficially owned by him for shares of Series C Preferred Stock and Investor Warrants, or shares of Common Stock on a dollar-for-dollar basis.
- (8) Includes (i) 10,799 shares of Common Stock; (ii) 15,123 shares of Common Stock issuable upon exercise of vested options; and (iii) 900 shares of Common Stock held by La Jolla Lenox Trust, a family trust of which the Trustee is someone other than Mr. Casamento. Mr. Casamento and members of his immediate family are the sole beneficiaries of the trust.
- (9) Includes (i) 13,204 shares of Common Stock and (ii) 18,123 shares of Common Stock issuable upon exercise of vested options. Excludes (i) 3,000 unvested restricted shares of Common Stock.
- (10) Includes 1,031 shares of Common Stock issuable upon exercise of vested options.
- (11) Includes 10,123 shares of Common Stock issuable upon exercise of vested options.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

***Promissory Notes, Series B Private Placement and Series B Exchange***

On December 20, 2019, Edward J. Borkowski, a Director, purchased a Promissory Note (the "*Borkowski Promissory Note*") for an original principal amount of \$100,000, together with related warrants exercisable for 51,547 shares of Common Stock at an exercise price of \$10.70, pursuant to a Note Purchase Agreement by and between us and certain accredited investors. The Borkowski Promissory Note accrued interest at a rate of 9% per annum and was convertible at the option of the holder into shares of Common Stock at a price of \$9.70 per share. On July 16, 2020, in connection with the Series B Private Placement and the Series B Exchange, Mr. Borkowski purchased \$250,000 worth of Series B Preferred Stock and related Series B Warrants for cash, and Mr. Borkowski also exchanged the balance of his outstanding Borkowski Promissory Note of \$105,128 (including outstanding principal amount and accrued and unpaid interest thereon) for approximately 13.65 shares of Series B Preferred Stock convertible into 13,653 shares of Common Stock, Series B Warrants for 6,826 shares of Common Stock and Exchange Warrants for 2,577 shares of Common Stock.

On July 16, 2020, in connection with the Series B Private Placement and the Exchange, James Sapirstein, President, Chief Executive Officer and Director purchased \$100,000 worth of Series B Preferred Stock and related Series B Warrants for cash. Mr. Sapirstein received approximately 12.99 shares of Series B Preferred Stock convertible into 12,987 shares of Common Stock and Series B Warrants for 6,493 shares of Common Stock.

As of February 7, 2022, Messrs. Sapirstein and Borkowski have entered into waiver agreements with the Company pursuant to which they have agreed to waive the exchange rights related to their Series B Convertible Preferred Stock holdings through December 31, 2022.

#### Policy and Procedures Governing Related Party Transactions

The Board is committed to upholding the highest legal and ethical conduct in fulfilling its responsibilities and recognizes that related party transactions can present a heightened risk of potential or actual conflicts of interest.

The SEC rules define a related party transaction to include any transaction, arrangement or relationship which: (i) we are a participant; (ii) the amount involved exceeds \$120,000; and (iii) executive officer, director or director nominee, or any person who is known to be the beneficial owner of more than 5% of our Common Stock, or any person who is an immediate family member of an executive officer, director or director nominee or beneficial owner of more than 5% of our Common Stock had or will have a direct or indirect material interest.

Although we do not maintain a formal written procedure for the review and approval of transactions with such related persons, it is our policy for the disinterested members of our Board to review all related party transactions on a case-by-case basis. To receive approval, a related-party transaction must have a legitimate business purpose for us and be on terms that are fair and reasonable to us and our stockholders and as favorable to us and our stockholders as would be available from non-related entities in comparable transactions.

All related party transactions must be disclosed in our applicable filings with the SEC as required under SEC rules.

#### Director Independence

The Board has determined that all of its members, other than Mr. Sapirstein, our President, Chief Executive Officer and Chair of our Board are "independent" within the meaning of Nasdaq Listing Rule 5605(a)(2) under the rules of the Nasdaq Stock Market ("*Nasdaq*"), and the Securities and Exchange Commission ("*SEC*") rules regarding independence.

#### ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Set forth below are fees billed or expected to be billed to us by our independent registered public accounting firm Mazars USA LLP for the years ended December 31, 2021 and 2020 for the professional services performed for us.

#### Audit Fees

The following table presents fees for professional services billed by Mazars USA LLP for the fiscal years ended December 31, 2021 and 2020.

	For the years ended	
	December 31,	
	2021	2020
Audit fees (1)	\$ 117,640	\$ 165,766
Audit-related fees (2)	114,315	34,700
Tax fees (3)	13,090	27,055
All other fees (4)	25,880	-
Total	\$ 270,925	\$ 227,521



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- (1) Professional services rendered by the Mazars USA LLP for the audit of our annual financial statements and review of financial statements included in our Form 10-Q's.
- (2) The aggregate fees billed for assurance and related services by Mazars USA LLP that are reasonably related to the performance of the audit or review of our financial statements and are not reported under Note 1 above, principally related to registration statement filings.
- (3) The aggregate fees billed for professional services rendered by Mazars USA LLP for tax compliance, tax advice, and tax planning.
- (4) The aggregate fees billed for products and services provided by Mazars USA LLP other than the services reported in Notes 1 through 3 above.

**Audit Committee Pre-Approval Policies and Procedures**

The Audit Committee has the sole authority for the appointment, compensation and oversight of the work of our independent auditors. The Audit Committee has established a policy regarding pre-approval of all auditing services and the terms thereof and non-audit services (other than non-audit services prohibited under Section 10A(g) of the Exchange Act or the applicable rules of the SEC or the Public Company Accounting Oversight Board) to be provided to us by the independent auditor. However, the pre-approval requirement may be waived with respect to the provision of non-audit services for us if the "de minimus" provisions of Section 10A(i)(1)(B) of the Exchange Act are satisfied.

The Audit Committee has considered whether the provision of audit-related fees, tax fees, and all other fees as described above is compatible with maintaining Mazars USA LLP's independence and has determined that such services for fiscal year 2020 were compatible. All such services were approved by the Audit Committee pursuant to Rule 2-01 of Regulation S-X under the Exchange Act to the extent that rule was applicable.

The Audit Committee is responsible for reviewing and discussing the audited financial statements with management, discussing with the independent registered public accountants the matters required in Auditing Standards No. 16, receiving written disclosures from the independent registered public accountants required by the applicable requirements of the Public Company Accounting Oversight Board regarding the independent registered public accountants' communications with the Audit Committee concerning independence and discussing with the independent registered public accountants their independence, and recommending to our board of directors that the audited financial statements be included in our annual report on Form 10-K.

**PART IV**

**ITEM 15. EXHIBITS**

<b>Exhibit No.</b>	<b>Description</b>
<a href="#">2.1#</a>	Agreement and Plan of Merger dated September 13, 2021, by and among the Company, Alpha Merger Sub, Inc., and Fortis Advisors LLC, as shareholder representative (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed with the SEC on September 13, 2021). ##
<a href="#">3.1*</a>	Amended and Restated Certificate of Incorporation of the Registrant, as amended.
<a href="#">3.2</a>	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 of the Company's Current Report on Form 8-K filed with the SEC on August 5, 2020).
<a href="#">4.1</a>	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Company's Registration Statement on Form S-1, filed with the SEC on July 29, 2016).
<a href="#">4.2</a>	Form of Investor Warrant (incorporated by reference to Exhibit 4.2 of the Company's Registration Statement on Form S-1 filed with the SEC on July 13, 2016).
<a href="#">4.3</a>	Form of Underwriter Warrant (incorporated by reference to Exhibit 4.3 to the Company's Registration Statement on Form S-1, filed with the SEC on July 29, 2016).
<a href="#">4.4</a>	Form of Series A Warrant, dated April 11, 2017 between the Company and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.3 filed with the Company's Current Report on Form 8-K filed with the SEC on April 12, 2017).
<a href="#">4.5</a>	Form of Series A Warrant, dated June 5, 2017 (incorporated by reference to Exhibit 10.3 filed with the Company's Current Report on Form 8-K filed with the SEC on June 9, 2017).
<a href="#">4.6</a>	Form of Series A-1 Warrant, dated June 5, 2017 (incorporated by reference to Exhibit 10.4 filed with the Company's Current Report on Form 8-K filed with the SEC on June 9, 2017).
<a href="#">4.7</a>	Form of Underwriter Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on May 4, 2018).
<a href="#">4.8</a>	Form of Selling Agent Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on April 3, 2019).
<a href="#">4.9</a>	Form of Selling Agent Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on May 14, 2019).
<a href="#">4.10</a>	Form of Wainwright Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on July 22, 2019).
<a href="#">4.11</a>	Form of Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on July 20, 2020).
<a href="#">4.12</a>	Form of Warrant for Convertible Notes Offering (incorporated by reference to Exhibit 4.2 of the Company's Registration Statement on Form S-3 filed with the SEC on July 27, 2020).
<a href="#">4.13</a>	Form of Pre-funded Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on January 4, 2021).
<a href="#">4.14</a>	Form of Private Placement Warrant (incorporated by reference to Exhibit 4.2 of the Company's Current Report on Form 8-K filed with the SEC on January 4, 2021).
<a href="#">4.15</a>	Form of Wainwright Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on January 8, 2021).
<a href="#">4.16</a>	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on March 10, 2021).
<a href="#">4.17</a>	Form of Warrant (incorporated by reference to Exhibit 4.2 of the Company's Current Report on Form 8-K filed with the SEC on March 10, 2021).
<a href="#">4.18</a>	Form of Wainwright Warrant (incorporated by reference to Exhibit 4.3 of the Company's Current Report on Form 8-K filed with the SEC on March 10, 2021).
<a href="#">4.19*</a>	Description of Capital Stock.
<a href="#">4.20</a>	Form of Wainwright Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on July 27, 2021).
<a href="#">4.21</a>	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the SEC on March 1, 2022).
<a href="#">4.22</a>	Form of Series C Warrant (incorporated by reference to Exhibit 4.2 of the Company's Current Report on Form 8-K filed with the SEC on March 1, 2022).
<a href="#">4.23</a>	Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.3 of the Company's Current Report on Form 8-K filed with the SEC on March 1, 2022).
<a href="#">4.24</a>	Form of Warrant Amendment Agreement (incorporated by reference to Exhibit 4.4 of the Company's Current Report on Form 8-K filed with the SEC on March 1, 2022).
<a href="#">10.1</a>	Stock Purchase Agreement dated May 21, 2014 between the Registrant, Protea Biosciences Group, Inc. and its wholly-owned subsidiary, Protea Biosciences, Inc (incorporated by reference to Exhibit 10.1 of the Company's Registration Statement on Form S-1 filed with the SEC on July 13, 2016).
<a href="#">10.2†</a>	Amended and Restated AzurRx BioPharma, Inc. 2014 Omnibus Equity Incentive Plan (incorporated by reference to Exhibit 10.3 of the Company's Registration Statement on Form S-1 filed with the SEC on July 13, 2016).
<a href="#">10.3</a>	Securities Purchase Agreement dated April 11, 2017 between the Registrant and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on April 12, 2017).
<a href="#">10.4</a>	Registration Rights Agreement dated April 11, 2017 between the Registrant and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 10.4 of the Company's Current Report on Form 8-K filed with the SEC on April 12, 2017).

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<a href="#">10.5</a>	Form of Securities Purchase Agreement dated June 5, 2017 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on June 9, 2017).
<a href="#">10.6</a>	Form of Registration Rights Agreement dated June 5, 2017 (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the SEC on April 12, 2017).
<a href="#">10.7</a>	Sublicense Agreement dated August 7, 2017 by and between the Registrant and TransChem, Inc. (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on August 11, 2017).
<a href="#">10.8</a>	Asset Sale and Purchase Agreement, dated December 7, 2018, by and between Protea Biosciences Group, Inc., Protea Biosciences, Inc. and AzurRx Biopharma, Inc. (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on December 13, 2018).
<a href="#">10.9</a>	Registration Rights Agreement, dated February 14, 2019 (incorporated by reference to Exhibit 10.6 of the Company's Current Report on Form 8-K filed with the SEC on February 20, 2019).
<a href="#">10.10</a>	Asset Purchase Agreement, by and between AzurRx BioPharma, Inc., AzurRx BioPharma SAS and Laboratoires Mayoly Spindler SAS, dated March 27, 2019 (incorporated by reference to Exhibit 10.25 of the Company's Annual Report on Form 10-K filed with the SEC on April 1, 2019).
<a href="#">10.11</a>	Patent License Agreement, by and between AzurRx BioPharma, Inc. and Laboratoires Mayoly Spindler SAS, dated March 27, 2019 (incorporated by reference to Exhibit 10.26 of the Company's Annual Report on Form 10-K filed with the SEC on April 1, 2019).
<a href="#">10.12†</a>	Employment Agreement by and between AzurRx BioPharma, Inc. and James Sapirstein, dated October 8, 2019 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on October 11, 2019).
<a href="#">10.13</a>	Securities Purchase Agreement, dated November 13, 2019 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on November 14, 2019).
<a href="#">10.14</a>	Registration Rights Agreement, dated November 13, 2019 (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the SEC on November 14, 2019).
<a href="#">10.15</a>	Form of Note Purchase Agreement (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on December 30, 2019).
<a href="#">10.16</a>	Form of Warrant (incorporated by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed with the SEC on December 30, 2019).
<a href="#">10.17</a>	Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.4 of the Company's Current Report on Form 8-K filed with the SEC on December 30, 2019).
<a href="#">10.18†</a>	Employment Agreement by and between AzurRx BioPharma, Inc. and Daniel Schneiderman, dated January 1, 2020 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on January 6, 2020).
<a href="#">10.19</a>	Form of Purchase Agreement, by and among the Company and the investors set forth on the signature pages thereto, including the form of Exchange Addendum (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on July 20, 2020).
<a href="#">10.20</a>	Form of Registration Rights Agreement, by and among the Company and the investors set forth on the signature page thereto (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the SEC on July 20, 2020).
<a href="#">10.21†</a>	First Amendment to 2014 Omnibus Equity Incentive Plan (incorporated by reference as Exhibit 10.3 of the Company's Current Report on Form 8-K filed with the SEC on July 20, 2020).
<a href="#">10.22†</a>	2020 Omnibus Equity Incentive Plan (incorporated by reference to Exhibit 10.4 of the Company's Quarterly Report on Form 10-Q filed with the SEC on November 16, 2020).
<a href="#">10.23</a>	Form of Purchase Agreement (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on January 4, 2021).
<a href="#">10.24</a>	Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the SEC on January 4, 2021).
<a href="#">10.25</a>	First Wave Purchase Agreement (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on January 8, 2021).
<a href="#">10.26#</a>	First Wave License Agreement (incorporated by reference to Exhibit 10.1 filed with the Company's Current Report on Form 8-K filed with the SEC on January 13, 2021).
<a href="#">10.27</a>	Form of Purchase Agreement (incorporated by reference to Exhibit 10.1 filed with the Company's Current Report on Form 8-K filed with the SEC on March 10, 2021).

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<a href="#">10.28</a>	At The Market Offering Agreement, dated May 26, 2021, by and between AzurRx BioPharma, Inc. and H.C. Wainwright & Co., LLC (incorporated by reference to Exhibit 1.2 of the Company's Registration Statement on Form S-3 filed with the SEC on May 26, 2021).
<a href="#">10.29</a>	Settlement Agreement, by and between the Company and Fortis Advisors LLC, dated November 15, 2021 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on November 16, 2021).
<a href="#">10.30</a>	Form of Waiver (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on February 7, 2022).
<a href="#">10.31†</a>	Employment Agreement by and between First Wave BioPharma, Inc. and Sarah Romano, dated February 14, 2022 (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on February 17, 2022).
<a href="#">10.32</a>	Form of Purchase Agreement (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on March 1, 2022).
<a href="#">21.1*</a>	Subsidiaries of the Registrant.
<a href="#">23.1*</a>	Consent of Mazars USA LLP.
<a href="#">31.1*</a>	Certification of CEO as Required by Rule 13a-14(a) or Rule 15d-14(a).
<a href="#">31.2*</a>	Certification of CFO as Required by Rule 13a-14(a) or Rule 15d-14(a).
<a href="#">32.1*</a>	Certification of CEO and CFO as Required by Rule 13a-14(a) and Rule 15d-14(b) (17 CFR 240.15d-14(b)) and Section 1350 of Chapter 63 of Title 18 of the United States Code.
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH*	Inline XBRL Taxonomy Extension Schema.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase.
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase.
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase.
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101).

\* Filed herewith.

# Certain portions of this exhibit (indicated by "[\*\*\*\*]") have been omitted as we have determined (1) it is not material and (2) is the type that the Company treats as private or confidential.

## Schedules and exhibits have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company hereby undertakes to furnish supplementally copies of any of the omitted schedules upon request by the SEC.

† Indicates a management contract or compensation plan, contract or arrangement.

**ITEM 16: FORM 10-K SUMMARY**

None.

**SIGNATURES**

In accordance with Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, there unto duly authorized.

**FIRST WAVE BIOPHARMA, INC.**

March 31, 2022

By: /s/ James Sapirstein  
Name: James Sapirstein  
Title: President and Chief Executive Officer

By: /s/ Sarah Romano  
Name: Sarah Romano  
Title: Chief Financial Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed by the following persons on behalf of the registrant and in the capacities held on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ James Sapirstein</u> James Sapirstein	President, Chief Executive Officer and Chair of the Board of Directors (principal executive officer)	March 31, 2022
<u>/s/ Sarah Romano</u> Sarah Romano	Chief Financial Officer (principal financial officer and accounting officer)	March 31, 2022
<u>/s/ Edward J. Borkowski</u> Edward J. Borkowski	Director	March 31, 2022
<u>/s/ Charles J. Casamento</u> Charles J. Casamento	Director	March 31, 2022
<u>/s/ Terry Coelho</u> Terry Coelho	Director	March 31, 2022
<u>/s/ Gregory Oakes</u> Gregory Oakes	Director	March 31, 2022
<u>/s/ Alastair Riddell</u> Alastair Riddell	Director	March 31, 2022

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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of First Wave BioPharma, Inc.

### Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of First Wave BioPharma, Inc. (f/k/a AzurRX BioPharma, Inc; the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the consolidated financial position of the Company as of December 31, 2021 and 2020, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

### Emphasis of a Matter

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred significant operating losses and negative cash flows from operations since inception. The Company also had an accumulated deficit of approximately \$153.9 million at December 31, 2021. The Company is dependent on obtaining additional working capital funding from the sale of equity and/or debt securities in order to continue to execute its development plans and continue operations. These conditions raise substantial doubt about its ability to continue as a going concern. Management's plans regarding those matters also are described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

### Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform an audit of the Company's internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

### Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

#### Impairment Assessment

##### Critical Audit Matter Description

As discussed in Note 2 to the consolidated financial statements, the Company's goodwill and long-lived assets arose as a result of the excess fair value over book value, and acquisition of certain intangible assets from prior business combinations. Goodwill and long-lived assets are tested for impairment at least annually. The determination of the fair value requires management to make significant estimates and assumptions related to forecasts of future revenues and expenses and discount rates.

Considering the significant estimation, judgement, and subjectivity required by management in determining the future cash flows and current fair value of assets, our audit of the impairment assessment of goodwill and long-lived assets required a high degree of auditor judgement and subjectivity.

##### How the Critical Matter Was Addressed in the Audit

Our audit procedures related to the intangible asset impairment included the following, among others:

- Evaluated and verified the events and circumstances described in management's qualitative analyses of intangible and goodwill impairment.
- Tested and assessed the reasonableness and appropriateness of assumptions used in management's analyses including sales volumes, sales prices, operating margins, discount rate, and growth rates.
- Tested and verified the mechanical and clerical accuracy of management's projections and calculations.
- Tested the completeness, accuracy, and relevance of underlying data used by management in the discounted cash flow model

#### Equity Classification and Valuation

##### Critical Audit Matter Description

As discussed in Notes 12, 13, and 14 to the consolidated financial statements, the Company issued new Series C convertible preferred stock along with private placement and pre-funded warrants. The classification between debt and equity of these instruments requires management to make significant and complex judgements in evaluating the characteristics of these instruments including the redemption features, voting rights, collateral requirements, covenant provisions, creditor and liquidation rights, dividends, conversion rights, and exchange rights. The valuation of these new instruments requires management to make significant estimates and complex judgements in determining the fair value of and relative fair value allocation amongst the original instruments, conversion options, and beneficial conversion features. Considering the significant judgement and estimation required by management in determining the proper classification and valuation of these equity instruments, our audit of the new equity instruments required a high degree of auditor judgement and subjectivity.

##### How the Critical Matter Was Addressed in the Audit

Our audit procedures related to the equity structures included the following, among others:

- We tested the Company's determination of the fair value for the equity transactions, as well as the respective relative fair value allocations for instruments that required bifurcation. Our testing included recalculating the fair value and allocations and assessing the reasonableness of certain assumptions used by the Company, as well as the completeness and accuracy of the data utilized.
- We verified management's records of new equity instruments by reading the original agreements for the equity instruments and assessing the terms relating to the technical accounting guidance.
- We evaluated management's conclusions regarding the balance sheet classification and valuation of the complex equity instruments
- We assessed the required financial statement disclosures related to the transactions for completeness and accuracy

#### /s/ Mazars USA LLP

We have served as the Company's auditor since 2015.

New York, NY  
March 31, 2022

**FIRST WAVE BIOPHARMA, INC.**  
**Consolidated Balance Sheets**

	December 31, 2021	December 31, 2020
<b>ASSETS</b>		
Current Assets:		
Cash and cash equivalents	\$ 8,248,684	\$ 6,062,141
Other receivables	-	551,489
Prepaid expenses	1,176,268	1,256,154
Total Current Assets	<u>9,424,952</u>	<u>7,869,784</u>
Property, equipment, and leasehold improvements, net	<u>73,110</u>	<u>18,329</u>
Other Assets:		
Patents, net	-	2,879,536
Goodwill	1,911,705	2,054,048
Operating lease right-of-use assets	336,197	74,238
Deposits	44,012	27,920
Total Other Assets	<u>2,291,914</u>	<u>5,035,742</u>
Total Assets	<u>\$ 11,789,976</u>	<u>\$ 12,923,855</u>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current Liabilities:		
Accounts payable and accrued expenses	\$ 3,100,984	\$ 1,685,603
Payable related to license agreement	-	13,250,000
Accrued dividend payable	465,361	-
Note payable	641,236	552,405
Other current liabilities	8,092,807	57,417
Total Current Liabilities	<u>12,300,388</u>	<u>15,545,425</u>
Other liabilities	<u>7,311,138</u>	<u>19,123</u>
Total Liabilities	<u>19,611,526</u>	<u>15,564,548</u>
Stockholders' Equity:		
Series C preferred stock- Par value \$ 0.0001 per share; 57,000 shares authorized; 0 shares issued and outstanding at December 31, 2021 and 2020.	-	-
Series B preferred stock- Par value \$ 0.0001 per share; 5,194.81 shares authorized; 662.25 and 2,773.6 shares issued and outstanding at December 31, 2021 and 2020, respectively.	-	-
Common stock - Par value \$ 0.0001 per share; 25,000,000 shares authorized; 14,855,848 and 3,115,030 shares issued and outstanding at December 31, 2021 and 2020, respectively.	1,485	312
Additional paid-in capital	147,305,147	93,837,739
Accumulated deficit	(153,904,047)	(95,366,198)
Accumulated other comprehensive loss	(1,224,135)	(1,112,546)
Total Stockholders' Equity	<u>(7,821,550)</u>	<u>(2,640,693)</u>
Total Liabilities and Stockholders' Equity	<u>\$ 11,789,976</u>	<u>\$ 12,923,855</u>

The accompanying notes are an integral part of these Consolidated Financial Statements.



**FIRST WAVE BIOPHARMA, INC.**  
**Consolidated Statements of Operations and Comprehensive Loss**

	Years Ended December 31,	
	2021	2020
Operating expenses:		
Research and development expenses	\$ 16,994,828	\$ 5,888,004
Research and development expenses - intellectual property acquired	21,325,527	13,250,000
General and administrative expenses	18,384,545	7,294,764
Intangible asset impairment	2,351,988	-
Total operating expenses	<u>59,056,888</u>	<u>26,432,768</u>
Loss from operations	<u>(59,056,888)</u>	<u>(26,432,768)</u>
Other income (expenses):		
Interest expense	(11,235)	(5,840,614)
Interest income	1,173	484
Gain on settlement	-	211,430
Gain (loss) on debt extinguishment	-	(609,998)
Change in fair value of liability	532,353	-
Other income	(3,252)	-
Total other income (expenses)	<u>519,039</u>	<u>(6,238,698)</u>
Net loss	<u>\$ (58,537,849)</u>	<u>\$ (32,671,466)</u>
Other comprehensive loss:		
Foreign currency translation adjustment	(111,589)	(154,009)
Total comprehensive loss	<u>\$ (58,649,438)</u>	<u>\$ (32,825,475)</u>
Net loss	\$ (58,537,849)	\$ (32,671,466)
Deemed dividend on preferred stock	(4,507,125)	(8,155,212)
Deemed dividend on preferred stock exchanges	(21,008,253)	-
Preferred stock dividends	(465,361)	(905,660)
Net loss applicable to common shareholders	<u>\$ (84,518,588)</u>	<u>\$ (41,732,338)</u>
Basic and diluted weighted average shares outstanding	8,925,728	2,843,629
Loss per share applicable to common shareholders - basic and diluted	\$ (9.47)	\$ (14.68)

The accompanying notes are an integral part of these Consolidated Financial Statements.

**FIRST WAVE BIOPHARMA, INC.**  
**Consolidated Statements of Changes in Stockholders' Equity**

	Series C Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid In Capital	Accumulated Deficit	Other Comprehensive Loss	Total
	Shares	Amount	Shares	Amount	Shares	Amount				
<b>Balance, January 1, 2020</b>	-	\$ -	-	\$ -	2,680,052	\$ 268	\$ 68,578,263	\$ (62,694,732)	\$ (1,266,555)	\$ 4,617,244
Issuance of Series B preferred stock and warrants for cash, conversion of promissory notes, net of offering costs	-	-	2,912	-	-	-	14,460,155	-	-	14,460,155
Warrants issued in connection with Series B convertible preferred stock private placement	-	-	-	-	-	-	5,952,516	-	-	5,952,516
Warrants issued as inducement to exchange promissory notes into Series B convertible preferred stock private placement	-	-	-	-	-	-	986,526	-	-	986,526
Beneficial conversion feature of Series B preferred stock	-	-	-	-	-	-	8,155,212	-	-	8,155,212
Deemed dividend of preferred stock	-	-	-	-	-	-	(8,155,212)	-	-	(8,155,212)
Deemed dividend related to exchange of promissory notes into Series B preferred stock	-	-	-	-	-	-	(1,129,742)	-	-	(1,129,742)
Issuance of Series B preferred PIK shares for accrued dividends	-	-	118	-	-	-	-	-	-	-
Common stock issued upon conversion of Series B preferred stock	-	-	(256)	-	256,581	26	(26)	-	-	-
Common stock issued to settle accounts payable	-	-	-	-	10,594	1	131,136	-	-	131,137
Common stock issued to consultants	-	-	-	-	18,284	2	144,403	-	-	144,405
Common stock issued to Lincoln Park for Equity Purchase agreement	-	-	-	-	149,520	15	988,333	-	-	988,348
Warrants issued in association with convertible debt issuances	-	-	-	-	-	-	1,252,558	-	-	1,252,558
Beneficial conversion feature on convertible debt issuances	-	-	-	-	-	-	1,838,422	-	-	1,838,422
Settlement with former chief executive officer	-	-	-	-	-	-	85,770	-	-	85,770
Stock-based compensation	-	-	-	-	-	-	549,425	-	-	549,425
Foreign currency translation adjustment	-	-	-	-	-	-	-	-	154,009	154,009
Net loss	-	-	-	-	-	-	-	(32,671,466)	-	(32,671,466)
<b>Balance, December 31, 2020</b>	-	\$ -	2,774	\$ -	3,115,031	\$ 312	\$ 93,837,739	\$ (95,366,198)	\$ (1,112,546)	\$ (2,640,693)

	Series C Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid In Capital	Accumulated Deficit	Other Comprehensive Loss	Total
	Shares	Amount	Shares	Amount	Shares	Amount				
<b>Balance, January 1, 2021</b>	-	\$ -	2,774	\$ -	3,115,031	\$ 312	\$ 93,837,739	\$ (95,366,198)	\$ (1,112,546)	\$ (2,640,693)
Issuance of Series C preferred stock and warrants for cash, net of offering costs	10,667	1	-	-	-	-	7,105,167	-	-	7,105,168
Issuance of Series C preferred stock for license acquired	3,290	1	-	-	-	-	2,467,648	-	-	2,467,649
Beneficial conversion feature of Series C preferred stock	-	-	-	-	-	-	4,507,125	-	-	4,507,125
Deemed dividend of Series C preferred stock	-	-	-	-	-	-	(4,507,125)	-	-	(4,507,125)
Issuance of Series C preferred stock upon exchange of Series B preferred stock	19,140	1	(1,839)	-	-	-	(1,431)	-	-	(1,430)
Warrants issued in connection with exchange of Series B preferred stock into Series C preferred stock	-	-	-	-	-	-	21,009,683	-	-	21,009,683
Deemed dividend related to exchange of Series B preferred stock into Series C preferred stock	-	-	-	-	-	-	(21,008,253)	-	-	(21,008,253)
Issuance of common stock upon exchange of Series B preferred stock	-	-	(14)	-	33,500	3	(3)	-	-	-
Common stock issued upon conversion of Series B preferred stock	-	-	(259)	-	258,278	26	(26)	-	-	-
Dividends on preferred stock	-	-	-	-	-	-	(465,361)	-	-	(465,361)
Common stock and pre-funded warrants issued upon conversion of Series C preferred stock	(33,097)	(3)	-	-	3,125,460	312	(309)	-	-	-
Issuance of common stock, pre-funded warrants and warrants for cash, net of offering costs	-	-	-	-	1,625,454	163	14,155,887	-	-	14,156,050
Effect of 10-for-1 reverse stock split	-	-	-	-	(1,706)	-	-	-	-	-
Issuance of common stock at-the-market for cash, net of offering costs	-	-	-	-	5,333,345	533	18,506,281	-	-	18,506,814
Common stock issued for intellectual property acquired, net	-	-	-	-	624,025	62	3,999,938	-	-	4,000,000
Common stock cancelled in connection with acquisition of First Wave Bio, Inc.	-	-	-	-	(332,913)	(33)	33	-	-	-
Common stock issued upon exercise of warrants	-	-	-	-	945,644	94	4,906,536	-	-	4,906,630
Common stock and warrants issued to consultants	-	-	-	-	122,230	12	1,326,050	-	-	1,326,062
Settlement with former placement agent	-	-	-	-	7,500	1	94,498	-	-	94,499
Stock-based compensation	-	-	-	-	-	-	1,371,070	-	-	1,371,070
Foreign currency translation adjustment	-	-	-	-	-	-	-	-	(111,589)	(111,589)
Net loss	-	-	-	-	-	-	-	(58,537,849)	-	(58,537,849)
<b>Balance, December 31, 2021</b>	-	\$ -	662	\$ -	14,855,848	\$ 1,485	\$ 147,305,147	\$ (153,904,047)	\$ (1,224,135)	\$ (7,821,550)

The accompanying notes are an integral part of these Consolidated Financial Statements.

**FIRST WAVE BIOPHARMA, INC.**  
**Consolidated Statements of Cash Flows**

	Years Ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	\$ (58,537,849)	\$ (32,671,466)
Adjustments to reconcile net loss to net cash used in operating activities:		
Intangible asset impairment	2,351,988	-
Depreciation	14,707	37,797
Amortization	527,548	527,548
Non-cash lease expense	(4,855)	(4,855)
Fixed assets written off	-	10,950
Change in fair value of liability	(532,353)	-
Stock-based compensation	1,371,070	522,133
Common stock issued for intellectual property acquired, net	4,000,000	-
Restricted stock granted to employees/directors	-	27,292
Common stock and warrants granted to consultants and former placement agent	1,420,561	166,905
Accreted interest on convertible debt	-	234,074
Accretion of debt discount	-	4,580,168
Loss on debt extinguishment	-	609,998
Gain on settlement	-	(211,430)
Beneficial conversion feature related to promissory note exchange	-	798,413
Changes in assets and liabilities:		
Other receivables	551,489	2,083,270
Prepaid expenses	79,886	(660,845)
Right of use assets	(257,104)	(110,835)
Deposits	(16,092)	(15,412)
Accounts payable and accrued expenses	1,415,381	(750,027)
Payables related to license agreement	-	13,250,000
Other liabilities related to Merger consideration	15,000,000	-
Other liabilities	327,405	354,784
Net cash used in operating activities	(32,288,218)	(11,221,538)
Cash flows from investing activities:		
Purchase of property and equipment	(69,488)	(4,167)
Proceeds from sale of property and equipment, net	-	91,517
Payment made related to license agreement	(10,250,000)	-
Net cash used in investing activities	(10,319,488)	87,350
Cash flows from financing activities:		
Proceeds from issuance of notes payable, net	-	799,772
Proceeds from issuance of preferred stock, net	7,105,168	13,197,740
Proceeds from issuance of common stock, net	14,156,050	988,348
Proceeds from exercise of warrants	4,906,630	-
Proceeds from issuance of convertible debt, net	-	3,227,002
Issuance of common stock at-the-market for cash, net of offering costs	18,506,814	-
Repayments of convertible debt	-	(475,000)
Issuance / (repayment) of note payable	88,831	(691,741)
Net cash provided by financing activities	44,763,493	17,046,121
Increase in cash and cash equivalents	2,155,787	5,911,933
Effect of exchange rate changes on cash	30,756	(25,588)
Cash and cash equivalents, beginning balance	6,062,141	175,796
Cash and cash equivalents, ending balance	<u>\$ 8,248,684</u>	<u>\$ 6,062,141</u>
Supplemental disclosures of cash flow information:		
Cash paid for interest	\$ -	\$ 105,460
Cash paid for income taxes	\$ -	\$ -
Non-cash investing and financing activities:		
Deemed dividend on preferred stock issuances	\$ (4,507,125)	\$ (8,155,212)
Deemed dividend on preferred stock exchanges	\$ (21,008,253)	\$ -
Accrued dividends on preferred stock	\$ (465,361)	\$ (905,650)
Issuance of preferred stock to settle liability related to license agreement	\$ 2,467,649	\$ -
Exchange of promissory notes into preferred stock and warrants	\$ -	\$ (609,998)

The accompanying notes are an integral part of these Consolidated Financial Statements.

**FIRST WAVE BIOPHARMA, INC.**  
**Notes to Consolidated Financial Statements**  
**December 31, 2021 and 2020**

**Note 1 - The Company and Basis of Presentation**

**The Company**

AzurRx BioPharma, Inc. ("AzurRx"), renamed itself First Wave BioPharma, Inc. ("First Wave" or "Parent") on September 21, 2021, in connection with its acquisition of First Wave Bio, Inc. ("FWB"). Parent and its wholly owned subsidiaries, including First Wave Bio, Inc., and AzurRx SAS, are collectively referred to as the "Company". Shares of the Company's Common Stock commenced trading on the Nasdaq Capital Market under the new ticker symbol "FWBI" and CUSIP number (33749P101) at the market open on September 22, 2021.

On September 13, 2021, AzurRx consummated its acquisition of FWB, a clinical-stage biotechnology company developing novel gut-targeted small molecules for inflammatory bowel disease ("IBD") and other serious gastrointestinal ("GI") conditions.

Also, on September 13, 2021, AzurRx effected a reverse stock split, whereby every ten shares of the Company's issued and outstanding Common Stock was converted automatically into one issued and outstanding share of Common Stock, with a corresponding 1-for-10 reduction in the number of authorized shares of Common Stock, but without any change in the par value per share. All share and per share amounts have been retroactively restated to reflect the 1-for-10 reverse stock split.

The Company is engaged in the research and development of targeted, non-systemic therapies for the treatment of patients with GI diseases. Non-systemic therapies are non-absorbable drugs that act locally, i.e. in the intestinal lumen, skin or mucosa, without reaching an individual's systemic circulation.

The Company is currently focused on developing its pipeline of gut-restricted GI clinical product candidates, including niclosamide, an oral small molecule with anti-viral and anti-inflammatory properties, and the biologic adrulipase (formerly MS1819), a recombinant lipase enzyme designed to enable the digestion of fats and other nutrients.

The Company is developing its product candidates for a host of GI diseases where there are significant unmet clinical needs and limited therapeutic options, resulting in painful, life threatening and discomforting consequences for patients. The Company's mission is to help protect the health and restore quality of life for the millions of people afflicted by these GI diseases.

Since its inception, the Company has devoted substantially all of its efforts to research and development, business development, and raising capital, and has financed its operations through issuance of common stock, convertible preferred stock, convertible debt and other debt/equity instruments. The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development and regulatory success, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, and ability to secure additional capital to fund operations.

Historically, the Company's major sources of cash have been comprised of proceeds from various public and private offerings of its capital stock. As of December 31, 2021, the Company had approximately \$8.2 million in cash and cash equivalents. The Company has incurred recurring losses, has experienced recurring negative operating cash flows and requires significant cash resources to execute its business plans. The Company has an accumulated deficit of approximately \$153.9 million as of December 31, 2021.

We have implemented business continuity plans designed to address and mitigate the impact of the COVID-19 pandemic on our business. The extent to which the ongoing COVID-19 pandemic impacts our business, our clinical development and regulatory efforts, our corporate development objectives and the value of and market for our Common Stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the U.S., Europe and other countries, and the effectiveness of actions taken globally to contain and treat the disease. The global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, we are subject to other challenges and risks specific to our business and our ability to execute on our strategy, as well as risks and uncertainties common to companies in the pharmaceutical industry with development and commercial operations, including, without limitation, risks and uncertainties associated with: obtaining regulatory approval of our product candidates; delays or problems in the manufacture and supply of our product candidates, loss of single source suppliers or failure to comply with manufacturing regulations; identifying, acquiring or in-licensing additional products or product candidates; pharmaceutical product development and the inherent uncertainty of clinical success; and the challenges of protecting and enhancing our intellectual property rights; complying with applicable regulatory requirements. In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties discussed above.

*Going Concern Uncertainty*

The accompanying consolidated financial statements have been prepared as if the Company will continue as a going concern. The Company has incurred significant operating losses and negative cash flows from operations since inception. On December 31, 2021, the Company had cash and cash equivalents of approximately \$8.2 million, and an accumulated deficit of approximately \$ 153.9 million. The Company has incurred recurring losses, has experienced recurring negative operating cash flows, and requires significant cash resources to execute its business plans. Historically, the Company's major sources of cash have been comprised of proceeds from various public and private offerings of its capital stock. The Company is dependent on obtaining additional working capital funding from the sale of equity and/or debt securities in order to continue to execute its development plans and continue operations. In November 2021, the Company reached an agreement with the hired representative of the former stockholders of FWB to substantially reduce the immediate payment obligations of the Company and defer certain remaining milestone and other payment obligations over time, with an immediate payment of \$2.0 million related to and periodic installments of \$ 500,000 per month payable from January 2022 through August 2022 and \$1.0 million per month payable from September 2022 through July 2023 until an aggregate of \$ 17.0 million is received.

***Basis of Presentation and Principles of Consolidation***

The accompanying consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("GAAP") and include the accounts of First Wave and its wholly-owned subsidiaries, AzurRx SAS, and First Wave Bio, Inc. Intercompany transactions and balances have been eliminated upon consolidation.

The accompanying consolidated financial statements have been prepared as if the Company will continue as a going concern. The Company has incurred significant operating losses and negative cash flows from operations since inception. At December 31, 2021, we had an accumulated deficit of approximately \$153.9 million and had negative working capital of approximately \$8.0 million. The Company is dependent on obtaining additional working capital funding from the sale of equity securities and/or debt in order to continue to execute its development plan and continue operations.

Subsequent to December 31, 2021, we have raised aggregate gross proceeds of approximately \$ 9.0 million from the sale of Common Stock and warrants in a registered direct offering transaction (See Note 21).

Without adequate working capital, the Company may not be able to meet its obligations and continue as a going concern. These conditions raise substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

**Note 2 - Significant Accounting Policies and Recent Accounting Pronouncements**

***Use of Estimates***

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The accompanying consolidated financial statements are prepared in conformity with GAAP and include certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements (including goodwill and intangible assets), and the reported amounts of revenue and expense during the reporting period, including contingencies. Accordingly, actual results may differ from those estimates

**Cash and Cash Equivalents**

The Company considers all highly liquid investments with maturities of three months or less from date of purchase to be cash equivalents. All cash and cash equivalent balances were highly liquid at December 31, 2021 and 2020, respectively.

**Concentrations of Credit Risk**

Financial instruments that potentially expose the Company to concentrations of credit risk consist of cash. The Company primarily maintains its cash balances with financial institutions in federally insured accounts in the U.S. The Company may from time to time have cash in banks in excess of FDIC insurance limits. At December 31, 2021 and 2020, the Company had approximately \$7.5 million and \$2.7 million, respectively, in one account in the U.S. in excess of these limits. The Company has not experienced any losses to date resulting from this practice. The Company mitigates its risk by maintaining the majority of its cash and equivalents with high quality financial institutions.

The Company also has exposure to foreign currency risk as its subsidiary in France has a functional currency in Euros.

**Cyber-Related Fraud**

In August 2019, management determined that it was a victim of a cyber-related fraud whereby a hacker impersonated one of the Company's key vendors to redirect payments, totaling approximately \$420,000. The Company, including the Audit Committee, completed its investigation and is reviewing all available avenues of recovery, including from the Company's financial institution to recover the payments. As of December 31, 2021, the Company had recovered approximately \$50,000 from its financial institution but management is unable to determine the probability of recovering anything further from the cyber-related fraud. As a result of the cyber-related fraud, the Company has instituted additional controls and procedures and all employees now undergone cybersecurity training.

**Debt Instruments**

Detachable warrants issued in conjunction with debt are recorded at their relative fair value, if they are determined to be equity instrument, or their respective fair values, if they are determined to be liability instruments, and recorded as a debt discount. Conversion features that are in the money at the commitment date constitute a beneficial conversion feature that is measured at its intrinsic value and recognized as debt discount. Debt discount is amortized as interest expense over the maturity period of the debt using the effective interest method. Contingent beneficial conversion features are recognized when the contingency has been resolved.

**Debt Issuance Costs**

Debt issuance costs are recorded as a direct reduction of the carrying amount of the related debt. Debt issuance costs are amortized over the maturity period of the related debt instrument using the effective interest method.

**Equity-Based Payments to Non-Employees**

Equity-based payments to non-employees are measured at fair value on the grant date per ASU No. 2018-07, Improvements to Nonemployee Share-Based Payment Accounting.

### **Fair Value Measurements**

The Company follows Accounting Standards Codification ("ASC") Topic 820-10, Fair Value Measurements and Disclosures ("ASC 820"), which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability.

As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices (unadjusted) in active markets for identical assets or liabilities;

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions, which reflect those that a market participant would use.

In certain cases, the inputs used to measure fair value may fall into different levels of the fair value hierarchy. In such cases, an instrument's level within the fair value hierarchy is based on the lowest level of input that is significant to the overall fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires judgment and considers factors specific to the financial instrument.

The Company recognizes transfers between levels as if the transfers occurred on the last day of the reporting period.

### **Foreign Currency Translation**

For foreign subsidiaries with operations denominated in a foreign currency, assets and liabilities are translated to U.S. dollars, which is the functional currency, at period end exchange rates. Income and expense items are translated at average rates of exchange prevailing during the periods presented. Gains and losses from translation adjustments are accumulated in a separate component of stockholders' equity.

### **Goodwill and Intangible Assets**

Goodwill represents the excess of the purchase price of the acquired business over the fair value of amounts assigned to assets acquired and liabilities assumed. Goodwill and other intangible assets with indefinite useful lives are reviewed for impairment annually or more frequently if events or circumstances indicate impairment may be present. Any excess in carrying value over the estimated fair value is charged to results of operations. The Company has not recognized any impairment charges through December 31, 2021 related to goodwill.

Intangible assets subject to amortization consist of in patents, process research and development and licenses, reported at the fair value at date of the acquisition less accumulated amortization. Amortization expense is provided using the straight-line method over their estimated useful lives. The carrying amounts of finite-lived intangible assets are evaluated for recoverability whenever events or changes in circumstances indicate that the Company may be unable to recover the asset's carrying amount. Given changes in the projected usage of the patents, the Company recognized impairment charges of approximately \$2.4 million at December 31, 2021.

### **Impairment of Long-Lived Assets**

The Company periodically evaluates its long-lived assets for potential impairment in accordance with ASC Topic 360, Property, Plant and Equipment ("ASC 360"). Potential impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. If impairments are identified, assets are written down to their estimated fair value. The Company has not recognized any impairment charges through December 31, 2021.

### **Income Taxes**

Income taxes are recorded in accordance with ASC 740, Accounting for Income Taxes ("ASC 740"), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. The Company determines its deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. At December 31, 2021 and 2020, the Company does not have any significant uncertain tax positions.

### **Leases**

Leases are recorded on the balance sheet as right of use assets and lease obligations.

### **Loss Per Share**

Basic loss per share ("*EPS*") is computed by dividing the loss attributable to common shareholders by the weighted average number of shares of Common Stock outstanding. Diluted EPS reflects the potential dilution that could occur from shares of Common Stock issuable through the exercise or conversion of stock options, restricted stock awards, warrants and convertible securities. In certain circumstances, the conversion of options is excluded from diluted EPS if the effect of such inclusion would be anti-dilutive.

The dilutive effect of stock options is determined using the treasury stock method. Stock options to purchase shares of Common Stock of the Company during fiscal 2021 and 2020 were not included in the computation of diluted EPS because the Company has incurred a loss for the years ended December 31, 2021 and 2020 and the effect would be anti-dilutive.

### **Research and Development**

Research and development costs are charged to operations when incurred and are included in operating expense, except for goodwill related to patents. Research and development costs consist principally of compensation of employees and consultants that perform the Company's research activities, payments to third parties for preclinical and non-clinical activities, expenses with clinical research organizations ("*CROs*"), investigative sites, consultants and contractors that conduct or provide other services relating to clinical trials, costs to acquire drug product, drug supply and clinical trial materials from contract development and manufacturing organization ("*CDMOs*") and third-party contractors relating to chemistry, manufacturing and controls ("*CMC*") efforts, the fees paid for and to maintain the Company's licenses, amortization of intangible assets related to the acquisition of adrulipase and research and development costs related to niclosamide.

### **Research and Development – Intellectual Property Acquired**

On December 31, 2020, the Company entered into a license agreement (the "*FWB License Agreement*") with FWB, pursuant to which FWB granted the Company an exclusive license to certain patents and patent applications related to a proprietary formulation of niclosamide for use in the fields of ICI-AC and COVID-19 GI infections. The acquisition of intellectual property and patents for the worldwide, exclusive right to develop, manufacture, and commercialize proprietary formulations of niclosamide for the fields of treating ICI-AC and COVID-19 in humans was accounted for as an asset acquisition and initial liabilities of approximately \$13.3 million in connection with the license acquisition were recorded as research and development expense, because it was determined to have no alternative future uses and therefore no separate economic value, which included cash payments totaling approximately \$10.3 million and the issuance of approximately \$3.0 million worth of preferred stock. Upon consummation of the Merger (as defined below) on September 13, 2021, the FWB License Agreement was effectively canceled.



On September 13, 2021, the Company completed its acquisition of FWB, which the Company concluded should be accounted for as an asset acquisition rather than a business combination under ASC 805, Business Combinations. The merger was accounted for as an asset acquisition because substantially all the fair value of the assets being acquired are concentrated in a single asset – intellectual property, which does not constitute a business.

The former FWB stockholders are also entitled to (i) up to \$ 207.0 million of cash milestone payments contingent upon the achievement of specified development, regulatory and sales goals for the use of the acquired assets, and (ii) certain revenue-sharing. During the year ended December 31, 2021, the Company achieved one development milestone pursuant to the FWB License Agreement totaling \$1.0 million, which was accrued and expensed in research and development. During the year ended December 31, 2021, the Company achieved one development milestone pursuant to the Merger Agreement totaling \$2.0 million, which was expensed in research and development. Depending on the status of development at the time a contingent payment is recognized the Company may determine that the payment should be expensed as research and development or be capitalized as an intangible asset. This determination will be based on the facts and circumstances that exist at the time a contingent payment is recognized.

#### **Stock-Based Compensation**

The Company's board of directors (the "*Board*") and stockholders have adopted and approved the Amended and Restated 2014 Omnibus Equity Incentive Plan (the "*2014 Plan*") which took effect on May 12, 2014, and the 2020 Omnibus Equity Incentive Plan, which took effect on September 11, 2020 (the "*2020 Plan*"). From the effective date of the 2020 Plan, no new awards have been or will be made under the 2014 Plan. The Company accounts for its stock-based compensation awards to employees and Board members in accordance with ASC Topic 718, Compensation—Stock Compensation ("*ASC 718*"). ASC 718 requires all stock-based payments to employees and Board members, including grants of employee stock options, to be recognized in the statements of operations by measuring the fair value of the award on the date of grant and recognizing this fair value as stock-based compensation using a straight-line method over the requisite service period, generally the vesting period.

For awards with performance conditions that affect their vesting, such as the occurrence of certain transactions or the achievement of certain operating or financial milestones, recognition of fair value of the award occurs when vesting becomes probable.

The Company estimates the grant date fair value of stock option awards using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the Common Stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the Common Stock.

#### **Recent Accounting Pronouncements**

In January 2017, the FASB issued ASU 2017-04, Intangibles - Goodwill and Other, Simplifying the Accounting for Goodwill Impairment. ASU 2017-04 removes Step 2 of the goodwill impairment test, which requires a hypothetical purchase price allocation. A goodwill impairment will now be the amount by which a reporting unit's carrying value exceeds its fair value, not to exceed the carrying amount of goodwill. All other goodwill impairment guidance will remain largely unchanged. Entities will continue to have the option to perform a qualitative assessment to determine if a quantitative impairment test is necessary. This new guidance will be applied prospectively and is effective for annual or any interim goodwill impairment tests in fiscal years beginning after December 15, 2019. This ASU, which the Company adopted as of January 1, 2020, did not have a material effect on the Company's consolidated financial statements.

In August 2020, the FASB issued accounting pronouncement (ASU 2020-06) related to the measurement and disclosure requirements for convertible instruments and contracts in an entity's own equity. The pronouncement simplifies and adds disclosure requirements for the accounting and measurement of convertible instruments and the settlement assessment for contracts in an entity's own equity. As a smaller reporting company, as defined by the U.S. Securities and Exchange Commission (the "*SEC*"), this pronouncement is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2023. The Company is currently evaluating the impact of this ASU on the consolidated financial statements.

**Note 3 - Fair Value Disclosures**

Fair value is the price that would be received from the sale of an asset or paid to transfer a liability assuming an orderly transaction in the most advantageous market at the measurement date. GAAP establishes a hierarchical disclosure framework that prioritizes and ranks the level of observability of inputs used in measuring fair value.

The fair value of the Company's financial instruments are as follows:

	Carrying Amount	Fair Value Measured at Reporting Date Using			Fair Value
		Level 1	Level 2	Level 3	
<b>December 31, 2021:</b>					
Other receivables	\$ -	\$ -	\$ -	\$ -	\$ -
<b>December 31, 2020:</b>					
Other receivables	\$ 551,489	\$ -	\$ -	\$ 551,489	\$ 551,489

The fair value of other receivables approximates carrying value as these consist primarily of French research and development tax credits that are normally received the following year.

**Note 4 – Asset Acquisition****The Asset Acquisition**

On September 13, 2021, the Company completed its acquisition of FWB, in accordance with the terms of an Agreement and Plan of Merger dated as of September 13, 2021 (the "Merger Agreement") by and among the Company, Alpha Merger Sub, Inc., a Delaware corporation and wholly owned subsidiary of the Company ("Merger Sub"), and FWB. On September 13, 2021, pursuant to the Merger Agreement, Merger Sub was merged with and into FWB (the "Merger"), with FWB being the surviving corporation and becoming a wholly owned subsidiary of the Company. In connection with the Merger, AzurRx changed its name to First Wave BioPharma, Inc.

At the effective time of the Merger, the former FWB stockholders received an applicable pro rata share of (i) \$ 3.0 million in cash and (ii) 624,025 shares of the Common Stock. The remaining non-contingent purchase price was payable to the former FWB stockholders on a pro rata basis upon the Company's payment of (i) \$8.0 million in cash, payable within 45 days of the Merger, (ii) \$ 7.0 million in cash, payable by March 31, 2022. As of November 15, 2021, the Company reached an agreement with the hired representative of the former stockholders of FWB to substantially reduce the immediate payment obligations of the Company and defer certain remaining milestone and other payment obligations over time, with an immediate payment of \$2.0 million related to a milestone payment and periodic installments of \$500,000 per month payable from January 2022 through August 2022 and \$1.0 million per month payable from September 2022 through July 2023 until an aggregate of \$17.0 million is received. In addition, the Company cancelled 332,913 shares of Common Stock held by FWB immediately prior to the Merger for no additional consideration, which shares of Common Stock are authorized and unissued.

The former FWB stockholders are also entitled to up to \$ 207 million of cash milestone payments contingent upon the achievement of specified development, regulatory and sales goals relating to the use of the acquired assets. All milestone payments will be payable in cash, provided that 25% of the milestone payments attributable to a certain IBD indications may be payable in Common Stock, at the option of the Company. In addition, the former FWB stockholders are entitled to 10% of certain specified revenue received by the Company from any third-party with a pre-existing niclosamide development program relating to COVID.

**Accounting Treatment**

The Company concluded that the Merger should be accounted for as an asset acquisition under ASC 805 because substantially all the fair value of the assets being acquired are concentrated in a single asset - intellectual property, which does not constitute a business. Because the acquired intellectual property has not received regulatory approval, the \$21.3 million non-contingent purchase price was immediately expensed in the Company's statement of operations as research and development - intellectual property acquired. The \$0.9 million of transaction expenses paid at closing were classified in general and administrative expenses. The Common Stock issued for the asset acquisition was valued at \$4.0 million which is equal to the 624,025 common shares issued multiplied by \$6.41 per share.

**Achievement of Milestone pursuant to Merger Agreement**

On October 4, 2021, the Company achieved a milestone for clinical development pursuant to the Merger Agreement in connection with dosing of the first patient in the Company's Phase 2 clinical trial for FW-UP for ulcerative proctitis resulting in a \$2.0 million payment to FWB, which is included in the \$17.0 million aggregate payment amount discussed under the heading "FWB Payments" below. This \$2.0 million milestone was accrued and expensed in research and development as the product candidate is still in clinical development.

**FWB Payments**

Fortis Advisors LLC is the hired representative (in such capacity, the "Representative") of the former stockholders of FWB in connection with the Merger Agreement. On October 29, 2021, the Representative filed a complaint against us in the Court of Chancery of the State of Delaware, seeking to enforce rights to payment of \$8.0 million due October 28, 2021, pursuant to the Merger Agreement, which the Company did not pay. On November 15, 2021, the Company reached an agreement with the Representative to settle the litigation, under terms that, among other things, involve a substantial reduction in immediate payment obligations and deferrals of certain remaining milestone and other payment obligations over time, with an immediate payment of \$2.0 million for the milestone and periodic installments of \$500,000 per month payable from January 2022 through August 2022 and \$ 1.0 million per month payable from September 2022 through July 2023 until an aggregate of \$17.0 million is received.

During the year ended December 31, 2021, the Company paid an aggregate of \$ 5.0 million in cash related to the Merger Agreement.

**Note 5 - Other Receivables**

Other receivables consisted of the following:

	December 31,	
	2021	2020
Research and development tax credits	\$ -	\$ 493,906
Other	-	57,583
Total other receivables	<u>\$ -</u>	<u>\$ 551,489</u>

At December 31, 2020, research and development tax credits was comprised of the 2020 refundable tax credits for research conducted in France and Europe. During the year ended December 31, 2020, the Company received the 2017, 2018 and 2019 refundable tax credits. During the year ended December 31, 2021, the Company received the 2020 refundable tax credits.

At December 31, 2020, other consisted of amounts due from U.S. research and development tax credits. There were no other receivables as of December 31, 2021.

**Note 6 - Property, Equipment and Leasehold Improvements**

Property, equipment and leasehold improvements consisted of the following:

	December 31,	
	2021	2020
Laboratory equipment	\$ -	\$ 2,410
Computer equipment and software	11,540	19,676
Office equipment	48,278	5,483
Leasehold improvements	28,000	29,163
Total property, plant, and equipment	87,818	56,732
Less accumulated depreciation	(14,708)	(38,403)
Property, plant and equipment, net	<u>\$ 73,110</u>	<u>\$ 18,329</u>

Depreciation expense was approximately \$15,000 for the year ended December 31, 2021 and \$38,000, including \$10,000 of write-offs for the year ended December 31, 2020.

For the year ended December 31, 2021, approximately \$15,000 of depreciation was included in general and administrative expense.

For the year ended December 31, 2020, approximately \$33,000 of depreciation was included in research and development expense and approximately \$15,000 of depreciation was included in general and administrative expense.

**Note 7 - Intangible Assets and Goodwill**

*Patents*

Pursuant to the Mayoly APA entered into in March 2019 (see Note 15), in which the Company purchased all remaining rights, title and interest in and to adrulipase from Mayoly, the Company recorded Patents in the amount of approximately \$3.8 million as follows:

Common stock issued at signing to Mayoly	\$ 1,740,959
Due to Mayoly at December 31, 2019	449,280
Due to Mayoly at December 31, 2020	393,120
Assumed Mayoly liabilities and forgiveness of Mayoly debt	1,219,386
	<u>\$ 3,802,745</u>

Intangible assets are as follows:

	December 31,	
	2021	2020
Patents	\$ 3,802,745	\$ 3,802,745
Less accumulated amortization	(1,450,757)	(923,209)
Intangible asset impairment	(2,351,988)	-
Patents, net	<u>\$ -</u>	<u>\$ 2,879,536</u>

Amortization expense was approximately \$528,000 for both years ended December 31, 2021, and 2020, respectively.

During the year ended December 31, 2021, the Company recorded impairment charges of approximately \$ 2.4 million related to patents that the Company determined were no longer sufficient for the commercialization of adrulipase.

Goodwill is as follows:

	<b>Goodwill</b>
Balance on January 1, 2020	\$ 1,886,686
Foreign currency translation	167,362
Balance on December 31, 2020	2,054,048
Foreign currency translation	(142,343)
Balance on December 31, 2021	<u>\$ 1,911,705</u>

#### **Note 8 - Accounts Payable and Accrued Expense**

Accounts payable and accrued expense consisted of the following:

	<b>December 31, 2021</b>	<b>December 31, 2020</b>
Trade payables	\$ 2,681,914	\$ 1,558,591
Accrued expenses	419,070	127,012
Total accounts payable and accrued expenses	<u>\$ 3,100,984</u>	<u>\$ 1,685,603</u>

#### **Note 9 - Note Payable**

##### *Directors and Officer's Liability Insurance*

On November 30, 2021, the Company entered into a 9-month financing agreement for its directors and officer's liability insurance in the amount of approximately \$957,000 that bears interest at an annual rate of 3.99%. Monthly payments, including principal and interest, of approximately \$81,000 per month. The balance due under this financing agreement was approximately \$641,000 at December 31, 2021.

On November 30, 2020, the Company entered into a 9-month financing agreement for its directors and officer's liability insurance in the amount of approximately \$620,000 that bears interest at an annual rate of 4.250%. Monthly payments, including principal and interest, of approximately \$70,000 per month. The balance due under this financing agreement was approximately \$552,000 at December 31, 2020.

##### *CARES ACT PPP Loan*

In April 2020, the Company applied for and received a CARES Act Paycheck Protection Program ("PPP") loan of approximately \$ 179,000 through the Small Business Administration ("SBA"). In May 2020, the Company returned the loan in full after analysis of the updated guidance from the U.S. Department of Treasury and the SBA regarding the eligibility for such loans.

#### **Note 10 – Convertible Debt**

##### *The ADEC Note Offering*

On February 14, 2019, the Company entered into a Note Purchase Agreement (the "ADEC NPA") with ADEC Private Equity Investments, LLC ("ADEC"), pursuant to which the Company issued to ADEC two Senior Convertible Notes (each an "ADEC Note," and together, the "ADEC Notes"), in the principal amount of \$1.0 million per ADEC Note, resulting in gross proceeds to the Company of \$2.0 million.

In December 2019, the Company repaid \$ 1,550,000 principal amount of the ADEC Notes and on January 2, 2020 repaid the remaining principal balance of \$450,000 plus outstanding accrued interest of approximately \$104,000. As of December 31, 2021 and 2020, no ADEC Notes were outstanding.

**Senior Convertible Promissory Note Offering**

On December 20, 2019, the Company began an offering of (i) Senior Convertible Promissory Notes (each a "Promissory Note," and together, the "Promissory Notes") in the principal amount of up to \$8.0 million to certain accredited investors (the "Note Investors"), and (ii) warrants ("Note Warrants") to purchase shares of Common Stock, each pursuant to Note Purchase Agreements entered into by and between the Company and each of the Note Investors (the "Promissory NPAs") (the "Promissory Note Offering").

In December 2019, the Company issued Promissory Notes to the Note Investors in the aggregate principal amount of approximately \$ 3.4 million. The Promissory Notes were scheduled to mature on September 20, 2020, accrue interest at a rate of 9% per annum, and were convertible, at the sole option of the holder, into shares of Common Stock (the "Promissory Note Conversion Shares") at a price of \$9.70 per share (the "Conversion Option"). The Promissory Notes could be prepaid by the Company at any time prior to the maturity date in cash without penalty or premium (the "Prepayment Option").

During January 2020, the Company issued Promissory Notes to the Note Investors in the aggregate principal amount of approximately \$ 3.5 million.

As additional consideration for the execution of the Promissory NPA, each Note Investor also received Note Warrants to purchase that number of shares of Common Stock equal to one-half (50%) of the Promissory Note Conversion Shares issuable upon conversion of the Promissory Notes (the "Note Warrant Shares"). The Note Warrants have an exercise price of \$10.70 per share and expire five years from the date of issuance. In addition, all of the Note Warrants, other than those issued in the December 20, 2019 closing (covering an aggregate of 237,435 shares of Common Stock) contain a provision prohibiting exercise until the expiration of six months from the date of issuance. The Company and each Note Investor executed a Registration Rights Agreement (the "RRA"), pursuant to which the Company agreed to file a registration statement. The Company filed a registration statement with the SEC on February 7, 2020 covering the Promissory Note Conversion Shares and Note Warrant Shares, but that registration statement was not declared effective and was subsequently withdrawn by the Company. On July 27, 2020, the Company filed a separate registration statement in connection with the Series B Private Placement and the Exchange described in Note 12, which also covers the Note Warrant Shares. That registration statement was declared effective on September 21, 2020.

In connection with the three closings in January 2020 of the Promissory Note Offering, the Company paid aggregate placement agent fees of approximately \$277,000, which fees were based on (i) 9% of the aggregate principal amount of the Promissory Notes issued to the Note Investors introduced by the placement agent, and (ii) a non-accountable expense allowance of 1% of the gross proceeds from the Promissory Note Offering. In addition, the placement agent was issued January Placement Agent Warrants, to purchase an aggregate of 19,973 shares of Common Stock. 4,150 of these January Placement Agent Warrants have an exercise price of \$ 12.10 per share and 15,824 of these January Placement Agent Warrants have an exercise price of \$ 14.20 per share.

The Company determined the Prepayment Option feature represents a contingent call option. The Company evaluated the Prepayment Option in accordance with ASC 815-15-25 and determined that the Prepayment Option feature is clearly and closely related to the debt host instrument and is not an embedded derivative requiring bifurcation. Additionally, the Company determined the Conversion Option represents an embedded call option. The Company evaluated the Conversion Option in accordance with ASC 815-15-25 and determined that the Conversion Option feature meets the scope exception from ASC 815 and is not an embedded derivative requiring bifurcation.

The Company evaluated the Promissory Notes for a beneficial conversion feature in accordance with ASC 470-20 and determined that at each commitment date the effective conversion price was below the closing stock price (market value), and the Convertible Notes contained a beneficial conversion feature.

Pursuant to the January 2020 closings of the Promissory Note Offering, the principal amount of approximately \$ 3.5 million was first allocated based on the relative fair value of the Promissory Notes and the Note Warrants. The fair value of the Note Warrants amounted to approximately \$2.4 million. Then the beneficial conversion feature was calculated, which amounted to approximately \$1.8 million. The Company incurred debt issuance costs of approximately \$ 0.5 million related to the offering. The initial carrying value of the Promissory Notes issued amounted to approximately \$0.1 million.

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On June 1, 2020, the Company entered into an amendment to a certain Promissory Note in the principal amount of \$ 100,000 issued on December 20, 2019 to Edward J. Borkowski, the chairman of the Board, to increase the Conversion Price to \$10.70 per share (the "Note Amendment"). The Company evaluated the Note Amendment transaction in accordance with ASC 470-50 and determined the Note Amendment did not constitute a substantive modification of the Promissory Note and that the transaction should be accounted for as a debt modification with no accounting treatment required.

During the year ended December 31, 2020, the Company recognized approximately \$ 4.9 million of interest expense related to these Promissory Notes, including amortization of debt discount related to the value of the Note Warrants of approximately \$1.5 million, amortization of the beneficial conversion feature of approximately \$ 2.3 million, amortization of debt discount related to debt issuance costs of approximately \$0.8 million, and accrued interest expense of approximately \$0.3 million.

As of December 31, 2021 and 2020, no Promissory Notes were outstanding.

*Exchange of Promissory Notes into Series B Convertible Preferred Stock*

As more fully discussed in Note 12, on July 16, 2020, in connection with the Series B Private Placement, approximately 937.00 shares of Series B Preferred Stock, Series B Warrants to purchase 468,499 shares of Common Stock, and Exchange Warrants to purchase 177,294 shares of Common Stock were issued to certain holders of the Promissory Notes in exchange for such Promissory Notes for aggregate consideration of approximately \$7.2 million consisting of approximately \$ 6.9 million aggregate outstanding principal amount, together with accrued and unpaid interest thereon through the date of the Series B Private Placement of approximately \$0.3 million.

The Company prepaid the remaining outstanding balance of \$25,000 aggregate principal amount of Promissory Notes, together with accrued and unpaid interest thereon through the prepayment date of approximately \$1,000, held by those holders who did not participate in the Exchange. Following these transactions, no Promissory Notes remain outstanding.

*Accounting for the Exchange of Promissory Notes into Series B Private Placement*

The Company determined the Exchange of the Promissory Notes into Series B Preferred Stock and related warrants should be recognized as an extinguishment of the Promissory Notes, which resulted in a loss on extinguishment of approximately \$0.6 million in the year ended December 31, 2020. Additionally, the Company recorded interest expense of approximately \$ 0.8 million in the year ended December 31, 2020 related to the remaining unamortized discount resulting from initial beneficial conversion feature of the Promissory Notes on closing date of the Exchange.

**Note 11 – Other Liabilities**

Other liabilities consisted of the following:

	December 31,	
	2021	2020
<b>Current</b>		
Lease liabilities	\$ 77,989	\$ 57,417
Other liabilities	14,818	-
Liabilities related to Merger consideration	8,000,000	-
	<u>\$ 8,092,807</u>	<u>\$ 57,417</u>
<b>Long-term</b>		
Lease liabilities	\$ 311,138	\$ 19,123
Liabilities related to Merger consideration	\$ 7,000,000	\$ -
	<u>\$ 7,311,138</u>	<u>\$ 19,123</u>

As of December 31, 2021, other current liabilities and other long-term liabilities included \$ 8,000,000 and \$7,000,000, respectively, related to the Merger Agreement (See Note 4).

#### **Note 12 – Equity**

Our certificate of incorporation, as amended and restated (the “*Charter*”) authorized the issuance of up to 50,000,000 shares of Common Stock, par value \$ 0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share.

On February 24, 2021 the Company held a Special Meeting of Stockholders (the “*Special Meeting*”), whereby, the shareholders approved, among others, the following proposals: (i) amending the Company’s Certificate of Incorporation to increase the authorized shares of its Common Stock to 250,000,000 shares from 150,000,000 shares, and (ii) amending the Company’s Charter to authorize the Board to effect a reverse stock split of both the issued and outstanding and authorized shares of Common Stock, at a specific ratio, ranging from one-for-five (1:5) to one-for-ten (1:10), any time prior to the one-year anniversary date of the Special Meeting, with the exact ratio to be determined by the Board (the “*Reverse Split*”). On September 13, 2021, the Company effected a reverse stock split, whereby every ten shares of the Company’s issued and outstanding common stock were converted automatically into one issued and outstanding share of common stock, with a corresponding 1-for-10 reduction in the number of authorized shares of common stock, but without any change in the par value per share. All share and per share amounts have been retroactively restated to reflect the Reverse Split and the Company effectively cancelled approximately 1,706 shares of Common Stock.

On February 14, 2022 the Company held its Annual Meeting of Stockholders (the “*Annual Meeting*”), whereby, the shareholders approved, among others, the following proposals: (i) amending the Company’s Certificate of Incorporation to increase the authorized shares of its Common Stock to 50,000,000 shares from 25,000,000 shares.

#### **Common Stock**

The Company had 14,855,848 and 3,115,030 shares of its Common Stock issued and outstanding at December 31, 2021 and 2020, respectively.

Each holder of Common Stock is entitled to one vote for each share of Common Stock held on all matters submitted to a vote of the stockholders. Our Charter and Amended and Restated Bylaws (the “*Bylaws*”) do not provide for cumulative voting rights.

In addition, the holders of our Common Stock will be entitled to receive ratably such dividends, if any, as may be declared by the Board out of legally available funds; however, the current policy of our Board is to retain earnings, if any, for operations and growth. Upon liquidation, dissolution or winding-up, the holders of our Common Stock will be entitled to share ratably in all assets that are legally available for distribution.

Holders of our Common Stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the Common Stock. The rights, preferences and privileges of the holders of Common Stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

#### **Preferred Stock**

The Board is authorized to divide the preferred stock into any number of series, fix the designation and number of each such series, and determine or change the designation, relative rights, preferences, and limitations of any series of preferred stock. The Board may increase or decrease the number of shares initially fixed for any series, but no decrease may reduce the number below the shares then outstanding and duly reserved for issuance.

On July 16, 2020, we authorized 5,194.805195 shares as Series B Preferred Stock and issued approximately 2,912.58 shares of Series B Preferred Stock, with approximately 2,282.22 shares of Series B Preferred Stock remaining authorized but undesignated and unissued.



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On January 5, 2021, we authorized 75,000 shares as Series C Preferred Stock. Shares of Series C Preferred Stock converted into Common Stock (or Prefunded Warrants, as applicable) or redeemed shall be canceled and shall not be reissued. As of December 31, 2021, 0 shares of Series C Preferred Stock were issued and outstanding, with approximately 41,903 shares of Series C Preferred Stock remaining authorized but unissued.

At December 31, 2021, the Company had approximately 662.25 shares of preferred stock issued and outstanding with approximately 9,999,337.75 shares of preferred stock remaining authorized but unissued.

**Series B Convertible Preferred Stock**

Pursuant to the Certificate of Designation of Rights and Preferences of the Series B Preferred Stock (the "*Series B Certificate of Designation*"), the terms of the Series B Preferred Stock are as follows:

Ranking

The Series B Preferred Stock will rank senior to the Common Stock with respect to distributions of assets upon the liquidation, dissolution or winding up of the Company.

Stated Value

Each share of Series B Preferred Stock has a stated value of \$ 7,700, subject to adjustment for stock splits, combinations and similar events (the "*Series B Stated Value*").

Dividends

Each holder of shares of Series B Preferred Stock, in preference and priority to the holders of all other classes or series of stock of the Company, is entitled to receive dividends, commencing from the date of issuance. Such dividends may be paid by the Company only when, as and if declared by the Board, out of assets legally available therefor, semiannually in arrears on the last day of June and December in each year, commencing December 31, 2020, at the dividend rate of 9.0% per year, which is cumulative and continues to accrue on a daily basis whether or not declared and whether or not the Company has assets legally available therefor. The Company may pay such dividends at its option either in cash or in kind in additional shares of Series B Preferred Stock (rounded down to the nearest whole share), provided the Company must pay in cash the fair value of any such fractional shares in excess of \$100.00. During the year ended December 31, 2020, the Company issued a total of approximately 117.62 shares of Series B Preferred Stock for payment of dividends amounting to approximately \$906,000. During the year ended December 31, 2021, the Company accrued dividends amounting to approximately \$678,000, of which approximately \$213,000 of accrued dividends were issued as shares of Common Stock in connection with holders of Series B Preferred Stock exercising the Series B Exchange Rights.

Liquidation Preference: Liquidation Rights

Under the Certificate of Designations, each share of Series B Preferred Stock carries a liquidation preference equal to the Series B Stated Value (as adjusted thereunder) plus accrued and unpaid dividends thereon (the "*Liquidation Preference*").

If the Company voluntarily or involuntarily liquidates, dissolves or winds up its affairs, each holder of the Series B Preferred Stock will be entitled to receive out of the Company's assets available for distribution to stockholders, after satisfaction of liabilities to creditors, if any, but before any distribution of assets is made on the Common Stock or any of the Company's shares of stock ranking junior as to such a distribution to the Series B Preferred Stock, a liquidating distribution in the amount of the Stated Value of all such holder's Series B Preferred Stock plus all accrued and unpaid dividends thereon. At December 31, 2021 and 2020, the value of the liquidation preference of the Series B Preferred stocks aggregated to approximately \$5.6 million and \$21.4 million, respectively.

Conversion

Each share of Series B Preferred Stock will be convertible at the holder's option at any time, into Common Stock at a conversion rate equal to the quotient of (i) the Series B Stated Value divided by (ii) the initial conversion price of \$7.70, subject to specified adjustments for stock splits, cash or stock dividends, reorganizations, reclassifications other similar events as set forth in the Series B Certificate of Designations. In addition, at any time after the six month anniversary of the Series B Closing Date, if the closing sale price per share of Common Stock exceeds 250% of the initial conversion price, or \$19.25, for 20 consecutive trading days, then all of the outstanding shares of Series B Preferred Stock will automatically convert (the "Automatic Conversion") into such number of shares of Common Stock as is obtained by multiplying the number of shares of Series B Preferred Stock to be so converted, plus the amount of any accrued and unpaid dividends thereon, by the Series B Stated Value per share and dividing the result by the then applicable conversion price. The Series B Preferred Stock contains limitations that prevent the holder thereof from acquiring shares of Common Stock upon conversion (including pursuant to the Automatic Conversion) that would result in the number of shares beneficially owned by such holder and its affiliates exceeding 9.99% of the total number of shares of Common Stock outstanding immediately after giving effect to the conversion, which percentage may be increased or decreased at the holder's election not to exceed 19.99%.

Most Favored Nations Exchange Right

In the event the Company effects any issuance by the Company or any of its subsidiaries of Common Stock or Common Stock equivalents for cash consideration, or a combination of units thereof (a "Subsequent Financing"), each holder of the Series B Preferred Stock has the right, subject to certain exceptions set forth in the Series B Certificate of Designations, at its option, to exchange (in lieu of cash subscription payments) all or some of the Series B Preferred Stock then held (with a value per share of Series B Preferred Stock equal to the stated value, plus accrued and unpaid dividends thereon, of the Series B Preferred Stock (the "Exchange Amount")) for any securities or units issued in a Subsequent Financing on dollar-for-dollar basis (the "Series B Exchange Right").

As of March 28, 2022, (i) holders of approximately 1,846.80 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$14.4 million had previously elected to exercise their Series B Exchange Rights into Series C Preferred Stock, convertible into an aggregate of 1,921,645 shares of Common Stock (which conversion the Company has elected to make in full), and additional Investor Warrants exercisable for up to an aggregate of 1,921,645 shares of Common Stock, (ii) holders of approximately 13.80 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$114,000 had previously elected to exercise their Series B Exchange Rights into 33,500 shares of Common Stock with no warrants, and (iii) holders of approximately 17.05 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$145,000 had previously elected to exercise their Series B Exchange Rights into 104,735 shares of Common Stock, and additional Series C Warrants exercisable for up to an aggregate of 104,735 shares of Common Stock.

Voting

The holders of the Series B Preferred Stock, voting as a separate class, will have customary consent rights with respect to certain corporate actions of the Company. The Company may not take the following actions without the prior consent of the holders of at least a majority of the Series B Preferred Stock then outstanding: (a) authorize, create, designate, establish, issue or sell an increased number of shares of Series B Preferred Stock or any other class or series of capital stock ranking senior to or on parity with the Series B Preferred Stock as to dividends or upon liquidation; (b) reclassify any shares of Common Stock or any other class or series of capital stock into shares having any preference or priority as to dividends or upon liquidation superior to or on parity with any such preference or priority of Series B Preferred Stock; (c) amend, alter or repeal the Certificate of Incorporation or Bylaws of the Company and the powers, preferences, privileges, relative, participating, optional and other special rights and qualifications, limitations and restrictions thereof, which would adversely affect any right, preference, privilege or voting power of the Series B Preferred Stock; (d) issue any indebtedness or debt security, other than trade accounts payable, insurance premium financings and/or letters of credit, performance bonds or other similar credit support incurred in the ordinary course of business, or amend, renew, increase, or otherwise alter in any material respect the terms of any such indebtedness existing as of the date of first issuance of shares of Series B Preferred Stock; (e) redeem, purchase, or otherwise acquire or pay or declare any dividend or other distribution on (or pay into or set aside for a sinking fund for any such purpose) any capital stock of the Company; (f) declare bankruptcy, dissolve, liquidate, or wind up the affairs of the Company; (g) effect, or enter into any agreement to effect, a Change of Control (as defined in the Certificate of Designations); or (h) materially modify or change the nature of the Company's business.

#### **2014 Equity Incentive Plan**

The Company's Board and stockholders adopted and approved the Amended and Restated 2014 Omnibus Equity Incentive Plan (the "2014 Plan"), which took effect on May 12, 2014. From the adoption and approval of the 2020 Plan on September 11, 2020, no new awards have been or will be made under the 2014 Plan.

The 2014 Plan allowed for the issuance of securities, including stock options to employees, Board members and consultants. The number of shares of Common Stock reserved for issuance under the 2014 Plan could not exceed ten percent (10%) of the issued and outstanding shares of Common Stock on an as converted basis (the "As Converted Shares") on a rolling basis. For calculation purposes, the As Converted Shares included all shares of Common Stock and all shares of Common Stock issuable upon the conversion of outstanding preferred stock and other convertible securities but did not include any shares of Common Stock issuable upon the exercise of options, or other convertible securities issued pursuant to the 2014 Plan. The number of authorized shares of Common Stock reserved for issuance under the 2014 Plan was automatically be increased concurrently with the Company's issuance of fully paid and non-assessable shares of As Converted Shares. Shares were deemed to have been issued under the 2014 Plan solely to the extent actually issued and delivered pursuant to an award.

On July 16, 2020, the Board approved an amendment to the 2014 Plan. The amendment eliminates individual grant limits under the 2014 Plan that were intended to comply with the exemption for "performance-based compensation" under Section 162(m) of the Internal Revenue Code, which section has been repealed.

The Company issued an aggregate of 0 and 287,001 stock options, during the years ended December 31, 2021 and 2020, respectively, under the 2014 Plan (see Note 14). As of December 31, 2021, there were an aggregate of 310,250 total shares available under the 2014 Plan, of which 271,550 are issued and outstanding, and 38,700 shares are reserved subject to issuance of restricted stock and RSUs. Upon adoption of the 2020 Omnibus Equity Incentive Plan on September 11, 2020, the Company may no longer make grants under the 2014 Plan.

#### **2020 Equity Incentive Plan**

The Company's Board and stockholders adopted and approved the 2020 Omnibus Equity Incentive Plan (the "2020 Plan"), which took effect on September 11, 2020. The 2020 Plan allows for the issuance of securities, including stock options to employees, Board members and consultants. The initial number of shares of Common Stock available for issuance under the 2020 Plan is 1,000,000 shares, which will, on January 1 of each calendar year, unless the Board decides otherwise, automatically increase to equal ten percent (10%) of the total number of shares of Common Stock outstanding on December 31 of the immediately preceding calendar year, calculated on an As Converted Basis. As Converted Shares include all outstanding shares of Common Stock and all shares of Common Stock issuable upon the conversion of outstanding preferred stock, warrants and other convertible securities, but will not include any shares of Common Stock issuable upon the exercise of options and other convertible securities issued pursuant to either the 2014 Plan or the 2020 Plan. The number of shares permitted to be issued as "incentive stock options" ("ISOs") from is 1,500,000 under the 2020 Plan.

The Company issued an aggregate of 175,246 and 1,000 stock options under the 2020 Plan during the year ended December 31, 2021 and 2020, respectively. As of December 31, 2021, 1,000,000 total shares were available under the 2020 Plan, of which 176,246 were issued and outstanding and 823,754 shares were available for potential issuances.

As of January 1, 2022, the number of shares of Common Stock available for issuance under the 2020 Plan automatically increased to 2,114,360.

#### **Equity Line with Lincoln Park**

In November 2019, the Company entered into a purchase agreement (the "Equity Line Agreement"), together with a registration rights agreement (the "Lincoln Park Registration Rights Agreement"), with Lincoln Park. Under the terms of the Equity Line Agreement, Lincoln Park has committed to purchase up to \$ 15,000,000 of our Common Stock (the "Equity Line"). Upon execution of the Equity Line Agreement, the Company issued Lincoln Park 48,717 shares of Common Stock (the "Commitment Shares") as a fee for its commitment to purchase shares of our Common Stock under the Equity Line Agreement. The Commitment Shares had a grant date fair value of approximately \$297,000 and had no effect on expenses or stockholders' equity.

The remaining shares of our Common Stock that may be issued under the Equity Line Agreement may be sold by the Company to Lincoln Park at our discretion from time-to-time over a 30-month period commencing after the satisfaction of certain conditions set forth in the Equity Line Agreement, subject to the continued effectiveness of a registration statement covering such shares of Common Stock sold to Lincoln Park by the Company. The registration statement was filed with the SEC on December 31, 2019 and was declared effective on January 14, 2020.

Under the Equity Line Agreement, on any business day over the term of the Equity Line Agreement, the Company has the right, in its sole discretion, to present Lincoln Park with a purchase notice (each, a "Purchase Notice") directing Lincoln Park to purchase up to 15,000 shares of Common Stock per business day (the "Regular Purchase"). In each case, Lincoln Park's maximum commitment in any single Regular Purchase may not exceed \$1,000,000. The Equity Line Agreement provides for a purchase price per Purchase Share (the "Purchase Price") equal to the lesser of:

- the lowest sale price of Common Stock on the purchase date; and;
- the average of the three lowest closing sale prices for the Common Stock during the ten consecutive business days ending on the business day immediately preceding the purchase date of such shares.

In addition, on any date on which the Company submits a Purchase Notice to Lincoln Park, the Company also has the right, in its sole discretion, to present Lincoln Park with an accelerated purchase notice (each, an "Accelerated Purchase Notice") directing Lincoln Park to purchase an amount of stock (the "Accelerated Purchase") equal to up to the lesser of (i) three times the number of shares purchased pursuant to such Regular Purchase; and (ii) 30% of the aggregate shares of Common Stock traded during all or, if certain trading volume or market price thresholds specified in the Equity Line Agreement are crossed on the applicable Accelerated Purchase date, the portion of the normal trading hours on the applicable Accelerated Purchase date prior to such time that any one of such thresholds is crossed (such period of time on the applicable Accelerated Purchase Date, the "Accelerated Purchase Measurement Period"), provided that Lincoln Park will not be required to buy shares pursuant to an Accelerated Purchase Notice that was received by Lincoln Park on any business day on which the last closing trade price of Common Stock on the Nasdaq Capital Market (or alternative national exchange) is below \$2.50 per share. The purchase price per share for each such Accelerated Purchase will be equal to the lesser of:

- 97% of the volume weighted average price of the Company's common stock during the applicable Accelerated Purchase Measurement Period on the applicable Accelerated Purchase date; and;
- the closing sale price of Common Stock on the applicable Accelerated Purchase Date.

The Company may also direct Lincoln Park on any business day on which an Accelerated Purchase has been completed and all of the shares to be purchased thereunder have been properly delivered to Lincoln Park in accordance with the Equity Line Agreement, to purchase an amount of stock (the "Additional Accelerated Purchase") equal to up to the lesser of (i) three times the number of shares purchased pursuant to such Regular Purchase; and (ii) 30% of the aggregate number of shares of Common Stock traded during a certain portion of the normal trading hours on the applicable Additional Accelerated Purchase date as determined in accordance with the Equity Line Agreement (such period of time on the applicable Additional Accelerated Purchase date, the "Additional Accelerated Purchase Measurement Period"), provided that the closing price of the Company's common stock on the business day immediately preceding such business day is not below \$2.50 per share. Additional Accelerated Purchases will be equal to the lower of:

- 97% of the volume weighted average price of the Company's common stock during the applicable Additional Accelerated Purchase Measurement Period on the applicable Additional Accelerated Purchase; and;
- the closing sale price of Common Stock on the applicable Additional Accelerated Purchase.

Pursuant to the terms of the Equity Line Agreement, without first obtaining stockholder approval, the aggregate number of shares that the Company is permitted to sell to Lincoln Park thereunder, when aggregated with certain other private offerings of Common Stock, as applicable, may not exceed 19.99% of the Common Stock outstanding immediately prior to the execution of the Equity Line Agreement on November 13, 2019, unless the average price of all applicable sales thereunder exceeds \$7.00 per share calculated by reference to the "Minimum Price" under Nasdaq Listing Rule 5635(d). On September 11, 2020, the Company received stockholder approval for the issuances of the full \$15 million available under the Equity Line Agreement. There is approximately \$14.0 million of availability left for issuance pursuant to the Equity Line Agreement.

The Company issued an aggregate of 0, and 149,520 shares of Common Stock, during the years ended December 31, 2021 and 2020, respectively, in connection with the Equity Line Agreement, resulting in net proceeds to the Company of approximately \$0 and \$1.0 million, respectively.

#### **At The Market Agreement with H.C. Wainwright**

On May 26, 2021, the Company entered into the ATM Agreement with H.C. Wainwright & Co., LLC ("Wainwright"), as sales agent, pursuant to which the Company may issue and sell, from time to time, through Wainwright, shares of its Common Stock, and pursuant to which Wainwright may sell its Common Stock by any method permitted by law deemed to be an "at the market offering" as defined by Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the "Securities Act"). The Company will pay Wainwright a commission of 3.0% of the aggregate gross proceeds from each sale of Common Stock. As of May 26, 2021, the Company was authorized to offer and sell up to \$50 million of its Common Stock pursuant to the ATM Agreement. During the year ended December 31, 2021, the Company issued and sold an aggregate of 5,333,345 shares of Common Stock under the ATM Agreement for which the Company received gross proceeds of approximately \$19.2 million, less issuance costs incurred of approximately \$601,000.

#### **Common Stock Issuances**

##### *2021 Issuances*

During the year ended December 31, 2021, the Company issued an aggregate of 122,230 shares of its Common Stock to consultants with a grant date fair value of approximately \$ 1.3 million for investor relations services provided, which was recorded as stock-based compensation and included as part of general and administrative expense.

During the year ended December 31, 2021, the Company issued an aggregate 7,500 shares of its Common Stock with a grant date fair value of approximately \$94,000 in connection with the settlement with the Company's former investment bank, which was recorded as stock-based compensation and included as part of general and administrative expense.

During the year ended December 31, 2021, the Company issued an aggregate of 3,125,460 shares of Common Stock upon the conversion of an aggregate of 33,097.10 shares of Series C Preferred Stock with a stated value of approximately \$24.7 million plus accrued dividends of approximately \$ 198,000.

During the year ended December 31, 2021, the Company issued an aggregate of 945,644 shares of Common Stock upon the exercise of an aggregate of 952,588 investor warrants, including an aggregate of 399,187 pre-funded warrants (see Note 13).

During the year ended December 31, 2021, the Company issued an aggregate of 258,278 shares of Common Stock upon the conversion of an aggregate of 258.08 shares of Series B Preferred Stock with a stated value of approximately \$2.0 million plus accrued dividends of approximately \$ 3,000.

During the year ended December 31, 2021, the Company issued an aggregate of 33,500 shares of Common Stock upon the exchange of 13.80 shares of Series B Preferred Stock with a stated value of approximately \$0.1 million plus accrued dividends of approximately \$ 8,000 into shares of Common Stock at \$ 3.40 per share.

During the year ended December 31, 2021, the Company issued an aggregate of 1,625,454 shares of Common Stock in connection with the March 2021 Offering and July 2021 Offering, as detailed below.

*2020 Issuances*

During the year ended December 31, 2020, holders of shares of Series B Preferred Stock converted approximately 254.54 shares of Series B Preferred Stock into an aggregate of 256,581 shares of Common Stock at the stated conversion price of \$7.70 per share.

During the year ended December 31, 2020, the Company issued an aggregate of 18,284 shares of its Common Stock to consultants with a total grant date fair value of approximately \$144,000 for investor relations services provided, which was recorded as stock-based compensation and included as part of general and administrative expense.

During the year ended December 31, 2020, the Company issued 6,252 restricted shares of Common Stock to a consultant as payment of \$ 135,000 of accounts payable for investor relations services.

During the year ended December 31, 2020, the Company issued an aggregate of 10,594 shares of its Common Stock to outside Board members as payment of Board fees with an aggregate grant date fair value of approximately \$131,000 that was recorded as stock-based compensation, included as part of general and administrative expense. The aggregate effective settlement price was \$12.40 per share, and each individual stock issuance was based on the closing stock price of the Common Stock on the initial date the payable was accrued.

***Restricted Stock and Restricted Stock Units***

Restricted stock refers to shares of Common Stock subject to vesting based on certain service, performance, and market conditions. Restricted stock unit awards ("RSUs") refer to an award under the 2014 Plan, which constitutes a promise to grant shares of Common Stock at the end of a specified restriction period.

During the year ended December 31, 2020, an aggregate of 1,008 restricted shares of Common Stock, subject to service conditions, vested with a total grant date fair value of approximately \$36,000 and was recorded as stock-based compensation, included as part of general and administrative expense.

During the year ended December 31, 2020, an aggregate 400 unvested restricted shares of Common Stock were forfeited.

As of December 31, 2021, and 2020, the Company had an aggregate unrecognized restricted Common Stock expense of approximately \$ 393,000 and \$393,000, respectively, which will be recognized when vesting of certain milestones will become probable.

***The Series B Private Placement and the Exchange***

On July 16, 2020 (the "*Series B Closing Date*"), the Company consummated a private placement offering (the "*Series B Private Placement*") whereby the Company entered into a Convertible Preferred Stock and Warrant Securities Purchase Agreement (the "*Series B Purchase Agreement*") with certain accredited and institutional investors (the "*Series B Investors*"). Pursuant to the Series B Purchase Agreement, the Company issued an aggregate of 2,912,583,005 shares of Series B Convertible Preferred Stock, par value \$ 0.0001 per share (the "*Series B Preferred Stock*"), at a price of \$7,700.00 per share, initially convertible into an aggregate of 2,912,576 shares of Common Stock at \$ 7.70 per share, together with warrants (the "*Series B Warrants*") to purchase an aggregate of 1,456,283 shares of Common Stock at an exercise price of \$ 8.50 per share. The amount of the Series B Warrants is equal to 50% of the shares of Common Stock into which the Series B Preferred Stock is initially convertible.

In connection with the Series B Private Placement, an aggregate of approximately 1,975.58 shares of Series B Preferred Stock initially convertible into 1,975,575 shares of Common Stock and related 987,784 Series B Warrants were issued for cash consideration, resulting in aggregate gross proceeds of approximately \$15.2 million and aggregate net proceeds to the Company of approximately \$13.2 million after deducting placement agent compensation and offering expenses.

An aggregate of approximately 937,000 shares of Series B Preferred Stock initially convertible into 937,001 shares of Common Stock and related Series B Warrants to purchase 468,499 shares of Common Stock were issued to certain Series B Investors (the "*Exchange Investors*") in exchange for consideration consisting of approximately \$6.9 million aggregate outstanding principal amount, together with accrued and unpaid interest thereon through the Series B Closing Date of approximately \$0.3 million, of certain Senior Convertible Promissory Notes (the "*Promissory Notes*") issued between December 20, 2019 and January 9, 2020 (the "*Exchange*"), pursuant to an Exchange Addendum (the "*Exchange Addendum*") executed by the Company and the Exchange Investors. As additional consideration to the Exchange Investors, the Company also issued certain additional warrants (the "*Exchange Warrants*") to purchase an aggregate of 177,294 shares of Common Stock at an exercise price of \$8.50 per share. The amount of the Exchange Warrants is equal to 25% of the shares of Common Stock into which such Promissory Notes were originally convertible upon the initial issuance thereof.

Pursuant to the Series B Private Placement and the Series B Purchase Agreement, for purposes of complying with Nasdaq Listing Rule 5635(c) and 5635(d), the Company was required to hold a meeting of its stockholders not later than 60 days following the Series B Closing Date to seek approval (the "*Stockholder Approval*") for, among other things, the issuance of shares of Common Stock upon (i) full conversion of the Series B Preferred Stock; and (ii) full exercise of the Series B Warrants and the Exchange Warrants. In the event the Stockholder Approval was not received on or prior to the 90th day following the Series B Closing Date, subject to extension upon the prior written approval of the holders of at least a majority of the Series B Preferred Stock then outstanding, the Company would have been required to repurchase all of the then outstanding shares of Series B Preferred Stock at a price equal to 150% of the stated value thereof plus accrued and unpaid dividends thereon, in cash. On September 11, 2020, the Company received Stockholder Approval.

The Company prepaid the remaining outstanding balance of \$25,000 aggregate principal amount of Promissory Notes, together with accrued and unpaid interest thereon through the prepayment date of approximately \$1,000, held by those holders who did not participate in the Exchange. Following these transactions, no Promissory Notes remain outstanding.

In connection with the Series B Private Placement, the Company paid the placement agent 9.0% of the gross cash proceeds received by the Company from investors introduced by the placement agent and 4.0% of the gross cash proceeds received by the Company for all other investors, or approximately \$1.3 million. The Company also paid the placement agent a non-accountable cash fee equal to 1.0% of the gross cash proceeds and a cash financial advisory fee equal to 3.0% of the outstanding principal balance of the Promissory Notes that were submitted in the Exchange, or approximately \$0.3 million in additional cash fees in the aggregate. In addition, the Company issued to the placement agent warrants to purchase up to 137,746 shares of Common Stock (the "*July Placement Agent Warrants*"). The July Placement Agent Warrants have substantially the same terms as the Series B Warrants, except the July Placement Agent Warrants have an exercise price of \$9.60 per share, are not callable, provide for cashless exercise and are not exercisable until the earlier of stockholder approval of the Series B Private Placement and the date that is six months following the issuance thereof.

#### *Accounting for the Series B Private Placement*

Upon receiving Shareholder Approval on September 11, 2020, the Company classified the Series B Preferred Stock as permanent equity because no features provide for redemption by the holders of the Series B Preferred Stock or conditional redemption, which is not solely within the Company's control, and there are no unconditional obligations in that (1) the Company must or may settle in a variable number of its equity shares and (2) the monetary value is predominantly fixed, varying with something other than the fair value of the Company's equity shares or varying inversely in relation to the Company's equity shares.

Because the Series B Preferred Stock contain certain embedded features that could affect the ultimate settlement of the Series B Preferred Stock, the Company analyzed the instrument for embedded derivatives that require bifurcation. The Company's analysis began with determining whether the Series B Preferred Stock is more akin to equity or debt. The Company evaluated the following criteria/features in this determination: redemption, voting rights, collateral requirements, covenant provisions, creditor and liquidation rights, dividends, conversion rights and exchange rights. The Company determined that the Series B Preferred Stock was more akin to equity than to debt when evaluating the economic characteristics and risks of the entire Series B Preferred Stock, including the embedded features. The Company then evaluated the embedded features to determine whether their economic characteristics and risks were clearly and closely related to the economic characteristics and risks of the Series B Preferred Stock. Since the Series B Preferred Stock was determined to be more akin to equity than debt, and the underlying that causes the value of the embedded features to fluctuate would be the value of the Company's common stock, the embedded features were considered clearly and closely related to the Series B Preferred Stock. As a result, the embedded features would not need to be bifurcated from the Series B Preferred Stock.

Any beneficial conversion features related to the exercise of the Most Favored Nation exchange right or the application of the Mandatory Conversion provision will be recognized upon the occurrence of the contingent events based on its intrinsic value at the commitment date.

The Company concluded the freestanding Series B Warrants did not contain any provision that would require liability classification and therefore should be classified in stockholder's equity, based on their relative fair value.

The proceeds from the Series B Private Placement were allocated to the Series B Preferred Stock and Series B Warrants based on their relative fair values. The total proceeds of approximately \$22.4 million were allocated as follows: approximately \$16.5 million to the Series B Preferred Stock, and approximately \$5.9 million to the Series B Warrants. After allocation of the proceeds, the effective conversion price of the Series B Preferred Stock was determined to be beneficial and, as a result, the Company recorded a deemed dividend of approximately \$8.2 million equal to the intrinsic value of the beneficial conversion feature and recognized on the closing date and recorded as a reduction of income available to common stockholders in computing basic and diluted loss per share. The total offering costs of approximately \$2.0 million were recognized in equity.

#### **January 2021 Offerings**

On December 31, 2020, the Company entered into a securities purchase agreement (the "*Series C Purchase Agreement*"), pursuant to which the Company agreed to sell in a registered direct offering 5,333,333 shares of Series C Preferred Stock, at a price of \$750.00 per share, initially convertible into an aggregate of 533,333 shares of Common Stock, at an initial stated value of \$750.00 per share and a conversion price of \$7.50 per share (the "*January 2021 Registered Direct Offering*").

Concurrently with the January 2021 Registered Direct Offering, in a private placement offering pursuant to the Series C Purchase Agreement (the "*January 2021 Private Placement*," and together with the January 2021 Registered Direct Offering, the "*January 2021 Offerings*"), the Company agreed to sell an additional 5,333,333 shares of Series C Preferred Stock at the same price as the Series C Preferred Stock offered in the January 2021 Registered Direct Offering and convertible on the same terms and warrants (the "*January 2021 Investor Warrants*") to purchase up to an aggregate of 1,066,666 shares of Common Stock, with an exercise price of \$8.00 per share and a maturity date of July 6, 2026.

In connection with the January 2021 Private Placement, the Company entered into a registration rights agreement, dated as of December 31, 2020, pursuant to which the Company filed a registration statement on Form S-1 (File No. 333-252087) to register the shares of Common Stock issuable upon the conversion of the Series C Preferred Stock sold in the January 2021 Private Placement and the exercise of the January 2021 Investor Warrants. The registration statement was declared effective by the SEC on January 21, 2021.

On January 6, 2021, the January 2021 Offerings closed, and the Company received aggregate gross proceeds of approximately \$8.0 million. The net proceeds to the Company from the January 2021 Offerings, after deducting the placement agent's fees and expenses, was approximately \$6.8 million. The Company used the net proceeds to fund the payment of cash consideration to FWB under the FWB License Agreement, and for other general corporate purposes.

The Company paid the placement agent a cash fee equal to 8.0% and a management fee equal to 1.0% of the aggregate gross proceeds received by the Company in the January 2021 Offerings, or approximately \$700,000. The Company also agreed to issue to the placement agent or its designees warrants (the "*January 2021 Placement Agent Warrants*") exercisable for up to 74,667 shares of Common Stock, which is equal to 7.0% of the amount determined by dividing the gross proceeds of the January 2021 Offerings by the offering price per share of Common Stock, or \$7.50. The January 2021 Placement Agent Warrants have substantially the same terms as the January 2021 Investor Warrants, except they are exercisable at \$9.375 per share, or 125% of the effective purchase price per share of the Series C Preferred Stock issued. The Company also reimbursed the placement agent \$35,000 for non-accountable expenses, \$125,000 for legal fees and expenses and other out-of-pocket expenses and \$12,900 for clearing fees.



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Pursuant to the January 2021 Private Placement and the Series C Purchase Agreement, the Company was required to hold a meeting of its stockholders not later than March 31, 2021 to seek approval (the "2021 Stockholder Approval") for, among other things, the issuance of shares of Common Stock upon (i) full conversion of the Series C Preferred Stock; and (ii) full exercise of the January 2021 Investors Warrants and the January 2021 Placement Agent Warrants, and to increase the authorized shares to 25,000,000 from 15,000,000.

On February 24, 2021, the Company received the 2021 Stockholder Approval, and all outstanding shares of Series C Preferred Stock were converted to Common Stock.

*Accounting for the January 2021 Offerings*

Upon receiving the 2021 Stockholder Approval on February 24, 2021, the Company classified the Series C Preferred Stock as permanent equity because no features provide for redemption by the holders of the Series C Preferred Stock or conditional redemption, which is not solely within the Company's control, and there are no unconditional obligations in that (1) the Company must or may settle in a variable number of its equity shares and (2) the monetary value is predominantly fixed, varying with something other than the fair value of the Company's equity shares or varying inversely in relation to the Company's equity shares.

Because the Series C Preferred Stock contains certain embedded features that could affect the ultimate settlement of the Series C Preferred Stock, the Company analyzed the instrument for embedded derivatives that require bifurcation. The Company's analysis began with determining whether the Series C Preferred Stock is more akin to equity or debt. The Company evaluated the following criteria/features in this determination: redemption, voting rights, collateral requirements, covenant provisions, creditor and liquidation rights, dividends, and conversion rights. The Company determined that the Series C Preferred Stock was more akin to equity than to debt when evaluating the economic characteristics and risks of the entire Series C Preferred Stock, including the embedded features. The Company then evaluated the embedded features to determine whether their economic characteristics and risks were clearly and closely related to the economic characteristics and risks of the Series C Preferred Stock. Since the Series C Preferred Stock was determined to be more akin to equity than debt, and the underlying that causes the value of the embedded features to fluctuate would be the value of the Company's common stock, the embedded features were considered clearly and closely related to the Series C Preferred Stock. As a result, the embedded features would not need to be bifurcated from the Series C Preferred Stock.

The Company concluded the freestanding January 2021 Investor Warrants did not contain any provision that would require liability classification and therefore should be classified in stockholder's equity, based on their relative fair value.

The proceeds from the January 2021 Offerings were allocated to the Series C Preferred Stock and the January 2021 Investor Warrants based on their relative fair values. The total proceeds of approximately \$6.8 million, net of \$1.2 million offering costs, were allocated as follows: approximately \$4.6 million to the Series C Preferred Stock and approximately \$3.4 million to the January 2021 Investor Warrants. After allocation of the proceeds, the effective conversion price of the Series C Preferred Stock was determined to be beneficial and, as a result, the Company recorded a deemed dividend of approximately \$4.5 million equal to the intrinsic value of the beneficial conversion feature and recognized on the closing date and recorded as a reduction of income available to common stockholders in computing basic and diluted loss per share. The total offering costs of approximately \$1.2 million were recognized in equity.

*Series B Most Favored Nations (MFN) Exchanges into the January 2021 Offerings*

Subject to consummating the January 2021 Offerings, the holders of the Series B Preferred Stock became entitled to exercise their Series B Exchange Right to exchange their Series B Preferred Stock at the Series B Exchange Amount into the Series C Preferred Stock and related January 2021 Investor Warrants.

During the year ended December 31, 2021, holders of approximately 1,877.64 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$14.5 million had elected to exercise their Series B Exchange Rights into 19,216.45 shares of Series C Preferred Stock, convertible into an aggregate of 1,921,645 shares of Common Stock and additional January 2021 Investor Warrants exercisable for up to an aggregate of 1,921,645 shares of Common Stock. Immediately upon issuance of the Series C Preferred Stock pursuant to the Series B Exchange Right prior to February 24, 2021, an aggregate of 13,166.62 shares of Series C Preferred Stock were converted into 1,316,662 shares of Common Stock, at an effective conversion price of \$ 7.70 per share, and an aggregate of 3,344.63 shares of Series C Preferred Stock, convertible into 33,446 shares of Common Stock, remained unconverted pending stockholder approval. Upon receiving the stockholder approval on February 24, 2021, the Company elected to convert all 334.46 remaining shares of Series C Preferred Stock issued pursuant to the Series B Exchange Right, plus accrued dividends thereon of approximately \$2,000 into 33,699 shares of Common Stock.

*Accounting for the Series B Exchanges into the January 2021 Offerings*

During the year ended December 31, 2021, pursuant to the Series B Exchange Right, the Company issued an aggregate of 19,140.14 shares of Series C Preferred Stock and warrants to purchase an aggregate of 1,913,971 shares of Common Stock in connection with the exchange of approximately 1,839.76 shares of Series B Preferred Stock. The exercise of all of these warrants and the conversion of a portion of these shares of Series C Preferred Stock were prohibited until the Company received stockholder approval on February 24, 2021. The Company analyzed the exchanges pursuant to the Series B Exchange Right from preferred stock to preferred stock qualitatively and determined that the exchanges result in a substantive change and should be accounted for as an extinguishment. As such, for the year ended December 31, 2021, the Company recognized an aggregate deemed dividend of approximately \$21.0 million as calculated by the difference in the carrying value of the Series B Preferred Stock exchanged and the fair value of the Series C Preferred Stock and January 2021 Investor Warrants issued on each exchange date.

**March 2021 Offering**

On March 7, 2021, the Company entered into a securities purchase agreement (the "*March 2021 Purchase Agreement*"), pursuant to which the Company agreed to sell, in a registered direct offering (the "*March 2021 Offering*") priced at the market under Nasdaq rules, (i) 580,000 shares of Common Stock, (ii) pre-funded warrants (the "*March 2021 Pre-Funded Warrants*") to purchase up to 205,854 shares of Common Stock, with an exercise price of \$ 0.01 per share and no expiration term and (iii) warrants (the "*March 2021 Warrants*") to purchase an aggregate of 392,927 shares of Common Stock with an exercise price of \$12.10 per share and an expiration term of five years from the date of issuance. The price per share of March 2021 Offering was \$ 12.725.

On March 10, 2021, the March 2021 Offering closed and the Company received aggregate gross proceeds of approximately \$ 10.0 million, excluding the net proceeds, if any, from the exercise of the March 2021 Warrants. The net proceeds to the Company from the March 2021 Offering were approximately \$9.1 million, after deducting the placement agent's fees and expenses.

The Company paid the placement agent a cash fee equal to 8.0% of the aggregate gross proceeds received by the Company, or approximately \$800,000. The Company also agreed to issue the placement agent or its designees warrants (the "*March 2021 Placement Agent Warrants*") exercisable for up to 55,010 shares of Common Stock, which is equal to 7.0% of the amount determined by dividing the gross proceeds of the March 2021 Offering by the offering price per share of Common Stock, or \$12.725. The March 2021 Placement Agent Warrants have substantially the same terms as the March 2021 Warrants, except they are exercisable at \$15.906 per share, or 125% of the effective purchase price per share of Common Stock issued. The Company also reimbursed the placement agent \$35,000 for non-accountable expenses, \$50,000 for legal fees and expenses and other out-of-pocket expenses and approximately \$16,000 for clearing fees.

The March 2021 Offering was made pursuant to the Company's effective shelf registration statement on Form S-3 (Registration No. 333-231954) originally filed with the SEC on June 21, 2019 and declared effective on June 25, 2019. The Company filed a prospectus supplement with the SEC in connection with the sale of such securities in the March 2021 Offering.

The Company concluded the freestanding March 2021 Warrants and the March 2021 Placement Agent Warrants did not contain any provisions that would require liability classification and therefore should be classified in stockholder's equity.

#### **July 2021 Offering**

On July 22, 2021, the Company entered into an underwriting agreement with Wainwright pursuant to which the Company agreed to sell, in an upsized firm commitment offering, 909,091 shares of Common Stock to Wainwright at an offering price to the public of \$5.50 per share, less underwriting discounts and commissions. On July 27, 2021, pursuant to the terms of the underwriting agreement, Wainwright exercised its 30-day over-allotment option in full to purchase an additional 136,363 shares of Common Stock at the same offering price to the public, less underwriting discounts and commissions. The offering closed on July 27, 2021.

The Company received net proceeds from the offering of approximately \$ 5.1 million. The Company paid Wainwright an underwriting discount equal to 8.0% of the gross proceeds of the offering, and reimbursed Wainwright for a non-accountable expense allowance of \$35,000, \$125,000 in legal fees and \$ 15,950 for clearing expenses. Additionally, as partial compensation for Wainwright's services as underwriter in the offering, the Company issued to Wainwright (or its designees) warrants to purchase 73,178 shares of Common Stock equal to 7.0% of the aggregate number of shares of Common Stock sold in the offering (the "July 2021 Wainwright Warrants"). The July 2021 Wainwright Warrants have a term of five (5) years from the date of the offering and an exercise price of \$6.875 per share (equal to 125% of the offering price per share), subject to adjustments as provided in the terms of the July 2021 Wainwright Warrants. The July 2021 Wainwright Warrants provide for liquidated damages and compensation for buy-ins, if the Company fails to timely deliver the underlying Common Stock within specified timeframes from exercise. The July 2021 Wainwright Warrants do not provide for any Black Scholes payout in the event of a fundamental transaction relating to the Company.

The Company concluded the freestanding July 2021 Wainwright Warrants did not contain any provisions that would require liability classification and therefore should be classified in stockholder's equity.

#### **Note 13 - Warrants**

During the year ended December 31, 2021, in connection with the January 2021 Offerings, the Company issued January 2021 Investor Warrants to the investor to purchase an aggregate of 1,066,666 shares of Common Stock. These January 2021 Investor Warrants were issued on January 6, 2021, are exercisable at \$8.00 per share and expire on July 6, 2026. The exercise of the January 2021 Investor Warrants was prohibited until the Company received stockholder approval on February 24, 2021. The total grant date fair value of these warrants was determined to be approximately \$6.0 million, as calculated using the Black-Scholes model, and were recorded as additional paid in capital based on their relative fair value of approximately \$3.4 million.

During the year ended December 31, 2021, in connection with the conversion of the Series C Preferred Stock issued in the January 2021 Offerings, the Company issued pre-funded warrants to the investor to purchase an aggregate of 193,333 shares of Common Stock. These pre-funded warrants were issued on January 6, 2021, are exercisable at \$0.01 per share and do not expire. The total grant date fair value of these pre-funded was determined to be approximately \$1.6 million and was recorded as additional paid in capital.

During the year ended December 31, 2021, in connection with the January 2021 Offerings, the Company issued January 2021 Placement Agent Warrants to the placement agent and/or their designees to purchase an aggregate of 74,667 shares of Common Stock. These January 2021 Placement Agent Warrants were issued on January 6, 2021, are exercisable at \$9.375 per share and expire on July 6, 2026. The total grant date fair value of these warrants was determined to be approximately \$ 392,000, as calculated using the Black-Scholes model, and had no effect on shareholders' equity.

During the year ended December 31, 2021, the Company issued January 2021 Investor Warrants to purchase an aggregate of 1,921,645 shares of Common Stock to holders of Series B Preferred Stock elected to exercise their Series B Exchange Rights into Series C Preferred Stock and related warrants, as referenced in Note 12. These January 2021 Investor Warrants were issued between January 13, 2021 and June 9, 2021, are exercisable at \$8.00 per share and expire on July 6, 2026. The exercise of these warrants was prohibited until the Company received stockholder approval on February 24, 2021. The total grant date fair value of these warrants was determined to be approximately \$21.0 million, as calculated using the Black-Scholes model, and were recorded as a deemed dividend and recognized on the exchange date and recorded as a reduction of income available to common stockholders in computing basic and diluted loss per share.

During the year ended December 31, 2021, in connection with the March 2021 Offering, the Company issued March 2021 Warrants to the investor to purchase an aggregate of 392,927 shares of Common Stock. These March 2021 Warrants were issued on March 10, 2021, are exercisable at \$12.10 per share and expire five years from the date of issuance. The total grant date fair value of these warrants was determined to be approximately \$3.5 million, as calculated using the Black-Scholes model, and were recorded as additional paid in capital.

During the year ended December 31, 2021, in connection with March 2021 Offering, the Company issued pre-funded warrants to the investor to purchase an aggregate of 205,855 shares of Common Stock. These pre-funded warrants were issued on March 10, 2021, are exercisable at \$0.10 per share and do not expire. The total grant date fair value of these pre-funded was determined to be approximately \$2.6 million and was recorded as additional paid in capital.

During the year ended December 31, 2021, in connection with the March 2021 Offering, the Company issued March 2021 Placement Agent Warrants to the placement agent and/or their designees to purchase an aggregate of 55,010 shares of Common Stock. These March 2021 Placement Agent Warrants were issued on March 10, 2021, are exercisable at \$15.906 per share and expire five years from the date of issuance. The total grant date fair value of these warrants was determined to be approximately \$ 453,000, as calculated using the Black-Scholes model, and had no effect on shareholders' equity.

During the year ended December 31, 2021, in connection with the July 2021 Offering, the Company issued July 2021 Placement Agent Warrants to the placement agent and/or their designees to purchase an aggregate of 73,181 shares of Common Stock. These July 2021 Placement Agent Warrants were issued on July 22, 2021, are exercisable at \$6.875 per share and expire five years from the date of issuance. The total grant date fair value of these warrants was determined to be approximately \$263,000, as calculated using the Black-Scholes model, and had no effect on shareholders' equity.

During the year ended December 31, 2021, the Company issued warrants to a consultant to purchase an aggregate of 20,000 shares of Common Stock that are subject to service-based milestone vesting conditions for investor relations services. These warrants were issued on February 8, 2021, are exercisable at \$16.90 per share and expire four years from the date of issuance. The total grant date fair value of these warrants was determined to be approximately \$214,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2021, warrants to purchase an aggregate of 952,588 shares of Common Stock, including the pre-funded warrants issued in January 2021 and March 2021, were exercised for 945,644 shares of Common Stock resulting in cash proceeds of approximately \$ 4.9 million.

For the year ended December 31, 2020, in connection with the January 2020 closings of the Promissory Note Offering, the Company issued Note Warrants to investors to purchase an aggregate of 181,326 shares of Common Stock with the issuance of the Promissory Notes (See Note 12). These Note Warrants were issued in January 2020, became exercisable commencing six (6) months following issuance at \$10.70 per share and expire five years from issuance. The total grant date fair value of these warrants was determined to be approximately \$1.6 million, as calculated using the Black-Scholes model, and were recorded as a debt discount based on their relative fair value.

Additionally, in connection with the January 2020 closings of the Promissory Note Offering, the Company issued the placement agent warrants to purchase an aggregate of 19,973 shares of Common Stock to the placement agent and/or their designees (See Note 12). These warrants were issued in January 2020, were immediately exercisable, and expire five years from issuance. 4,147 of these warrants are exercisable at \$ 12.10 per share and 15,824 of these warrants are exercisable at \$ 14.20 per share. The total grant date fair value of these warrants was determined to be approximately \$174,000, as calculated using the Black-Scholes model, and was charged to debt discount and amortized over the life of the debt.

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For the year ended December 31, 2020, in connection with the closing of the Exchange (see Note 12), the Company issued Exchange Warrants to certain investors to purchase an aggregate of 177,294 shares of Common Stock with the issuance of the Series B Preferred Stock as referenced in Note 12. These Exchange Warrants were issued on July 16, 2020, are exercisable commencing six (6) months following the issuance date at \$8.50 per share and expire five years from issuance. The total grant date fair value of the Exchange warrants was determined to be approximately \$987,000, as calculated using the Black-Scholes model, and were recorded as part of the loss on extinguishment (See Note 10).

For the year ended December 31, 2020, in connection with the closing of the Series B Private Placement, the Company issued placement agent warrants to purchase an aggregate of 137,746 shares of Common Stock to the placement agent and/or their designees. These warrants were issued in July 2020, became exercisable commencing six (6) months following issuance at \$9.60 per share and expire five years from issuance. The total grant date fair value of these warrants was determined to be approximately \$745,000, as calculated using the Black-Scholes model, and were recorded as equity.

For the year ended December 31, 2020, in connection with the settlement and release with our former Chief Executive Officer, Johan "Thijs" Spoor in July 2020, the Company granted Mr. Spoor warrants to purchase an aggregate of 15,000 shares of Common Stock. The warrants were immediately exercisable, have an exercise price equal to \$ 10.00 per share, a five-year term and may be exercised pursuant to a cashless exercise provision commencing six months from the issuance date. The total grant date fair value of these warrants was determined to be approximately \$86,000, as calculated using the Black-Scholes model, and were included in the gain on settlement.

During year ended December 31, 2020, warrants to purchase an aggregate of 8,075 shares of Common Stock expired with exercise prices ranging between \$32.50 and \$73.70 per share.

Warrant transactions for the years ending December 31, 2021 and 2020 were as follows:

	Warrants	Exercise Price Per Share	Weighted Average Price
<b>Warrants outstanding and exercisable on January 1, 2020</b>	<b>537,829</b>	<b>\$ 10.70 - 73.70</b>	<b>\$ 25.30</b>
Granted during the period	1,987,968	\$ 8.50 - 14.20	\$ 8.80
Expired during the period	(8,075)	\$ 32.50 - 73.70	\$ 41.10
Exercised during the period	-	-	-
<b>Warrants outstanding and exercisable on December 31, 2020</b>	<b>2,517,722</b>	<b>\$ 8.50 - 73.70</b>	<b>\$ 12.20</b>
<b>Warrants outstanding and exercisable on January 1, 2021</b>	<b>2,517,722</b>	<b>\$ 8.50 - 73.70</b>	<b>\$ 12.20</b>
Granted during the period	4,095,602	\$ 0.01 - 16.90	7.46
Expired during the period	(133,346)	\$ 0.01 - 14.20	\$ 33.98
Exercised during the period	(952,588)	\$ 15.00 - 73.70	\$ 5.32
<b>Warrants outstanding and exercisable on December 31, 2021</b>	<b>5,527,390</b>	<b>\$ 0.80 - 6.60</b>	<b>\$ 9.49</b>

Warrants exercisable at December 31, 2021 were as follows:

	Exercise Price	Number of Shares Under Warrants	Weighted Average Remaining Contract Life in Years	Weighted Average Exercise Price
	\$ 0.00 - 9.99	4,582,860	4.12	
	\$ 10.00 - 19.99	803,631	3.54	
	\$ 20.00 - 29.99	32,003	1.56	
	\$ 30.00 - 39.99	43,463	0.57	
	\$ 40.00 - 49.99	16,425	0.27	
	\$ 50.00 - 59.99	48,208	0.40	
	\$ 60.00 - 69.99	800	0.42	
<b>Totals</b>		<b>5,527,390</b>	<b>3.95</b>	<b>\$ 9.49</b>

The weighted average fair value of warrants granted during the years ended December 31, 2021 and 2020, was \$ 8.63 and \$5.90 per share, respectively. The grant date fair values were calculated using the Black-Scholes model with the following weighted average assumptions:

	December 31,	
	2021	2020
Expected life (in years)	4.38	5
Volatility	83.8- 90.8%	81.0- 85.0%
Risk-free interest rate	0.36- 0.90%	0.28- 1.67%
Dividend yield	-%	-%

**Note 14 – Stock Options**

Under the 2014 Plan and the 2020 Plan, the fair value of options granted is estimated on the grant date using the Black-Scholes option valuation model. This valuation model for stock-based compensation expense requires the Company to make assumptions and judgments about the variables used in the calculation, including the expected term (weighted-average period of time that the options granted are expected to be outstanding), the volatility of the common stock price and the assumed risk-free interest rate. The Company recognizes stock-based compensation expense for only those shares expected to vest over the requisite service period of the award. No compensation cost is recorded for options that do not vest and the compensation cost from vested options, whether forfeited or not, is not reversed.

On June 30, 2021, the Board rescinded and cancelled certain stock option awards previously made under the 2014 Plan (the "Prior Awards") to James Sapirstein, the Company's President, Chief Executive Officer and Chairman of the Board, and Daniel Schneiderman, the Company's former Chief Financial Officer, and issued new stock options awards (the "New Awards") under the 2020 Plan in an equivalent amount and with equivalent exercise price, vesting and expiration terms to the Prior Awards. This action was approved by the Board following the recommendation of a special committee of the Board upon review of certain matters raised in a stockholder litigation demand letter received by the Company on or about July 27, 2020, as previously disclosed in the Company's definitive proxy statement, dated August 11, 2020, in connection with stockholder approval of the 2020 Plan.

The terms of the New Awards to Mr. Sapirstein (the "New Sapirstein Awards") covering 90,000 shares of the Common Stock at an exercise price of \$ 8.50 per share comprised of (i) stock options to purchase 30,000 shares of Common Stock that vest over a term of 18 months in 18 equal monthly installments starting with the first monthly installment on February 16, 2022, (ii) stock options to purchase 20,000 shares of Common Stock that vested immediately upon the grant of such stock options, and (iii) stock options to purchase 40,000 shares of Common Stock subject to milestone-based vesting based upon the achievement of certain strategic milestones specified by the Board. The Company determined the cancellation and reissue of the New Sapirstein Awards did not result in modification accounting under ASC 718 as there was no change between the fair value of the original stock options immediately prior to the modification and the grant date fair value of the replacement stock options and no change to vesting conditions. The Company will recognize a total of approximately \$359,000, representing the original unexpensed amount over the remaining requisite service periods of the New Sapirstein Awards.

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The terms of the New Awards to Mr. Schneiderman (the "New Schneiderman Awards") covering an aggregate of 28,500 shares of Common Stock at an exercise price of \$ 8.50 per share comprised of (i) stock options to purchase 25,000 shares of Common Stock, of which stock options to purchase 7,986 shares of Common Stock vested immediately upon the grant of such stock options and the remaining stock options to purchase 17,014 shares of Common Stock will vest over a term of 2 years and 1 month in 25 equal monthly installments, and (ii) stock options to purchase 3,500 shares of Common Stock, of which stock options to purchase 1,750 shares of Common Stock vested immediately upon the grant of such stock options and the remaining options to purchase 1,750 shares of Common Stock vest over a term of 19 months in 19 equal monthly installments. The Company determined the cancellation and reissue of the New Schneiderman Awards did not result in modification accounting under ASC 718 as there was no change between the fair value of the original stock options immediately prior to the modification and the grant date fair value of the replacement stock options and no change to vesting conditions. The Company will recognize a total of \$192,000 over the remaining requisite service periods of the New Schneiderman Awards, which amounts to the unexpensed amount of the original stock option grants.

During the year ended December 31, 2021, the Company issued stock options under the 2020 Plan to employees, excluding the New Awards to purchase an aggregate of 35,100 shares of Common Stock with strike prices ranging from \$6.40 to \$15.40 per share and a term of ten years that vest in equal monthly installments over three years. These options had a total fair value of approximately \$247,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2021, the Company issued stock options under the 2020 Plan to outside Board members to purchase an aggregate of 21,646 shares of Common Stock with strike prices ranging from \$6.40 to \$9.70 per share and a term of ten years that vest in equal monthly installments over fiscal year 2021. These options had a total fair value of approximately \$153,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2021, excluding the Prior Awards described above, stock options to purchase an aggregate of 134,477 shares of Common Stock under the 2014 Plan were cancelled with strike prices ranging between \$8.50 and \$36.00 per share.

During the year ended December 31, 2021, excluding the Prior Awards described above, stock options to purchase an aggregate of 8,604 shares of Common Stock under the 2020 Plan were cancelled with strike prices ranging between \$9.23 and \$14.30 per share.

During the year ended December 31, 2021, stock options to purchase an aggregate of 91,362 shares of Common Stock, subject to service-based milestone vesting conditions, vested with a total grant date fair value of approximately \$552,000 which was recorded as stock-based compensation, of which approximately \$ 435,000 was included as part of general and administrative expense and approximately \$117,000 was included as part of research and development expense.

During the year ended December 31, 2021, stock options to purchase an aggregate of 95,500 shares of Common Stock, subject to performance-based milestone vesting conditions, vested due to the Company achieving certain clinical milestones, with a total grant date fair value of approximately \$623,000 which was recorded as stock-based compensation, of which approximately \$ 253,000 was included as part of general and administrative expense and approximately \$370,000 was included as part of research and development expense. Stock options to purchase an aggregate of 43,750 shares of Common Stock, with a total grant date fair value of approximately \$ 427,000, vested due to the Company completing enrollment of the Phase 2 OPTION 2 clinical trial. Stock options to purchase an aggregate of 21,000 shares of Common Stock, with a total grant date fair value of approximately \$148,000, vested due to the Company's public announcement of topline data for the Phase 2 OPTION 2 clinical trial. Stock options to purchase an aggregate of 750 shares of Common Stock, with a total grant date fair value of approximately \$8,000, vested due to the Company completing enrollment of the Phase 2 Combination Trial in Europe. Stock options to purchase an aggregate of 10,000 shares of Common Stock, with a total grant date fair value of approximately \$40,000, vested due to the Company determining that initiating a U.S. Phase 1 clinical trial for any product other than adripilase became probable in connection with the initiation of the COVID-19 niclosamide trial.

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During the year ended December 31, 2020, the Company issued stock options under the 2014 Plan to purchase an aggregate of 33,500 shares of Common Stock with a strike price of \$ 10.30 per share and a term of ten years to its chief financial officer that vest in equal monthly installments over three years. These options had a total grant date fair value of approximately \$ 281,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2020, the Board approved an amended and restated option grant to its chief financial officer, amending and restating a grant previously made on January 2, 2020, to reduce the amount of shares issuable upon exercise of such option to be the maximum number of shares Mr. Schneiderman was eligible to receive under the 2014 Plan on the original grant date, or 30,000 shares (on a split adjusted basis), due to the 2014 Plan provisions relating to the individual grant limits that were intended to comply with the exemption for "performance-based compensation" under Section 162(m) of the Internal Revenue Code, which section has been repealed. The Board also approved the issuance of a replacement option covering the balance of shares intended to be issued at that time, or 3,500 shares. The original stock option has an exercise price of \$ 10.30, the closing sale price of Common Stock on January 2, 2020, which was the date of its original grant, and the replacement stock option has an exercise price of \$8.50, the closing sale price of the Common Stock on its date of grant. Both the original stock option and the replacement stock option vest over a term of three years, in 36 equal monthly installments on each monthly anniversary of January 2, 2020. On the issuance date, 633 shares had vested, and 2,867 shares were unvested with approximately \$24,000 of unrecognized expense. The Company determined the cancellation and reissue of these stock options resulted in an effective repricing of the stock options and modification accounting should be applied under ASC 718. The fair value of the original stock options immediately prior to the modification was approximately \$23,000 and the grant date fair value of the replacement stock options was approximately \$24,000. The Company will recognize a total of approximately \$25,000 over the remaining requisite service period through January 1, 2023.

During the year ended December 31, 2020, the Company issued stock options under the 2014 Plan to purchase an aggregate of 46,000 shares of Common Stock with a strike price of \$ 9.70 per share and a term of ten years to certain Board members that vested in equal installments over 2020. These options had a total grant date fair value of approximately \$210,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2020, the Company issued stock options under the 2014 Plan to purchase an aggregate of 204,000 shares of Common Stock with a strike price of \$ 8.50 per share and a term of ten years to its employees. 60,000 of these stock options are subject to performance-based milestone vesting conditions and 144,000 of these stock options vest in equal monthly installments over three years. These options had a total grant date fair value of approximately \$1.4 million, as calculated using the Black-Scholes model.

During the year ended December 31, 2020, the Company issued stock options under the 2020 Plan to purchase an aggregate of 1,000 shares of Common Stock with a strike price of \$ 9.70 per share and a term of ten years to a consultant that are subject to performance-based milestone vesting conditions. These options had a total grant date fair value of approximately \$8,000, as calculated using the Black-Scholes model.

During the year ended December 31, 2020, stock options under the 2014 Plan to purchase an aggregate of 60,008 shares of Common Stock, subject to service-based milestone vesting conditions, vested with a total grant date fair value of approximately \$ 361,000 and recorded as stock-based compensation, of which approximately \$341,000 was included as part of general and administrative expense and approximately \$20,000 was included as part of research and development expense.

During the year ended December 31, 2020, stock options under the 2014 Plan to purchase an aggregate of 5,000 shares of Common Stock, subject to performance-based vesting conditions, vested with a total grant date fair value of approximately \$20,000 and were recorded as stock-based compensation, and included as part of general and administrative expense due to the Company achieving clinical milestones.

During the year ended December 31, 2020, stock options under the 2014 Plan to purchase an aggregate of 48,722 shares of Common Stock were cancelled with strike prices ranging between \$8.50 and \$44.80 per share.



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The weighted average fair value of stock options granted during the year ended December 31, 2021 and 2020 was \$ 9.05 and \$8.90, respectively per share.

The fair values were estimated on the grant dates using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	December 31,	
	2021	2020
Contractual term (in years)	9-10	5 - 10
Volatility	83.8 - 90.6%	81.0 - 85.0%
Risk-free interest rate	0.93 - 1.69%	0.62 - 1.88%
Dividend yield	-%	-%

The expected term of the options is based on expected future employee exercise behavior. Volatility is based on the historical volatility of the Company's Common Stock if available or of several public entities that are similar to the Company. The Company bases volatility this way because it may not have sufficient historical transactions in its own shares on which to solely base expected volatility. The risk-free interest rate is based on the U.S. Treasury rates at the date of grant with maturity dates approximately equal to the expected term at the grant date. The Company has not historically declared any dividends and does not expect to in the future.

The Company realized no income tax benefit from stock option exercises in each of the periods presented due to recurring losses and valuation allowances.

During the years ended December 31, 2021 and 2020, stock option activity under the 2014 Plan and 2020 Plan was as follows:

	Number of Shares	Average Exercise Price	Remaining Contract Life (Years)	Intrinsic Value
<b>Stock options outstanding on January 1, 2021</b>	<b>407,028</b>	<b>\$ 13.80</b>	<b>7.94</b>	<b>\$ -</b>
Granted during the period	175,246	\$ 8.61	8.32	\$ -
Canceled during the period	(143,082)	\$ 10.47	2.87	\$ -
<b>Stock options outstanding on December 31, 2021</b>	<b>439,192</b>	<b>\$ 11.58</b>	<b>7.28</b>	<b>\$ -</b>
<b>Exercisable on December 31, 2021</b>	<b>281,418</b>	<b>\$ 13.41</b>	<b>6.55</b>	<b>\$ -</b>
<b>Non-vested stock options outstanding on January 1, 2021</b>	<b>274,065</b>	<b>\$ 9.90</b>	<b>8.42</b>	<b>\$ -</b>
Granted during the period	175,246	\$ 8.61	8.32	\$ -
Vested during the period	(186,862)	\$ 10.41	-	\$ -
Canceled during the period	(104,521)	\$ 9.84	-	\$ -
<b>Non-vested stock options outstanding on December 31, 2021</b>	<b>157,928</b>	<b>\$ 8.32</b>	<b>8.58</b>	<b>\$ -</b>

	Number of Shares	Average Exercise Price	Remaining Contract Life (Years)	Intrinsic Value
<b>Stock options outstanding on January 1, 2020</b>	<b>167,750</b>	<b>\$ 21.70</b>	<b>5.37</b>	<b>\$ -</b>
Granted during the period	288,001	\$ 8.90	9.06	\$ -
Canceled during the period	(48,723)	\$ 27.70	-	\$ -
<b>Stock options outstanding on December 31, 2020</b>	<b>407,028</b>	<b>\$ 13.80</b>	<b>7.94</b>	<b>\$ -</b>
<b>Exercisable on December 31, 2020</b>	<b>132,963</b>	<b>\$ 17.80</b>	<b>6.67</b>	<b>\$ -</b>
<b>Non-vested stock options outstanding on January 1, 2020</b>	<b>88,350</b>	<b>\$ 13.30</b>	<b>6.26</b>	<b>\$ -</b>
Granted during the period	288,001	\$ 8.90	9.06	\$ -
Vested during the period	(84,063)	\$ 9.80	-	\$ -
Canceled during the period	(18,223)	\$ 17.50	-	\$ -
<b>Non-vested stock options outstanding on December 31, 2020</b>	<b>274,065</b>	<b>\$ 9.90</b>	<b>8.42</b>	<b>\$ -</b>

As of December 31, 2021, the Company had unrecognized stock-based compensation expense of approximately \$ 1.1 million. Approximately \$0.9 million of this unrecognized expense will be recognized over the average remaining vesting term of the stock options of 1.85 years. Approximately \$40,000 of this unrecognized expense will vest upon initiating a Phase 3 clinical trial in the U.S. for adrulipase. Approximately, \$140,000 of this unrecognized expense will vest upon the public release of topline data of the complete Combination Trial results. Approximately, \$ 140,000 of this unrecognized expense will vest upon signing of a definitive term sheet with Board approval for either (i) a strategic licensing, distribution, or commercialization agreement for adrulipase with a bona fide partner, or (ii) the substantial sale of the Company or the adrulipase asset, on or before December 31, 2021. The Company will recognize the expense related to these milestones when the milestones become probable.

As of December 31, 2020, the Company had unrecognized stock-based compensation expense of approximately \$ 2.0 million. Approximately \$1.0 million of this unrecognized expense will be recognized over the average remaining vesting term of the stock options of 8.42 years.

Approximately \$440,000 of this unrecognized expense will vest upon enrollment completion of the ongoing OPTION 2 Trial. Approximately \$41,000 of this unrecognized expense will vest upon enrollment completion of the ongoing Combination Trial. Approximately \$168,000 of this unrecognized expense will vest upon the public release of topline data of the complete OPTION 2 Trial results. Approximately \$40,000 of this unrecognized expense will vest upon initiating a Phase 3 clinical trial in the U.S. for adrulipase. Approximately \$40,000 of this unrecognized expense will vest upon initiating a U.S. Phase 1 clinical trial for any product other than adrulipase. Approximately, \$140,000 of this unrecognized expense will vest upon the public release of topline data of the complete Combination Trial results. Approximately, \$ 140,000 of this unrecognized expense will vest upon signing of a definitive term sheet with Board approval for either (i) a strategic licensing, distribution or commercialization agreement for adrulipase with a bona fide partner, or (ii) the substantial sale of the Company or the adrulipase asset, on or before December 31, 2021. The Company will recognize the expense related to these milestones when the milestones become probable.

#### Note 15 – Agreements

##### *License Agreement with First Wave Bio, Inc.*

On December 31, 2020, we entered into the FWB License Agreement, pursuant to which FWB granted us a worldwide, exclusive right to develop, manufacture, and commercialize FWB's proprietary immediate release and enema formulations of niclosamide (the "*Niclosamide Product*") for the fields of treating ICI-AC and COVID-19 in humans.

In consideration of the license and other rights granted by FWB, we agreed to pay FWB a \$ 9.0 million upfront cash payment due within 10 days, which was paid in January 2021 and are obligated to make an additional payment of \$1.25 million due on June 30, 2021. In addition, we are obligated to pay potential milestone payments to FWB totaling up to \$37.0 million for each indication, based upon the achievement of specified development and regulatory milestones. Under the FWB License Agreement we were obligated to pay FWB royalties as a mid-single digit percentage of net sales of the Niclosamide Product, subject to specified reductions. We were also obligated to issue to FWB junior convertible preferred stock, initially convertible into \$3.0 million worth of Common Stock based upon the volume weighted average price of the Common Stock for the five-day period immediately preceding the date of the FWB License Agreement, or \$ 9.118 per share, convertible into an aggregate of 32,902 shares of Common Stock. This was classified as a liability in the consolidated balance sheet because of certain NASDAQ restrictions and the requirement to obtain stockholder approval.

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On January 8, 2021, we entered into a securities purchase agreement with FWB (the "*FWB Purchase Agreement*") to issue the junior convertible preferred stock to the FWB License Agreement. Pursuant to the FWB Purchase Agreement, we issued to FWB 3,290,196 shares of Series C Preferred Stock, at an initial stated value of \$750.00 per share and a conversion price of \$ 7.50 per share, which is convertible into an aggregate of 32,902 shares of Common Stock. The shares of Series C Preferred Stock automatically converted into Common Stock upon the stockholder approval on February 24, 2021. The FWB Purchase Agreement contains demand and piggyback registration rights with respect to the Common Stock issuable upon conversion.

The conversion price of the Series C Preferred Stock was determined to be beneficial and, as a result, the Company recorded a deemed dividend of approximately \$ 230,000 equal to the intrinsic value of the beneficial conversion feature and recognized on the issuance date and recorded as a reduction of income available to common stockholders in computing basic and diluted loss per share.

Upon the 2021 Stockholder Approval on February 24, 2021, the Company recognized a change in fair value of approximately \$ 0.5 million based on the difference in fair value of the \$ 3.0 million liability initially recorded pursuant to the FWB License Agreement as of December 31, 2020 and the fair value of approximately \$2.5 million of Series C Preferred Stock issued pursuant to the FWB Purchase Agreement to settle the liability.

Following the 2021 Stockholder Approval, the shares of Series C Preferred Stock were automatically converted into Common Stock.

Upon consummating the Merger on September 13, 2021, the FWB License Agreement was effectively canceled.

**Mayoly Agreement**

On March 27, 2019, the Company and Laboratories Mayoly Spinder ("*Mayoly*") entered into an Asset Purchase Agreement (the "*Mayoly APA*"), pursuant to which the Company purchased substantially all remaining rights, title and interest in and to adrulipase. Further, upon execution of the Mayoly APA, the Joint Development and License Agreement (the "*JDLA*") previously executed by AzurRx SAS and Mayoly was assumed by the Company. In addition, the Company granted to Mayoly an exclusive, royalty-bearing right to revenue received from commercialization of adrulipase within certain territories.

**Employment Agreements**

*James Sapirstein*

Effective October 8, 2019, the Company entered into an employment agreement with Mr. Sapirstein to serve as its President and Chief Executive Officer for a term of three years, subject to further renewal upon agreement of the parties. The employment agreement with Mr. Sapirstein originally provided for a base salary of \$450,000 per year, which was subsequently increased to \$ 480,000 per year during the year ended December 31, 2020. In addition to the base salary, Mr. Sapirstein is eligible to receive (i) a cash bonus of up to 40% of his base salary on an annual basis, based on certain milestones that are yet to be determined; (ii) 1% of net fees received by the Company upon entering into license agreements with any third-party with respect to any product current in development or upon the sale of all or substantially all assets of the Company; (iii) an award grant of 20,000 restricted stock units ("*RSUs*") which are scheduled to vest as follows (a) 10,000 shares upon the first commercial sale of adrulipase in the U.S. and (b) 10,000 shares upon the total market capitalization of the Company exceeding \$ 1.0 billion for 20 consecutive trading days; (iv) a grant of 30,000 10-year stock options to purchase shares of common stock with an exercise price equal to \$5.60 per share, which are scheduled to vest as follows (a) 5,000 shares upon the Company initiating its next Phase 2 clinical trial in the U.S. for adrulipase, (b) 5,000 shares upon the Company completing its next or subsequent Phase 2 clinical trial in the U.S. for adrulipase, (c) 10,000 shares upon the Company initiating a Phase 3 clinical trial in the U.S. for adrulipase, and (d) 10,000 shares upon the Company initiating a Phase 1 clinical trial in the U.S. for any product other than adrulipase. Mr. Sapirstein is entitled to receive 20 days of paid vacation, participate in full employee health benefits and receive reimbursement for all reasonable expenses incurred in connection with his services to the Company.

In the event that Mr. Sapirstein's employment is terminated by the Company for Cause, as defined in his employment agreement, or by Mr. Sapirstein voluntarily, then he will not be entitled to receive any payments beyond amounts already earned, and any unvested equity awards will terminate. In the event that Mr. Sapirstein's employment is terminated as a result of an Involuntary Termination Other than for Cause, as defined in his employment agreement, Mr. Sapirstein will be entitled to receive the following compensation: (i) severance in the form of continuation of his salary (at the base salary rate in effect at the time of termination, but prior to any reduction triggering Good Reason (as such term is defined in Mr. Sapirstein's employment agreement) for a period of twelve months following the termination date; (ii) payment of Mr. Sapirstein's premiums to cover COBRA for a period of twelve months following the termination date; and (iii) a prorated annual bonus.

*Daniel Schneiderman*

Effective January 2, 2020, the Company entered into an employment agreement with Mr. Schneiderman to serve as the Company's Chief Financial Officer for a term of three years, subject to further renewal upon agreement of the parties. The employment agreement with Mr. Schneiderman provides for a base salary of \$285,000 per year. In addition to the base salary, Mr. Schneiderman is eligible to receive (a) an annual milestone cash bonus based on certain milestones that will be established by the Company's Board or the Compensation Committee, and (b) a grant of stock options to purchase 33,500 shares of common stock with an exercise price of \$10.30 per share, which shall vest in three equal portions on each anniversary date of the execution of Mr. Schneiderman's employment agreement, commencing on January 2, 2021, the first anniversary date of the agreement. Mr. Schneiderman is entitled to receive 20 days of paid vacation, participate in full employee health benefits and receive reimbursement for all reasonable expenses incurred in connection with his service to the Company. The Company may terminate Mr. Schneiderman's employment agreement at any time, with or without Cause, as such term is defined in his employment agreement.

In the event that Mr. Schneiderman's employment is terminated by the Company for Cause, as defined in Mr. Schneiderman's employment agreement, or by Mr. Schneiderman voluntarily, then he will not be entitled to receive any payments beyond amounts already earned, and any unvested equity awards will terminate. If the Company terminates his employment agreement without Cause, not in connection with a Change of Control, as such term is defined in Mr. Schneiderman's employment agreement, he will be entitled to (i) all salary owed through the date of termination; (ii) any unpaid annual milestone bonus; (iii) severance in the form of continuation of his salary for the greater of a period of six months following the termination date or the remaining term of the employment agreement; (iv) payment of premiums to cover COBRA for a period of six months following the termination date; (v) a prorated annual bonus equal to the target annual milestone bonus, if any, for the year of termination multiplied by the formula set forth in the agreement. If the Company terminates Mr. Schneiderman's employment agreement without Cause, in connection with a Change of Control, he will be entitled to the above and immediate accelerated vesting of any unvested options or other unvested awards.

Mr. Schneiderman resigned from his position as our Chief Financial Officer effective February 28, 2022. Mr. Schneiderman's resignation from his executive role with the Company was not due to any disagreements with respect to the Company's operations, policies or practices.

In connection with Mr. Schneiderman's resignation, we entered into a settlement and release agreement, whereby the Company will: (i) pay Mr. Schneiderman a lump sum severance payment in an amount equal to six (6) months of his salary; (ii) reimburse premiums to cover all benefits available under the Consolidated Omnibus Budget Reconciliation Act (COBRA) for a period of six (6) months following the termination date if so elected by Mr. Schneiderman; and (iii) vest all unvested stock options issued to Mr. Schneiderman and provide for the exercise of all stock options through their remaining life. In addition, the Company and Mr. Schneiderman have entered into a separate consulting agreement for Mr. Schneiderman to provide consulting services to the Company for a period of two (2) months during the transition period.

*Dr. James E. Pennington*

Effective May 28, 2018, the Company entered into an employment agreement with Dr. Pennington to serve as its Chief Medical Officer. The employment agreement with Dr. Pennington provides for a base annual salary of \$250,000, which was subsequently increased to \$425,000 per year during the year ended December 31, 2021. In addition to his salary, Dr. Pennington is eligible to receive an annual milestone bonus, awarded at the sole discretion of the Board based on his attainment of certain financial, clinical development, and/or business milestones established annually by the Board or Compensation Committee. The Company may terminate Dr. Pennington's employment agreement at any time, with or without Cause, as such term is defined in Dr. Pennington's employment agreement. In the event of termination by the Company other than for Cause, Dr. Pennington is entitled to three months' severance payable over such period. In the event of termination by the Company other than for Cause in connection with a Change of Control as such term is defined in Dr. Pennington's employment agreement, Dr. Pennington will receive six months' severance payable over such period.

**Note 16 - Leases**

The Company leases its offices and research facilities under operating leases which are subject to various rent provisions and escalation clauses.

Effective June 1, 2021, the Company commenced a sixty-three-month lease agreement for its corporate headquarters located in approximately 3,472 square feet of office space at 777 Yamato Road, Suite 502, Boca Raton, FL 33431.

During the year ended December 31, 2020, the Company entered into a month-to-month lease for office space in Delray Beach, FL, a one-year residential lease in Delray Beach, FL and a two-year lease extension (amendment) to its Hayward, CA office. During the year ended December 31, 2020, the Company's lease for its research laboratory in France expired and was not renewed.

The Company determined that the modification to the Hayward, CA lease did not grant an additional right of use and concluded that the modification was not a separate new lease, but rather that it should reassess and remeasure the entire modified lease on the effective date of the modification. The Company accounted for the lease amendment prospectively.

The Company's leases expire at various dates through 2026. The escalation clauses are indeterminable and considered not material and have been excluded from minimum future annual rental payments.

Lease expense amounted to approximately \$261,000 and \$205,000 for the years ended December 31, 2021 and 2020, respectively.

The weighted-average remaining lease term and weighted-average discount rate under operating leases at December 31, 2021 were:

	<u>December 31,</u> <u>2021</u>	<u>December 31,</u> <u>2020</u>
<b>Lease term and discount rate</b>		
Weighted-average remaining lease term	4.1 years	1.42 years
Weighted-average discount rate	6.87%	6.00%

Maturities of operating lease liabilities at December 31, 2021 were as follows:

2022	\$	81,254
2023		83,691
2024		86,202
2025		88,788
2026		60,593
Total lease payments		<u>400,528</u>
Less imputed interest		<u>(11,401)</u>
Present value of lease liabilities	\$	<u>389,127</u>

**Note 17 - Income Taxes**

The Company is subject to taxation at the federal level in both the United States and France and at the state level in the United States. At December 31, 2021 and 2020, the Company had no tax provision for either jurisdictions.

At December 31, 2021 and 2020, the Company had gross deferred tax assets of approximately \$ 31.6 million and \$26.1 million, respectively. As the Company cannot determine that it is more likely than not that the Company will realize the benefit of the deferred tax asset, a valuation allowance of approximately \$31.6 million and \$26.1 million has been established at December 31, 2021 and 2020, respectively. The change in the valuation allowance was approximately \$5.6 million and \$9.7 million in 2021 and 2020, respectively.

The significant components of the Company's net deferred tax assets consisted of:

	December 31,	
	2021	2020
Gross deferred tax assets:		
Net operating loss carry-forwards	\$ 30,576,000	\$ 24,269,000
Temporary differences:		
Stock compensation	112,000	1,408,000
Accruals	30,000	76,000
Change in accounts payable	138,000	-
Other	791,000	639,000
Amortization	-	(319,000)
Deferred tax asset valuation allowance	(31,647,000)	(26,073,000)
Net deferred tax asset	<u>\$ -</u>	<u>\$ -</u>

Income taxes computed using the federal statutory income tax rate differs from the Company's effective tax rate primarily due to the following:

	December 31,	
	2021	2020
Income taxes benefit (expense) at statutory rate	21.0%	21.0%
State income tax	4.2%	14.0%
Non-deductible expense	(10.3%)	(12.0%)
Change in valuation allowance	(9.5%)	(23.0%)
Prior year adjustments	(4.7%)	-%
Other	(0.7%)	-%
	<u>0%</u>	<u>0%</u>

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The Company has gross net operating loss ("NOL") carryforwards for U.S. federal and state income tax purposes of approximately \$79.1 million and \$51.4 million, at December 31, 2021 and 2020, respectively. The NOLs expire between the years 2034 and 2039. The Company's ability to use its NOL carryforwards may be limited if it experiences an "ownership change" as defined in Section 382 of the Internal Revenue Code of 1986, as amended. An ownership change generally occurs if certain stockholders increase their aggregate percentage ownership of a corporation's stock by more than 50 percentage points over their lowest percentage ownership at any time during the testing period, which is generally the three-year period preceding any potential ownership change. The Company has not completed a study to determine whether transactions that have occurred over the past three years may have triggered an ownership change limitation.

The Company had approximately \$27.1 million and \$23.0 million in net operating losses, at December 31, 2021 and 2020, respectively, which it can carryforward indefinitely to offset against future French income.

The Company had taken no uncertain tax positions that would require disclosure under ASC 740, Accounting for Income Taxes, at December 31, 2021 and 2020, respectively.

**Note 18 - Net Loss per Common Share**

Basic net loss per share is computed by dividing net loss available to Common Stockholders by the weighted average number of common shares outstanding during the period. Diluted earnings per share reflect, in periods in which they have a dilutive effect, the impact of common shares issuable upon exercise of stock options and warrants and conversion of convertible debt that are not deemed to be anti-dilutive. The dilutive effect of the outstanding stock options and warrants is computed using the treasury stock method.

At December 31, 2021, diluted net loss per share did not include the effect of 721,663 shares of Common Stock issuable upon the conversion of Series B preferred stock, 5,527,390 shares of Common Stock issuable upon the exercise of outstanding warrants, 37,500 shares of restricted stock not yet issued, and 447,796 shares of Common Stock issuable upon the exercise of outstanding options as their effect would be antidilutive during the periods prior to conversion. Also excluded from the diluted net loss per are the potentially dilutive effect of shares of Common Stock potentially issuable pursuant the Series B Exchange Right.

At December 31, 2020, diluted net loss per share did not include the effect of 2,773,602 shares of Common Stock issuable upon the conversion of Series B preferred stock, 2,517,919 shares of Common Stock issuable upon the exercise of outstanding warrants, 11,200 shares of restricted stock not yet issued, and 407,028 shares of Common Stock issuable upon the exercise of outstanding options as their effect would be antidilutive during the periods prior to conversion. Also excluded from the diluted net loss per are the potentially dilutive effect of 329,020 shares of Common Stock from the First Wave License Agreement, and the potentially dilutive effect 1,066,667 shares of Common Stock underlying the Series C Preferred Stock and 1,066,666 shares of Common Stock issuable upon exercise of Investor Warrants potentially issuable pursuant the Registered Direct Offering and Private Placement entered into on December 31, 2020.

**Note 19 - Related Party Transactions**

*Insider Participation in the Private Placement and Exchange*

On July 16, 2020, in connection with the Series B Private Placement and the Exchange, James Sapirstein, President, Chief Executive Officer and Chair of the Board purchased \$100,000 worth of Series B Preferred Stock and related Series B Warrants for cash. Mr. Sapirstein received approximately 12.99 shares of Series B Preferred Stock convertible into 12,987 shares of Common Stock and Series B Warrants for 6,494 shares of Common Stock. Edward J. Borkowski, lead independent director, purchased \$250,000 worth of Series B Preferred Stock and related Series B Warrants for cash and exchanged \$105,129 of Promissory Notes (including outstanding principal amount and accrued and unpaid interest thereon) for Series B Preferred Stock and related Series B Warrants and Exchange Warrants in the Exchange.

## Note 20 - Employee Benefit Plans

### 401(k) Plan

Since 2015, the Company has sponsored a multiple employer defined contribution benefit plan, which complies with Section 401(k) of the Internal Revenue Code covering substantially all employees of the Company.

All employees are eligible to participate in the plan. Employees may contribute from 1% to 100% of their compensation and the Company matches an amount equal to 100% on the first 6% of the employee contribution and may also make discretionary profit-sharing contributions.

Employer contributions under this 401(k) plan amounted to approximately \$ 107,000 and \$92,000 for the years ended December 31, 2021 and 2020, respectively.

## Note 21 – Subsequent Events

### Nasdaq Deficiency Notice

On November 26, 2021, the Company received a letter from the Listing Qualifications Department of The Nasdaq Stock Market LLC ("*Nasdaq*") indicating that the Company was not in compliance with the minimum stockholders' equity requirement for continued listing on the Nasdaq Capital Market, under Listing Rule 5550(b)(1), because its stockholders' equity of \$(6,969,988) as reported in its Quarterly Report on Form 10-Q for the period ended September 30, 2021 was below the required minimum of \$2.5 million, and because, as of November 24, 2021, it did not meet the alternative compliance standards, relating to the market value of listed securities of \$35 million or net income from continuing operations of \$500,000 in the most recently completed fiscal year or in two of the last three most recently completed fiscal years.

On January 10, 2022, the Company submitted to Nasdaq a plan to regain compliance with Listing Rule 5550(b)(1). On February 15, 2022, Nasdaq notified the Company that they have granted the Company an extension of up to 180 calendar days from November 26, 2021, or through May 25, 2022, to regain compliance. If the Company fails to evidence compliance upon filing its periodic report for the quarter ending June 30, 2022, the Company may be subject to delisting. If Nasdaq determines to delist the Company's common stock, the Company will have the right to appeal to a Nasdaq hearings panel.

### Waiver Agreements with Certain Holders of Series B Convertible Preferred Stock

In February 2022, the Company entered into waiver agreements (the "*Waiver*") with certain holders of the Company's Series B Convertible Preferred Stock, par value \$ 0.0001 per share (the "*Series B Preferred Stock*"), pursuant to which the Company agreed to pay a cash waiver fee equal to ten percent of the stated value of the shares of Series B Preferred Stock held by such holder (other than holders who are insiders of the Company who did not receive a cash waiver fee) and such holder agreed to irrevocably waive its Series B Exchange Right (as defined below) with respect to any Subsequent Financing (as defined below) that occurs from and after the date of the Waiver until December 31, 2022.

Pursuant to the Series B Preferred Stock Certificate of Designations (the "*Certificate of Designations*"), in the event of any issuance by the Company or any of its subsidiaries of its Common Stock, or Common Stock equivalents for cash consideration or a combination of units thereof (a "*Subsequent Financing*"), each holder of the Company's Series B Preferred Stock has the right, subject to certain exceptions set forth in the Certificate of Designations, at its option, to exchange (in lieu of cash subscription payments) all or some of the Series B Preferred Stock then held (with a value per share of Series B Preferred Stock equal to the stated value of each share of Series B Preferred Stock, or \$7,700.00, plus accrued and unpaid dividends thereon, of the Series B Preferred Stock) for any securities or units issued in a Subsequent Financing on a dollar-for-dollar basis (the "*Series B Exchange Right*").

The Company entered into Waivers with holders of approximately \$ 2.88 million of stated value of Series B Preferred Stock. The Company also entered into Waivers with Company insiders of approximately \$474,000 of stated value of our Series B Preferred Stock for which the Company did not pay a waiver fee.



*March 2022 Registered Direct Offering*

On February 27, 2022, the Company entered into a securities purchase agreement with a single institutional investor (the "*March 2022 Purchase Agreement*") pursuant to which the Company agreed to sell, in a registered direct offering (the "*March 2022 Registered Direct Offering*") priced at the market under Nasdaq rules, an aggregate of (i) 1,650,000 shares of Common Stock, (ii) pre-funded warrants (the "*March 2022 Pre-Funded Warrants*") exercisable for an aggregate of up to 4,848,195 shares of Common Stock, and (iii) Series C warrants (the "*Series C Warrants*") exercisable for an aggregate of up to 6,498,195 shares of Common Stock. The public offering price for each share of Common Stock and accompanying Series C Warrant to purchase one share of Common Stock was \$1.385, and the public offering price for each March 2022 Pre-Funded Warrant and accompanying Series C Warrant to purchase one share of Common Stock was \$ 1.375. The March 2022 Registered Direct Offering closed on March 2, 2022.

The net proceeds of the March 2022 Registered Direct Offering, after deducting the placement agent's fees and expenses and other estimated offering expenses payable by the Company and excluding the net proceeds, if any, from the exercise of the Series C Warrants, were approximately \$8.1 million. The Company intends to use the net proceeds from the March 2022 Registered Direct Offering to pay a portion of the cash purchase price for its acquisition of First Wave Bio, Inc. and for other general corporate purposes, which may include product manufacturing, clinical development and/or increases in working capital.

In the March 2022 Purchase Agreement, the Company has agreed not to issue, enter into any agreement to issue or announce the issuance or proposed issuance of, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or file any registration statement or prospectus, or any amendment or supplement thereto for 60 days after the closing date of the March 2022 Registered Direct Offering. In addition, the Company has agreed not to effect or enter into an agreement to effect any issuance of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock involving a variable rate transaction (as defined in the March 2022 Purchase Agreement) until the one-year anniversary of the date of the March 2022 Purchase Agreement, subject to certain exceptions.

The March 2022 Purchase Agreement contain customary representations, warranties and agreements by the Company, customary conditions to closing, indemnification obligations of the Company and the purchasers, including for liabilities arising under the Securities Act, other obligations of the parties and termination provisions. The representations, warranties and covenants contained in the March 2022 Purchase Agreement were made only for the purposes of such agreements and as of specific dates, were solely for the benefit of the parties to such agreements and may be subject to limitations agreed upon by the contracting parties.

*Series B Most Favored Nations (MFN) Exchanges*

Under the Certificate of Designations for the Series B Certificate of Designations, in the event the Company effects any issuance of Common Stock or Common Stock equivalents for cash consideration, or a combination of units thereof (a "*Subsequent Financing*"), each holder of Series B Preferred Stock, has the right to exchange the Exchange Amount of the Series B Preferred Stock for any securities issued in the Subsequent Financing, in lieu of any cash subscription payments therefor (the "*Series B Exchange Right*").

The Company entered into the March 2022 Purchase Agreement as part of the March 2022 Registered Direct Offering, and the holders of the Series B Preferred Stock became entitled to exercise their Series B Exchange Right to exchange into shares of Common Stock and related Series C Warrants. As of March 28, 2022, holders of approximately 17.05 shares of Series B Preferred Stock with an aggregate Exchange Amount of approximately \$145,000 had previously elected to exercise their Series B Exchange Rights into 104,735 shares of Common Stock, and additional Series C Warrants exercisable for up to an aggregate of 104,735 shares of Common Stock.

*Issuance of Stock Options*

On January 3, 2022, the Company issued employees ten-year stock options to purchase 161,000 shares of Common Stock with a strike price of \$ 1.45 per share, subject to service-based milestone vesting over three years under the 2020 Plan as payment for services rendered. Such issuance was exempt from registration under 4(a)(2) of the Securities Act.