

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the Fiscal Year Ended December 31, 2022

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: 001-39070

MONOPAR THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

32-0463781

(I.R.S. employer identification number)

1000 Skokie Blvd., Suite 350, Wilmette, IL

(Address of principal executive offices)

60091

(zip code)

(847) 388-0349

(Registrant's telephone number, including area code)

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

Title of each class

Trading Symbol(s)

Name of each exchange on which registered

Common stock, \$0.001 par value

MNPR

The Nasdaq Stock Market LLC
(Nasdaq Capital Market)

Securities registered pursuant to 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 and post such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or 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

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

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

State the aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter. The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant as of June 30, 2022 was \$10,000,462 based on the closing price reported for such date on the Nasdaq Capital Market.

The number of shares outstanding with respect to each of the classes of our common stock, as of March 10, 2023, is set forth below:

Class

Number of shares outstanding

Common stock, par value \$0.001 per share

13,193,172

The documents incorporated by reference are as follows: portions of the Registrant's Proxy Statement for its 2023 annual meeting of stockholders are incorporated by reference into Part III.

**MONOPAR THERAPEUTICS INC.
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Forward-Looking Statements

This Annual Report on Form 10-K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Act”), and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts included in this Annual Report on Form 10-K are forward-looking statements. The words “hopes,” “believes,” “anticipates,” “plans,” “seeks,” “estimates,” “projects,” “expects,” “intends,” “may,” “could,” “should,” “would,” “will,” “continue,” and similar expressions are intended to identify forward-looking statements. The following uncertainties and factors, among others, could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- the results of the go/no go interim analysis decision from our independent data monitoring committee with respect to the Phase 2b portion of our ongoing Validive clinical trial, anticipated by the end of March 2023;
- our ability to raise sufficient funds within the next 12 months in order for us to (1) assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, complete the Phase 3 portion of our ongoing Validive Phase 2b/3 clinical trial and, if required, complete a second confirmatory Phase 3 clinical trial, (2) continue the clinical development of camsirubicin through and beyond our ongoing Phase 1b dose escalation clinical trial, (3) support further preclinical and clinical development of MNPR-101 for radiopharmaceutical use in advanced cancers, and (4) support further development of MNPR-202 and related compounds; as well as our ability to further raise additional funds in the future to support any future product candidate programs through completion of clinical trials, and our current and future product candidate programs through the approval processes and, if applicable, commercialization;
- our ability to find a suitable pharmaceutical partner or partners to further our development efforts, under acceptable financial terms;
- risks and uncertainties associated with our research and development activities, including our clinical trials, regulatory submissions, and manufacturing and quality expenses;
- estimated timeframes for our clinical trials and regulatory reviews for approval to market products are uncertain;
- the rate of market acceptance and competitiveness in terms of pricing, efficacy and safety, of any products for which we receive marketing approval, and our ability to competitively market any such products as compared to larger pharmaceutical firms;
- the difficulties of commercialization, marketing and product manufacturing and overall strategy;
- uncertainties of intellectual property position and strategy including new discoveries and patent filings;
- our ability to attract and retain experienced and qualified key personnel and/or to find and utilize external sources of experience, expertise and scientific, medical and commercialization knowledge to complete product development and commercialization of new products;
- the risks inherent in our estimates regarding the level of needed expenses, capital requirements and the availability of required additional financing at acceptable terms;
- the impact of government laws and regulations including increased governmental control of healthcare and pharmaceuticals, resulting in direct price controls driving lower prices, other governmental regulations affecting cost requirements and structures for selling therapeutic products, and recent governmental legislation affecting other industries which may indirectly increase our costs of obtaining goods and services;
- the uncertain continuing impact of COVID-19 on our ability to advance our clinical programs and raise additional financing;
- the cumulative impact of domestic and global inflation, volatility in financial markets and the banking industry and/or the potential for an economic recession increasing our costs of obtaining goods and services or making financing more difficult to obtain on acceptable terms or at all;
- the uncertain impact of the Russia-Ukraine war on our clinical material manufacturing expenses and timelines, as well as on general economic, trade and financial market conditions; and
- uncertainty of our financial projections and operational timelines and the development of new competitive products and technologies.

Although we believe that the risk assessments identified in such forward-looking statements are appropriate, we can give no assurance that such risks will materialize. Cautionary statements are disclosed in this Annual Report on Form 10-K, including without limitation statements in the section entitled “Item 1A - Risk Factors,” addressing forward-looking statements. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements. We undertake no obligation to update any statements made in this Annual Report on Form 10-K or elsewhere, including without limitation any forward-looking statements, except as required by law.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other 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 these forward-looking statements. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances projected in this information.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in “Item 1A - Risk Factors” located elsewhere in this Annual Report on Form 10-K. These risks include, among others, the following:

- We are a clinical stage biopharmaceutical company with a history of financial losses. We expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain cash self-sufficiency or profitability, which could result in a decline in the market value of our common stock.
- We expect the results of the go/no go interim analysis decision from our independent data monitoring committee with respect to the Phase 2b portion of our ongoing Validive clinical trial by the end of March 2023. A negative decision would require us to refocus our development efforts on our other product candidates and could result in a decline in the market value of our common stock.
- Funds raised to date are not sufficient to 1) assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, complete the Phase 3 portion of our ongoing Validive Phase 2b/3 (“VOICE”) clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial; 2) continue the clinical development of camsirubicin through and beyond our ongoing Phase 1b dose escalation clinical trial; 3) support further development of MNPR-101 for radiopharmaceutical use in advanced cancers; or 4) support continued development of MNPR-202 and related compounds. If we are unable to raise enough funds within the next 12 months from the sale of our common stock or other financing efforts, or conclude a strategic agreement or collaboration such as out-licensing Validive or other product candidates, or entering into a clinical or commercial partnership, we will likely have to terminate one or more programs. There can be no assurance that we will be able to secure such financing or find a suitable development partner on satisfactory terms.
- We do not have and may never have any approved products on the market. Our business is highly dependent upon receiving marketing approvals from various U.S. and international governmental agencies and would be severely harmed if we are not granted approvals to manufacture and sell our product candidates.
- Our clinical trials may not yield sufficiently conclusive results for regulatory agencies to approve the use of our products, which would adversely affect our financial condition.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals will be delayed or prevented, which would materially delay our program schedules and adversely affect our financial condition.
- If we or our licensees, development collaborators, or suppliers are unable to manufacture our products in sufficient quantities or at defined quality specifications, or are unable to obtain regulatory approvals for the manufacturing facility, we may be unable to develop and/or meet demand for our products and lose time to market and potential revenues.
- We rely on qualified third parties to conduct our active pharmaceutical ingredient manufacturing, our drug product manufacturing, non-clinical studies, and our clinical trials. If these third parties do not or cannot successfully carry out their contractual duties and meet expected deadlines or performance goals, the initiation or conduct of our clinical trials would be delayed and we may be unable to obtain regulatory approval for, or commercialize, our current product candidates or any future products, and our financial condition would be adversely affected.

- The Russia-Ukraine war, and resulting sanctions against Russia and Russian entities, and Russian reduction in gas shipments to the EU and other allies, have increased fuel costs, reduced access to critical supplies and may cause shipping delays. The broader economic, trade and financial market consequences are uncertain at this time, which may increase the cost of supplies for our clinical materials, may delay the manufacture of our clinical materials, may increase costs of other goods and services or make it more difficult or costly to raise additional financing, any of which could cause an adverse effect on our clinical programs and on our financial condition.
- Market variables, such as inflation of product costs, labor rates and fuel, freight and energy costs, as well as geopolitical events could likely cause us to suffer significant increases in our operating and administrative expenses.
- Unstable market and economic conditions, such as the recent volatility in the markets due to concerns about bank stability and economic challenges due to inflation, may have serious adverse consequences on our ability to raise funds, which may cause us to delay, restructure or cease our operations.
- The effects of economic and political pressure to lower pharmaceutical prices are a major threat to the economic viability of new research-based pharmaceutical products, and any significant decrease in drug prices could materially and adversely affect the financial appeal of our products and investment prospects.
- We face significant competition from other biotechnology and pharmaceutical companies, and from research-based academic medical institutions, in our targeted medical indications, and our operating results would be adversely affected if we fail to compete effectively. Many competitors have greater organizational capabilities in our industry, much higher available capital resources, and established marketing resources and sales in the targeted markets. Competition and technological change may make our product candidates obsolete or non-competitive.
- The termination of third-party licenses would adversely affect our rights to important compounds or technologies which are essential to develop and market our products.
- If we and our third-party licensors do not obtain and preserve protection for our respective intellectual property rights, our competitors may be able to develop and market competing drugs, which would adversely affect our financial condition.
- If we lose key management leadership, and/or the expertise and experience of our scientific personnel, and if we cannot recruit qualified employees or other highly qualified and experienced personnel for future requirements, we would be at risk to experience significant program delays and increased compensation and operational costs, and our business would be materially disrupted.
- The long-term effects of COVID-19 are highly uncertain, and their scope and impact could have a substantial negative bearing on our business, financial condition, operating results, stock price and ability to raise additional funds.

PART I

Item 1. Business

You should read the following discussion in conjunction with our financial statements as of December 31, 2022, and the notes to such financial statements included elsewhere in this Annual Report on Form 10-K.

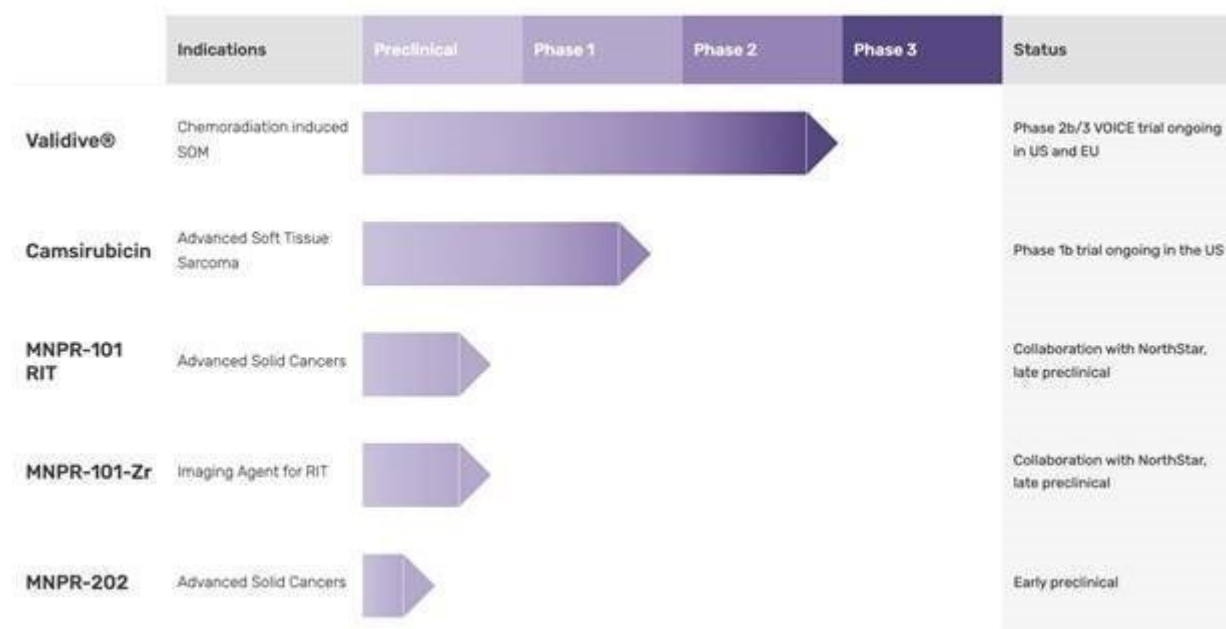
Overview

We are a clinical stage biopharmaceutical company focused on developing proprietary therapeutics designed to extend life or improve quality of life for cancer patients. We are building a drug development pipeline through the licensing and acquisition of therapeutics in late preclinical and clinical development stages. We leverage our scientific and clinical experience to help reduce the risk and accelerate the clinical development of our drug product candidates.

During 2022, we expanded the number of clinical trial sites in our global Phase 2b/3 clinical trial of our lead product candidate, Validive® (clonidine hydrochloride mucobuccal tablet; clonidine HCl MBT), for the prevention of chemoradiotherapy (“CRT”)-induced severe oral mucositis (“SOM”) in patients with oropharyngeal cancer (“VOICE” trial). We currently have active sites in the U.S., Spain, France, Germany and Poland and have completed enrollment of the Phase 2b portion of the clinical trial with a go/no go interim analysis decision from our independent data monitoring committee anticipated by the end of March 2023. We also continued enrolling in our U.S.-based open-label, Phase 1b clinical trial of camsirubicin for the treatment of advanced soft tissue sarcoma (“ASTS”). We also, in collaboration with our partner, NorthStar Medical Radioisotopes, LLC, continue to move forward with the development of MNPR-101 for radiopharmaceutical use in advanced cancers. Finally, we continue to develop MNPR-202, an analog of camsirubicin designed to potentially treat doxorubicin- and camsirubicin-resistant cancers, which is being tested in preclinical models by our collaborator, the Cancer Science Institute of Singapore at the National University of Singapore.

To complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will require additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive) which we are planning to pursue within the next 12 months. We also require additional funding to continue to develop camsirubicin through and beyond our ongoing Phase 1b clinical trial and to further fund our current and future product pipeline.

Our Product Pipeline



Our Product Candidates

Validive (clonidine hydrochloride mucobuccal tablet; clonidine HCl MBT)

Validive is designed to be used prophylactically to prevent SOM in patients undergoing CRT for oropharyngeal cancer (“OPC”). SOM is a painful and debilitating inflammation and ulceration of the mucous membranes lining the oral cavity and oropharynx in response to chemoradiation. The majority of patients receiving CRT to treat their OPC develop

SOM, which remains one of the most common and devastating side effects of treatment in this indication. The potential clinical benefits to preventing SOM in patients include: reduced treatment discontinuations leading to potentially improved overall survival outcomes; reduced mouth and throat pain avoiding the need for feeding tube intervention; decreased long-term and often permanent debilitation arising from swallowing difficulties, neck and throat spasms, and lung complications due to food aspiration; and decreased reliance on pain medication. Our mucobuccal tablet (“MBT”) formulation is a novel delivery system for clonidine that allows for prolonged and enhanced local delivery of drug in the regions of mucosal radiation damage in patients with OPC. Validive has been granted fast track designation in the U.S., orphan drug designation in the EU, and has global intellectual property patent protection through mid-2029 not accounting for possible patent extensions.

In September 2017, we exercised an option to license Validive from Onxeo S.A., the company that developed Validive through its Phase 2 clinical trial. In the completed Phase 2 clinical trial, Validive demonstrated clinically meaningful efficacy signals within the 64-patient OPC population randomized to placebo, Validive 50 µg dose and Validive 100 µg dose. The absolute incidence of SOM in OPC patients who received a dose of Validive 100 µg once per day was reduced by 26.3% (incidence rate of 65.2% in placebo, 45.0% in Validive 50 µg group, and 38.9% in Validive 100 µg group). The median time to onset of SOM was 37 days in the placebo cohort; 45 days in the Validive 50 µg cohort and no median time of onset was reached in the Validive 100 µg group since fewer than half of this cohort of patients developed SOM. There was also a 37.8% reduction in the median duration of the SOM for the Validive 100 µg group versus placebo (41.0 days placebo group, 34.0 days Validive 50 µg group, and 25.5 days Validive 100 µg group) in patients that developed SOM. Median duration of SOM across all patients, inclusive of both those that did and did not develop SOM, was 17 days in the placebo group and 0 days in each of the Validive 50 and 100 µg groups. A positive dose response was seen in each of these three clinical endpoints. Additionally, patients in the Validive cohorts in the Phase 2 clinical trial demonstrated a safety profile similar to that of placebo. Onxeo’s promising preclinical studies and Phase 2 clinical trial have informed the design and conduct of what we believe will be an effective Phase 2b/3 and, if required, second confirmatory Phase 3 clinical program.

In February 2021, we dosed the first patient in our Phase 2b/3 VOICE trial. In August 2021, we successfully reached our original target of 20 activated clinical trial sites for the Phase 2b portion of the 2b/3 Validive® VOICE trial, and in September 2021 we received authorization to proceed with the VOICE clinical trial in multiple countries in Europe. In 2022, we completed enrollment of the Phase 2b portion of the VOICE trial and commenced enrolling the Phase 3 portion. As of March 10, 2023, we have 81 clinical sites activated and enrolling patients in the U.S. and Europe. To be prepared for a positive go/no-go decision based on the interim analysis, anticipated to occur by the end of March 2023, we continue to activate additional sites globally. To complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will require additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive), which we are planning to pursue within the next 12 months.

SOM typically arises in the immune tissue at the back of the tongue and throat, which comprise the oropharynx, and consists of acute severe tissue damage and pain that prevents patients from swallowing, eating and drinking. Validive stimulates the alpha-2 adrenergic receptor (alpha-2AR) on macrophages (white blood cells present in the immune tissues of the oropharynx) suppressing pro-inflammatory cytokine expression. Validive exerts its effects locally in the oral cavity and oropharynx over a prolonged period of time through its unique MBT formulation. Patients who develop SOM are also at increased risk of developing late onset toxicities, including trismus (jaw, neck, and throat spasms), dysphagia, and lung complications, which are often irreversible and lead to increased hospitalization and the need for further interventions sometimes years after completion of CRT. We believe that the prevention of SOM by Validive will have the potential to reduce treatment discontinuation and/or treatment delays potentially leading to improved survival outcomes and reducing or eliminating these long-term morbidities resulting from CRT.

The OPC target population for Validive is the most rapidly growing segment of head and neck cancer (“HNC”) patients, with an estimated greater than 40,000 new cases of OPC in the U.S alone in 2023. The growth in OPC is driven by the increasing prevalence of oral human papilloma virus (“HPV”) infections in the U.S. and around the world. Despite the availability of a pediatric/adolescent HPV vaccine, the rate of OPC incidence in adults is not anticipated to be materially reduced for decades due to low adoption of the vaccine to date. As a result, the incidence of HPV-driven OPC is projected to increase for years to come and will continue to represent a clinical need for Validive for the prevention of CRT-induced SOM in patients with OPC since CRT is the standard of care treatment, and we anticipate that radiation will remain an important treatment modality for these patients for years to come.

Validive is an MBT of clonidine. The MBT formulation was developed to enhance drug delivery to the oral mucosa while minimizing systemic absorption. The Validive tablet is tasteless and odorless and is self-administered once daily by affixing it to the outside of the patient’s upper gum where it dissolves slowly over a period of several hours, resulting in the extended release of clonidine into the oral cavity and oropharynx, the sites of SOM following CRT for OPC. Validive treatment begins on the first day of CRT and continue daily through the last day of radiation.

The majority of patients receiving CRT to treat their OPC develop SOM, which is one of the most common and devastating side effects of treatment in this indication. We believe Validive has the potential to address several critical elements that affect SOM patients, including:

Reduction in the incidence of SOM. SOM can increase the risk of acute and chronic comorbidities, including dysphagia, trismus and lung complications, which are often irreversible and lead to increased hospitalization and the need for additional interventions. In a Phase 2 clinical trial, the OPC patient cohort treated with Validive 100 µg demonstrated a reduction in the absolute incidence of SOM compared to placebo of 26.3% (incidence rate of 65.2% in placebo, 45.0% in Validive 50 µg group, 38.9% in Validive 100 µg group). A reduced incidence of SOM in OPC patients may lower the risk of acute and chronic comorbidities, and improve clinical outcomes and quality of life.

Delay in the time to onset of SOM. SOM can cause cancer treatment delay and/or discontinuation, which seriously impacts overall survival outcomes. In the Phase 2 clinical trial, OPC patients had a time to onset of SOM of 37 days in the placebo cohort; 45-day time to onset of SOM in the Validive 50 µg cohort; and a median time was not reached in the Validive 100 µg group as fewer than half of the patients developed SOM. Prolonging time to onset of SOM typically leads to fewer missed CRT treatments, resulting in improved overall survival outcomes.

Decrease in the duration of SOM. Longer duration of SOM leads to a higher risk of the need for parenteral nutrition and lower quality of life. SOM patients experience difficulty or inability to drink and/or eat, and difficulty in swallowing often results in malnourishment and feeding tube intervention. The Phase 2 clinical trial data demonstrated a 15.5-day reduction (by 37.8%) in the duration of SOM for patients treated with Validive 100 µg (41-day median duration with placebo, 34 days with the Validive 50 µg group, and 25.5 days for the Validive 100 µg group) in patients that developed SOM. Median duration across all patients, inclusive of both those that did and did not develop SOM, was 17 days in the placebo group and 0 days in each of the Validive 50 µg and 100 µg groups. Reduced duration of SOM has the capacity to result in lower risk of malnourishment and feeding tube intervention, and fewer treatment terminations/delays.

While not designed by us, Onxeo's promising preclinical studies and Phase 2 clinical trial have informed the design and conduct of what we believe will be an effective Phase 2b/3 VOICE clinical trial.

In response to COVID-19 and its effects on clinical trials, in 2020, we adjusted our clinical development plan accordingly to fit what is feasible in the current environment. We simplified the design of the previously planned Phase 3 clinical trial for Validive for the prevention of CRT-induced severe oral mucositis in patients with oropharyngeal cancer ("VOICE"), to a seamless Phase 2b/3 design. This design is based on a binary primary endpoint, incidence of SOM, and minimizes touch points with the clinical trial sites and patients. Validive is a once daily self-administered mucoadhesive tablet which can be taken in the patient's home setting. The VOICE trial (NCT04648020) is a randomized, placebo-controlled and double blinded global clinical trial with trial sites in the U.S., Spain, France, Germany and Poland. In 2022, we completed enrollment of the Phase 2b portion of the VOICE trial and commenced enrollment in the Phase 3 portion. As of March 10, 2023, we have 81 clinical sites activated and enrolling patients in the U.S. and Europe.

The blinded interim analysis of clinical data from the Phase 2b patient cohort of the trial, to be performed by an independent data monitoring committee, will be used to guide us as to whether or not to continue enrolling the Phase 3 portion of the trial. This analysis should be completed and reported out by the end of March 2023. To be prepared for a positive go/no-go decision based on the interim analysis, we continue to activate additional sites globally. The entire trial has been designed to enroll up to 260 evaluable patients. This modification in design allowed us to activate and commence dosing the VOICE trial in early 2021 without requiring near-term financing. If the interim analysis results in a no-go decision, we would need to reconsider our efforts with respect to Validive and refocus our development efforts on our other product candidates. Because the interim analysis is being performed by an independent data monitoring committee, we do not know what the results will be as of the date of this Annual Report.

Assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, to complete the Phase 3 portion of the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will require additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive), which we are planning to pursue within the next 12 months. Validive has been granted fast track designation in the U.S., orphan drug designation in the EU, and has global intellectual property patent protection through mid-2029 not accounting for possible patent extensions.

Validive U.S. Market Opportunity

The incidence of HNC (all anatomical types, including larynx, oral cavity, oropharynx, etc.) in the U.S. was estimated to be approximately 65,630 cases in 2020 (American Society of Clinical Oncology, cancer.net). The most rapidly growing type of HNC is OPC. The oropharynx is comprised largely of immune tissue and includes the soft palate, the base (rear one third) of the tongue, and the tonsils. In the U.S., the incidence of OPC is estimated to be greater than 40,000 cases in 2023. The majority of these OPC patients (approximately 70%) are human papilloma virus positive ("HPV+"). The incidence of OPC is also increasing in the rest of the world (>30% of HNC), with >50% of all OPC being HPV+. While certain types of HNC have been in decline in the U.S., such as laryngeal cancer as a result of a reduction in

the smoking population, the total incidence of HNC has been growing steadily primarily due to OPC. The increase in OPC is directly associated with increased infection with the human papilloma virus. The incidence of HPV+ OPC has outpaced the incidence of HPV- HNC by 4-5-fold over the past decade. This trend of HPV+ OPC driving an increase in overall HNC is expected to continue for some time as the relatively recent introduction of a vaccine designed to prevent the transfer and colonization with HPV is only effective if administered prior to infection, and until October 2018, it was only recommended for those under the age of 26 (newer U.S. Food and Drug Administration (“FDA”) guidelines include those up to age 45). Even for those under the age of 26 who are eligible for the vaccine, oral HPV infections are predicted to increase due to the lack of adequate use of HPV vaccinations. Approximately 50% of eligible females and 33% of eligible males are presently being vaccinated.

Most OPC is caused by the HPV16 strain, with virus detectable in the tumor. More than 3% of adult men and 1% of adult woman have HPV16 detectable in their saliva at any one time. The virus is transmitted through sexual contact and CDC estimates 10% of men and 3.6% of women in the U.S. have an active oral HPV infection. The latency period for that proportion that do go on to develop HPV+ OPC is 15-20+ years. This HPV+ OPC population is expected to be a long-term driver of the incidence of OPC, and the resultant SOM associated with what is frequently curative therapy for this serious malignancy.

In previous studies describing SOM in OPC patients receiving the CRT regimen we are using in our VOICE clinical program, patients had a SOM incidence rate of 55-90% across studies. In the Validive Phase 2 trial, the incidence of SOM in OPC patients receiving placebo was 65.2% (see “*Validive Phase 2 Clinical Trial Data*” section below). Currently there is no way to predict which patients will develop SOM, so any active preventive treatment for SOM will likely be used in most OPC patients receiving CRT. With the consistently growing incidence of OPC as a result of the human papillomavirus, there is the potential for a substantial and growing market for Validive.

Validive Mechanism of Action

Validive is designed to deliver high local concentrations of clonidine, an agonist of alpha-2AR, to the oral cavity and oropharynx, the site of irradiation in the treatment of OPC. In the oropharynx, alpha-2AR is expressed on macrophages, immune cells that produce inflammatory cytokines, the molecules that are responsible for the development of SOM, in response to CRT. Several published clinical reports have demonstrated that chemoradiation treatment substantially increased salivary cytokine levels and a recent study demonstrated that these were positively associated with the formation of SOM in patients with head and neck cancer. Patients with HPV+ OPC demonstrate an increased accumulation of macrophages in the tumor microenvironment compared to patients with OPC that were negative for human papilloma virus (“HPV-”), thus further priming HPV+ OPC patients for the development of SOM. The alpha-2AR regulates the expression of cytokines by macrophages, and clonidine reduces this cytokine production. Macrophages are the primary immune cells in the oropharynx that express alpha-2AR, making clonidine’s mechanism of cytokine suppression macrophage selective and distinct from the mechanism of other anti-inflammatory drugs. Further, Validive delivers clonidine to the mucosal surface, the site most affected by chemoradiation treatment in OPC. This results in high salivary concentrations of clonidine, minimizing systemic absorption, and allowing for maximal exposure the at-risk oral mucosa and the OPC microenvironment to drug. Preclinical studies and a Phase 2 clinical trial of Validive have provided data that support Validive’s mechanism of action and therapeutic potential for reducing the incidence of SOM in patients with OPC, improving oral mucositis-related symptoms, and decreasing CRT-related adverse events, while exhibiting a favorable safety profile and high compliance rate in patients.

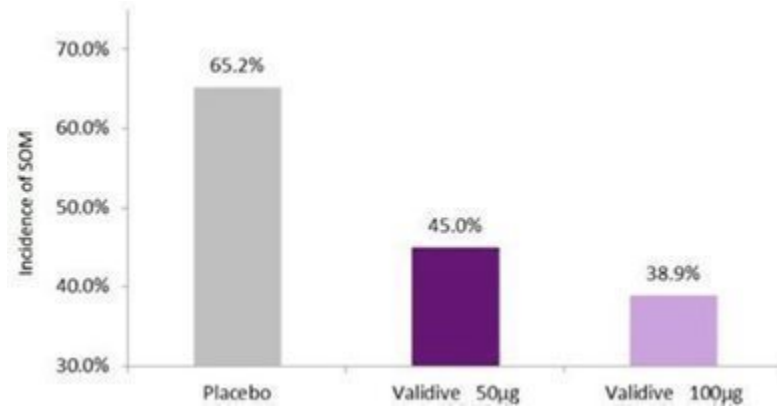
Validive Phase 2 Clinical Trial Data

In October 2015, the results from an international Phase 2 clinical trial of Validive were announced, demonstrating promising signs of clinical activity and safety compared to placebo. The trial enrolled 183 HNC patients and was conducted in more than thirty centers in Europe and the United States. Patients who had undergone surgical resection of their head and neck cancer with curative intent and who were planned to receive at least 50 Gray (Gy) of radiation in combination with chemotherapy, regardless of anatomical location of disease, were included in this study. This global, multi-center, double-blind, randomized, placebo-controlled, three-arm study (NCT01385748) compared the efficacy and safety of Validive 50 µg and 100 µg to placebo in patients with HNC receiving CRT. Of the 183 HNC patients, 64 had OPC (placebo = 24, Validive 50 µg = 21, Validive 100 µg = 19). Validive and placebo were administered once daily beginning 1 to 3 days prior to CRT and continuing until the end of chemoradiation.

We believe the Phase 2 clinical trial data support the development of Validive for the prevention of SOM in OPC patients. The analysis of OPC patients in this study showed:

- The incidence of SOM (primary endpoint) was reduced by 26.3% (40% relative to placebo) in OPC patients treated with Validive 100 µg (p=0.09, a meaningful trend but not statistically significant). 65.2% of OPC patients on placebo experienced SOM compared to only 38.9% of OPC patients on Validive 100 µg.

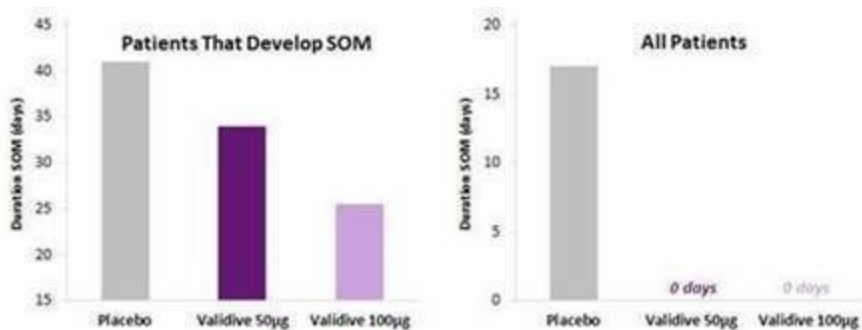
■ Incidence of SOM in OPC Patients



Validive has demonstrated reduced incidence of SOM in a Phase 2 clinical trial (p=0.09)

- Patients on Validive experienced a delay in the time to onset of SOM. Patients receiving placebo experienced a median time to onset of SOM of 37 days; patients receiving Validive (50 µg one per day) experienced a 45-day median time to onset of SOM; and patients receiving Validive (100 µg once per day) did not reach a median time to onset. A comparison of hazards for time to onset demonstrated that patients that received Validive 100 µg had a hazard ratio (HR)=0.48 compared to placebo.
- Patients receiving Validive experienced a decrease in the median duration of SOM. In patients that developed SOM, a 15.5-day reduction (by 37.8%) in the median duration of SOM was observed in patients treated with Validive 100 µg (41-day median duration with placebo, 34 days in the Validive 50 µg group, and 25.5 days in the Validive 100 µg group). Median duration across all patients, inclusive of both those that did and did not develop SOM, was 17 days in the placebo group and 0 days in each of the Validive 50 and 100 µg groups.

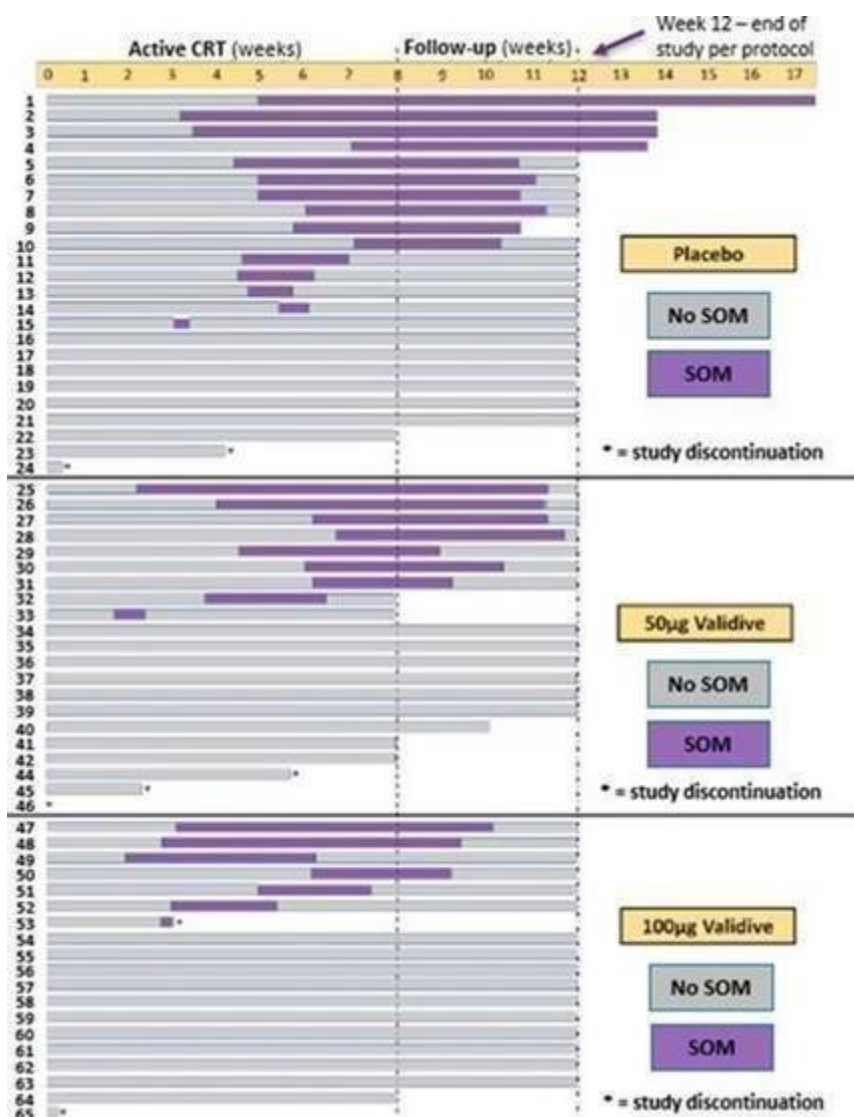
■ Median Duration of SOM in OPC Patients



Validive decreased duration of SOM in a Phase 2 clinical trial

- Severe drinking, eating, and speaking limitations due to mouth and throat soreness (“MTS”) score were also reduced in the Validive 100 µg treated cohort.
- Improvements in other indicators of clinical benefit, including decreased weight loss, decreased opiate use and increased cumulative dose of radiation received, strongly favored the Validive 100 µg treated group.
- A dose response was observed with the Validive 100 µg dose, demonstrating a trend toward superiority over the Validive 50 µg dose as well as placebo. Individual patient-level data supports advancing the Validive 100 µg dose into Phase 2b/3.

Individual Patient Data Showing Incidence, Time to Onset, and Duration of SOM in OPC patients Treated with Placebo and Two Different Doses of Validive (50 and 100 µg/day)



For the full 183-patient Phase 2 population, which included various types of head and neck cancer such as oral and laryngeal cancer in addition to OPC, the incidence of SOM was lower in patients treated with Validive (45.3% when the 50 and 100 µg dose groups were pooled together) than in patients receiving placebo (60.0%) ($p = 0.064$). Additionally, Validive was very well tolerated, with the occurrence of adverse events of any type or grade being similar between placebo and Validive treated groups. Patients treated with Validive experienced less nausea and dysphagia compared to placebo. No clinically meaningful decreases in systolic blood pressure or diastolic blood pressure were noted between the placebo and Validive arms. There was no statistical difference in the number of patients having experienced at least one treatment emergent adverse event related to the study treatment between placebo and Validive as summarized in the table below. Two patients in the placebo group and 2 patients in the Validive 50 µg group experienced a serious treatment-emergent adverse event (“STEAE”). No STEAEs were observed in the Validive 100 µg cohort. No patients in the Validive-treated cohorts were discontinued due to study drug. The 2-year survival rate was not statistically different between patients treated with placebo and Validive indicating that Validive did not interfere with primary disease treatment.

All Serious Treatment-Emergent Adverse Events Related to Study Drug

System Organ Class	Preferred Term	Placebo (n=62)	Clonidine MBT 50µg (n=55)	Clonidine MBT 100µg (n=64)
Vascular Disorders	Hypertension	0 (0%)	2 (3.6%)	0 (0%)
Gastrointestinal Disorders	Dysphagia	1 (1.6%)	0 (0%)	0 (0%)
Metabolism and Nutritional Disorders	Dehydration	1 (1.6%)	0 (0%)	0 (0%)
All	All	2 (3.2%)	2 (3.6%)	0 (0%)

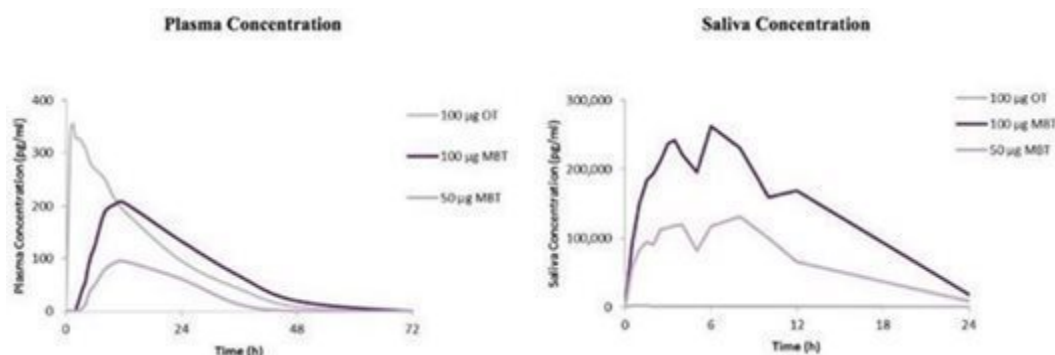
MBT=mucoadhesive buccal tablet; n=number of patients studied

The mean overall patient compliance as assessed by the investigators was approximately 90%, and similar across all treatment groups. Overall compliance according to patient diaries was also similar in all treatment groups and consistent with the compliance according to the investigator's evaluation. The mean incidence of swallowing the MBT was low (4.7%) for all patients based on 7,366 daily MBT applications across all treatment groups.

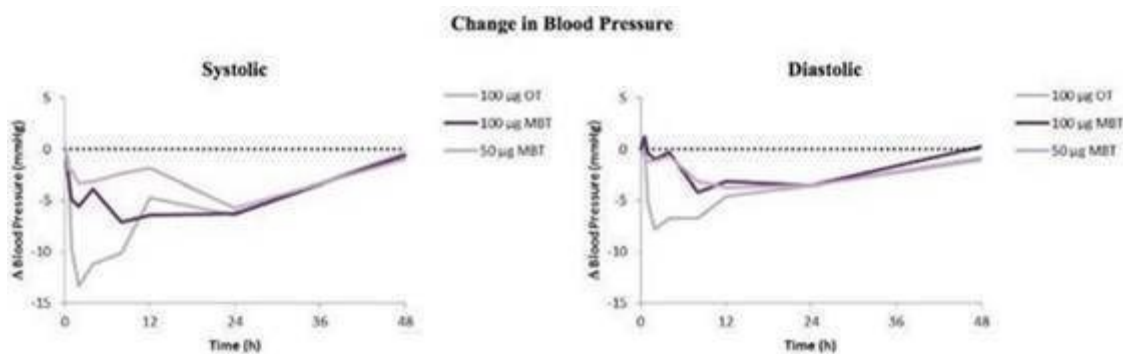
Our review of the Phase 2 clinical trial data suggests that the effect of Validive was much greater in OPC compared to non-OPC patients. We believe the Phase 2 data along with the mechanism of action of Validive provide a rationale for developing Validive for the treatment of chemoradiation induced SOM in OPC patients as a first indication. The most rapidly growing sub-population of HNC in the U.S. and Europe is OPC, largely driven by HPV+ disease. The oropharynx is the part of the throat at the back of the mouth, which includes the soft palate, the base (rear one third) of the tongue, and the tonsils. HPV+ OPC is a molecularly defined population of HNC characterized by the expression of a protein biomarker, p16 INK4a, and the presence of HPV DNA in the tumor. Evaluation of HPV status is part of the routine clinical assessment of patients with OPC prior to initiating treatment.

Validive Phase 1 Clinical Trial Data

A Phase 1 clinical trial in 36 healthy volunteers comparing the pharmacokinetics of the systemic (oral tablet) clonidine HCl with clonidine MBT (local and sustained delivery of clonidine to oral mucosa and oropharynx – Validive's formulation) was completed. This was a single-center, Phase 1, single-blind randomized, three-period, three-sequence, single-dose crossover study was conducted between August and November 2015. Healthy volunteers receiving Validive had far less systemic exposure to clonidine with the 50 µg and 100 µg clonidine MBTs (Validive) versus 100 µg clonidine HCl tablets (swallowed oral tablet). In contrast, levels of clonidine in saliva in volunteers receiving a single dose of 50 µg and 100 µg clonidine MBT (Validive) was much greater than saliva levels in volunteers receiving a single dose of 100 µg clonidine HCl tablets. Additionally, no significant effects on blood pressure were observed with the clonidine MBTs (Validive). Blood pressure effects were tested because clonidine is known to lower blood pressure when absorbed systemically. These results are consistent with the expectation that the MBT formulation (Validive) is designed to release clonidine in the oral cavity and oropharynx, as opposed to distributed systemically.



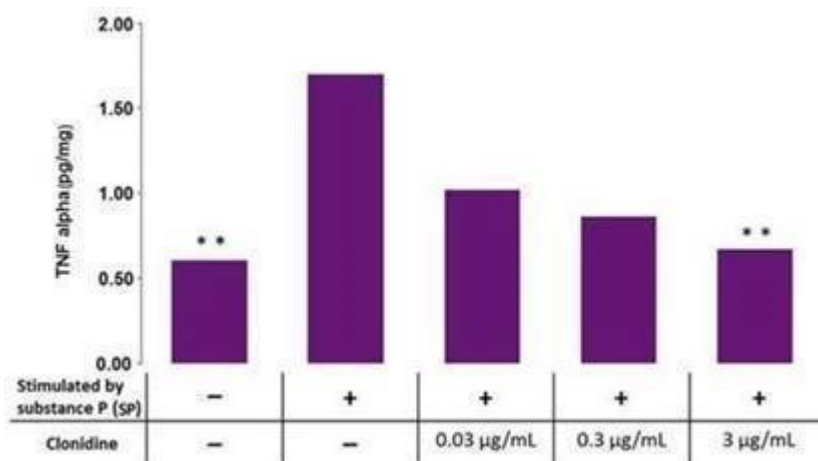
Both Validive 50 µg and 100 µg showed high salivary exposure (as seen above), with low systematic and blood pressure effect (as seen below):



Validive Preclinical Data

The anti-inflammatory properties of clonidine were studied in a human oral mucosa organotypic culture model, as pro-inflammatory cytokines are believed to drive the development of SOM. Samples of healthy non-keratinized human oral mucosa were obtained from patients undergoing surgery. The experimental oral mucosa pro-inflammatory process was mediated by the addition of neuropeptide substance P (“SP”) to the culture medium. The addition of SP on human gingiva induced a significant increase in TNF-alpha, an important pro-inflammatory molecule involved in mucositis pathogenesis. Overall, on human gingiva stimulated by SP, a concentration dependent decrease in TNF-alpha production was observed with clonidine, which was statistically significant at 3 µg/ml clonidine; see below:

Clonidine Inhibits the Production of Pro-Inflammatory Cytokine Release from Oral Tissue



** = different from SP treatment alone, p<0.01

Camsirubicin (5-imino-13-deoxydoxorubicin; formerly MNPR-201, GPX-150)

Our second product candidate, camsirubicin, is a novel analog of doxorubicin which has been designed to reduce the cardiotoxic side effects generated by doxorubicin while retaining anti-cancer activity. A Phase 2 clinical trial for camsirubicin has been completed in patients with advanced (e.g., unresectable or metastatic) soft tissue sarcoma (“ASTS”). Average life expectancy for these patients is 12-15 months. In this study, 52.6% of patients evaluable for tumor progression demonstrated clinical benefit (partial response or stable disease), which was proportional to dose and consistently observed at higher cumulative doses of camsirubicin (>1000 mg/m²). Camsirubicin was very well tolerated in this study and underscored the ability to potentially administer camsirubicin without restriction of cumulative dose in patients with ASTS. Although doxorubicin has been the standard of care treatment for ASTS for over 40 years, doxorubicin is limited to a lifetime cumulative dose maximum of 450 mg/m². Even if a patient is responding to doxorubicin, their treatment is discontinued once this lifetime cumulative dose has been reached.

Camsirubicin is a proprietary doxorubicin analog that is selective for topoisomerase II-alpha. Doxorubicin is used to treat adult and pediatric solid and blood (hematologic) cancers, including soft tissue sarcomas, breast, gastric, ovarian and bladder cancers, leukemias and lymphomas. Despite clinical studies demonstrating the anti-cancer benefit of higher cumulative doses of doxorubicin, the clinical efficacy of doxorubicin has historically been limited by the risk of patients developing irreversible, potentially life-threatening cardiotoxicity. For example, several clinical studies completed in the 1990s demonstrated that concurrent doxorubicin (60 mg/m², 8 cycles) and paclitaxel gave a 94% overall response rate in patients with metastatic breast cancer but led to 18% of these patients developing congestive heart failure. Reduction of doxorubicin to 4-6 cycles of treatment decreased the incidence of congestive heart failure, but also reduced response rates to 45-55%. In a clinical study looking at dose response, sarcoma patients on the high dose (75 mg/m²) doxorubicin had a response rate of 37% compared to just 18% in the low dose (45 mg/m²) doxorubicin group. With the cumulative dose restriction on doxorubicin, the median progression free survival for ASTS patients is approximately 6 months, with median overall survival of 12-15 months. There is a significant unmet opportunity to develop a replacement for doxorubicin that can be dosed higher and for longer to improve anti-tumor activity

Camsirubicin has been engineered specifically to retain the anticancer activity of doxorubicin while minimizing its toxic effects on the heart. Similar to doxorubicin, the antitumor effects of camsirubicin are mediated through the stabilization of the topoisomerase II complex after a DNA strand break and DNA intercalation leading to tumor cell apoptosis (cell death). Inhibiting the topoisomerase II-alpha isoform is desired for the anti-cancer effect, while inhibiting the topoisomerase II-beta isoform has been demonstrated to mediate, at least in part, the cardiotoxicity associated with all anthracycline drugs currently used in the clinic. Camsirubicin is substantially more selective than doxorubicin for inhibiting topoisomerase II-alpha versus topoisomerase II-beta. This selectivity may partly explain the minimal cardiotoxicity that has been observed for camsirubicin in preclinical and clinical studies to date. We believe that these attributes provide a strong rationale for developing camsirubicin as a monotherapy as well as in combination with other anticancer agents, without potential restrictions on cumulative dose, and offer the opportunity to pursue a large market opportunity for camsirubicin in a broad spectrum of cancer types.

Based on the encouraging clinical results to date, in September 2021, we commenced an open-label, Phase 1b dose escalation trial of camsirubicin plus growth factor support (pegfilgrastim/G-CSF) in the U.S. as first-line treatment for patients with ASTS. The aim is to administer camsirubicin without restricting cumulative dose, thereby potentially improving efficacy by keeping patients who are responding on treatment. These are patients who are not candidates for surgery or radiation treatment, and are largely made up of patients with metastatic disease. Doxorubicin is the current standard of care in the first-line setting for these patients. Although this Phase 1b is designed to determine the maximum tolerated dose of camsirubicin, given the historical dose-dependent anti-tumor response repeatedly demonstrated with doxorubicin, efficacy measurements are being tracked in these patients as the dose is increased. In November 2021, the first dose level of camsirubicin had been completed, with a positive recommendation from the trial safety review committee to proceed to the next higher dose level. We are presently enrolling patients at the fifth dose level. The fifth dose level is over twice the highest dose reached in any prior camsirubicin clinical trial (650 mg/m² versus 265 mg/m²) and no drug-related cardiotoxicity has been observed to date up to the current dose-level. The open-label Phase 1b camsirubicin dose-escalation trial is planning to enroll additional cohorts until the maximum tolerable dose is reached. In November 2022, we presented an abstract and poster of the Phase 1b clinical trial data at the Connective Tissue Oncology Society Annual Meeting in Vancouver, BC.

We currently anticipate topline results in the camsirubicin Phase 1b clinical trial by the end of 2023 and believe we have sufficient funds to advance the trial through that date. However, if camsirubicin reaches higher dose levels than we are anticipating, the Phase 1b clinical trial may still be dosing patients beyond the end of 2023 and topline results may be deferred. Although we would likely consider this a positive development, it is possible that we would require additional funding to complete an extended Phase 1b clinical trial in this situation. Regardless, additional funding is expected to be required to support further development through and beyond our ongoing Phase 1b clinical trial.

In June 2019, we entered into a clinical collaboration with Grupo Español de Investigación en Sarcomas (“GEIS”). GEIS is an internationally renowned non-profit organization focused on the research, development and management of clinical trials for sarcoma, that has worked with many of the leading biotech and global pharmaceutical companies. Following completion of our Phase 1b clinical trial, we continue to expect that GEIS will sponsor and lead a multi-country, randomized, open-label Phase 2 clinical trial evaluating camsirubicin head-to-head against doxorubicin, the current first-line treatment for ASTS. The Phase 2 clinical trial is estimated to enroll 170 ASTS patients with the primary endpoint of the trial being progression-free survival, with secondary endpoints including response rate, overall survival and incidence of treatment-emergent adverse events. We will provide study drug to GEIS and supplemental financial support for the clinical trial. In addition to camsirubicin’s orphan drug designation in the U.S. by the FDA, the European Commission also granted orphan drug designation for camsirubicin for the treatment of soft tissue sarcoma in the EU in November 2019.

Camsirubicin U.S. Market Opportunity

Camsirubicin is an analog of doxorubicin, the first anthracycline to gain FDA approval. Anthracyclines are a class of drugs that are among the most commonly used agents in the treatment of cancer. They have demonstrated efficacy in a wide variety of cancers, including soft tissue sarcoma, breast cancer, lung cancer, ovarian cancer, and lymphomas, among other types. Although doxorubicin was approved decades ago, it is still widely used. According to QY Research, in 2020 the global doxorubicin market was \$1.1836 billion, and expected to grow at a 7.7% compounded annual growth rate, with projections surpassing \$1.8 billion by 2026. According to IQVIA, in 2015 the European Union had over \$270 million in sales between doxorubicin HCl and liposomal doxorubicin. Liposomal versions of doxorubicin (e.g., Doxil[®]) demonstrated that a different formulation of doxorubicin with improved clinical benefits can command a significantly higher price premium compared to generic doxorubicin HCl.

The market opportunity for the first indication, ASTS, is anticipated to be substantial. In 2020, there were an estimated 13,130 new cases of soft tissue sarcoma (STS) in the U.S., and approximately 5,350 deaths from STS, mainly from metastatic disease. Additionally, a few years ago a PDGFR-targeted antibody (olaparumab) was granted accelerated approval based on data from an open label Phase 2 trial. In 2019, the olaparumab Phase 3 trial as first line for advanced soft tissue sarcoma came back negative, resulting in the drug being pulled from the market. Olaparumab had just completed its second full year on the market in the U.S. and abroad before being pulled, reaching over \$304 million in sales in 2018, demonstrating the large unmet medical need and considerable market opportunity in ASTS.

Camsirubicin Clinical Data

Several clinical studies of camsirubicin have been completed.

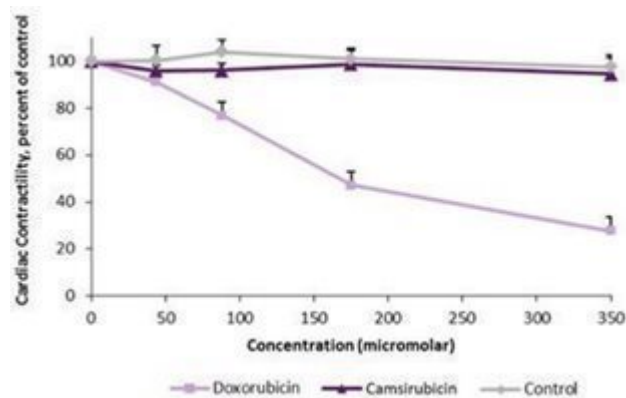
In October 2013, a Phase 1 dose escalation study conducted at the University of Iowa completed enrollment of 24 patients who received one of eight different dose levels of camsirubicin ranging from 14 to 265 mg/m². No evidence of irreversible cardiotoxicity was observed in any of these patients, including 4 patients who received prior anthracycline (doxorubicin or related molecules) treatment. Stable disease was observed in 55.0% of patients in this Phase 1 study, including 3 out of 4 patients with leiomyosarcoma, which is a type of soft tissue sarcoma that originates in connective tissue and smooth muscle most commonly in the uterus, stomach and small intestine. No growth factor support (G-CSF) was given to patients, and the limiting toxicity was neutropenia.

In January 2015, a multi-center open label single arm Phase 2 clinical trial was initiated in doxorubicin-naïve patients with ASTS. This Phase 2 clinical trial enrolled 22 patients and was completed in August 2016. Camsirubicin was administered intravenously at 265 mg/m² every 3 weeks for up to 16 doses, with all patients being given growth factor support, and there was clear indication of anticancer activity at this well-tolerated dose and schedule. The majority of patients (52.6%) evaluable for tumor progression demonstrated clinical benefit (stable disease or partial response), which was proportional to dose and consistently observed at higher cumulative doses of camsirubicin (>1000 mg/m²). The progression-free survival at 6 months was 38%, higher than the 6-month PFS of doxorubicin in three of the more recent studies, which showed 23%, 25%, and 33% 6-month PFS for doxorubicin. Camsirubicin was very well tolerated in this study and underscored the potential ability to administer camsirubicin without restriction for cumulative dose in patients with ASTS. Under compassionate use access, one patient received 20 cycles of camsirubicin (cumulative dose 5,300 mg/m²). Apart from one patient who developed febrile neutropenia and severe leukopenia, there were no grade 4 toxicities reported and no grade 3 side effects other than anemia. A transient decrease in left ventricular ejection fraction (“LVEF”) was observed in four patients treated with camsirubicin. These decreases in LVEF in camsirubicin treated patients were not serious adverse events and were transient, with LVEF subsequently returning to normal levels in all four subjects. Despite some subjects in this study receiving camsirubicin for up to 20 cycles, effects on cardiac function were of no clinical significance and there was no evidence of irreversible heart failure in any subject.

Camsirubicin Preclinical Data

In preclinical studies, camsirubicin showed a lack of acute as well as chronic functional cardiotoxicity and did not cause the cardiac histopathologic lesions observed with doxorubicin in a chronic rabbit model. Below is *in vitro* data showing the lack of altered contractility with acute exposure of rabbit atria to camsirubicin, even at high concentrations:

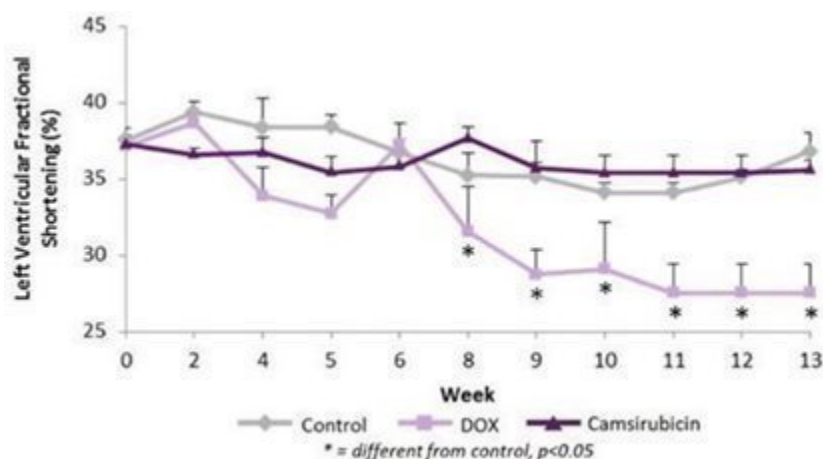
Camsirubicin Cardiac Contractility



Camsirubicin demonstrated limited effect on cardiac contractility, in-line with control

Chronic IV administration of camsirubicin two times per week into rabbits over the course of 13 weeks also showed a lack of cardiotoxicity of camsirubicin when compared to doxorubicin (“DOX”). Echocardiography was performed weekly to obtain left ventricular fractional shortening (“LVFS”) measurements to assess cardiac function. At sacrifice, all six doxorubicin-treated rabbits showed cardiac dysfunction by echocardiography, and LVFS was significantly different from control values ($p < 0.001$). In contrast, none of the camsirubicin-treated rabbits exhibited cardiac dysfunction by echocardiography at any time during the study. Below is a graph of the results:

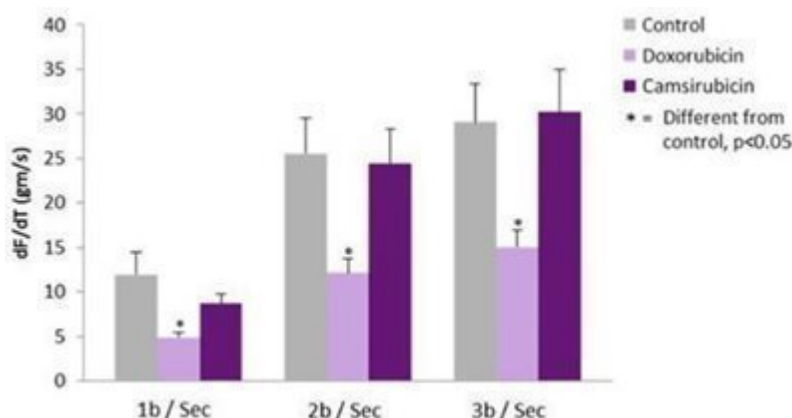
Weekly Cardiac Echoes



None of the camsirubicin treated rabbits showed significant cardiac dysfunction compared to the vehicle control.

At the conclusion of the 13 weeks of drug dosing, the rabbits were sacrificed, and the left atria were studied to assess cardiac function *ex vivo*. Atria from the doxorubicin-treated rabbits had impaired cardiac contractility (dF/dt) compared to controls over the entire force-frequency range (1, 2 and 3 Hz). Cardiac contractility for the camsirubicin treated cohort was not significantly different than the vehicle control. Below is a graph of the results:

Camsirubicin Cardiac Contractility



Cardiac contractility (dF/dt) of isolated atria at the three contraction rates (1, 2, and 3 contractions/sec) obtained from rabbits chronically infused with either doxorubicin, camsirubicin or saline vehicle (control).

Values are mean, error bars are standard error of the mean (SEM). Camsirubicin demonstrated limited effect on cardiac contractility, in-line with placebo.

Finally, cardiac scoring of the left ventricle walls obtained from the rabbits in this study by a histopathologist showed increased microscopic injury in hearts from doxorubicin-treated rabbits compared to hearts from rabbits administered the vehicle control. Heart tissues from camsirubicin-treated rabbits were the same as the vehicle controls.

MNPR-101 for Radiopharmaceutical Use

Our third program is based on MNPR-101 (formerly huATN-658), a novel first-in-class humanized monoclonal antibody to the urokinase plasminogen activator receptor (“uPAR”), for its use as a radiopharmaceutical in advanced cancers. uPAR is highly expressed in tumors while healthy tissue rarely, if ever, expresses uPAR. The expression of uPAR on diseased cells and tissues allows for selective targeting of MNPR-101, which may be modified to carry imaging and therapeutic payloads.

MNPR-101 represents a novel approach for drug targeting of uPAR as it does not interfere with normal binding of uPA to uPAR. It instead blocks the CD11b (alpha-M)-uPAR interaction. MNPR-101 is on its own believed to have potential activity against many different cancer types because it:

- is selectively expressed on metastatic tumor, tumor-associated immune, and angiogenic endothelial cells, but not on most normal cells. Several Phase 1 positron emission tomography (“PET”) imaging studies in human advanced cancer patients show that uPAR can only be detected in the tumor and not in normal tissues;
- is central to several extracellular and intracellular oncogenic pathways required for metastasis (inhibiting the uPA system in turn inhibits many other downstream targets, such as MAPK, AKT, MEK, and FAK, that are currently being targeted by other companies);
- is expressed on immune cells that allow the tumor to evade recognition by the immune system;
- mediates antibody-dependent cellular cytotoxicity (ADCC); and
- has the potential to interfere at several different signaling pathways that converge at uPAR.

Based upon the anticipated non-overlapping toxicity and distinct mechanism of action, we believe MNPR-101 has the potential to be used in combination with existing cancer therapies. The selective expression of uPAR in tumors underpins our expectation that MNPR-101 will be well-tolerated and amenable to a radiopharmaceutical treatment approach.

MNPR-101-Zr as a Potential Imaging Agent

MNPR-101-Zr is being developed as an imaging agent for the diagnosis and surveillance of multiple cancer types. In February 2023, we announced that based on promising recently generated preclinical imaging results with MNPR-101-Zr showing high uptake across multiple cancer types, we and NorthStar were committing to additional funding with the aim of initiating a first-in-human imaging study with MNPR-101-Zr as early as the end of this year.

MNPR-101-Zr is a zirconium-89 labeled version of MNPR-101. Positron emission tomography (“PET”) imaging of preclinical mouse models for triple-negative breast, colorectal, and pancreatic tumors displayed high and selective uptake of MNPR-101-Zr in these uPAR-expressing tumors.

These proof-of-concept studies provide support for a first-in-human PET imaging study with MNPR-101-Zr and a future therapeutic study using actinium-225 labeled radioimmunotherapeutic version of MNPR-101. Overall, the imaging results demonstrate the potential utility of MNPR-101 as a precision targeting agent for both imaging and therapy in multiple cancer indications.

MNPR-101 RIT

Also pursuant to our collaboration with NorthStar, we continue to develop potential radioimmunotherapeutics (“RITs”) based on MNPR-101. Our collaboration combines NorthStar’s expertise in the innovative production, supply, and distribution of important medical radioisotopes with our expertise in therapeutic drug development. NorthStar and we have filed provisional composition of matter patents covering the actinium-based radiopharmaceutical drug candidate (MNPR-101-PCTA-Ac-225). We are currently evaluating pathways to initiating a first-in-human study with this drug candidate.

MNPR-202 and Related Analogs

In June 2021, we entered into a collaboration agreement with the Cancer Science Institute of Singapore (“CSI Singapore”), one of Asia’s premier cancer research centers, at the National University of Singapore (“NUS”) (consistently ranked as one of the world’s top universities) to evaluate the activity of MNPR-202 and related analogs in multiple types of cancer. MNPR-202 was designed to retain the same potentially non-cardiotoxic backbone as camptothecin but is modified at other positions which may enable it to work in certain cancers that are resistant to camptothecin and doxorubicin. In December 2020, we announced the issuance of our composition of matter U.S. patent (US10,450,340) covering MNPR-202 and related analogs. CSI Singapore has tested MNPR-202 in preclinical cancer models with promising results and is currently conducting additional preclinical studies with MNPR-202. In December 2022, in collaboration with Dr. Anand Jeyasekharan of CSI Singapore, we presented an abstract and poster of the preclinical data of MNPR-202 at the American Society of Hematology 64th Annual Meeting in New Orleans, LA.

License, Development and Collaboration Agreements

Onxeo S.A.

In June 2016, we executed an agreement with Onxeo S.A., a French public company, which gave us the exclusive option to license (on a world-wide exclusive basis) Validive (clonidine hydrochloride mucobuccal tablet; clonidine HCl MBT) a mucoadhesive tablet of clonidine based on the Lauriad mucoadhesive technology. The agreement includes clinical, regulatory, developmental and sales milestones that could reach up to \$108 million if we achieve all milestones, and escalating royalties from 5% to 10% on net sales. In September 2017, we exercised the option to license Validive from Onxeo for \$1 million, but as of March 10, 2023, we have not been required to pay Onxeo any other funds under the agreement. We will need to raise significant funds or enter into a collaboration partnership to support the completion of clinical development and potential marketing approval of Validive.

Under the agreement, we are required to pay royalties to Onxeo on a product-by-product and country-by-country basis until the later of (1) the date when a given product is no longer within the scope of a patent claim in the country of sale or manufacture, (2) the expiry of any extended exclusivity period in the relevant country (such as orphan drug exclusivity, pediatric exclusivity, new chemical entity exclusivity, or other exclusivity granted beyond the expiry of the relevant patent), or (3) a specific time period after the first commercial sale of the product in such country. In most countries, including the U.S., the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country, not taking into consideration any potential patent term adjustment that may be filed in the future or any regulatory extensions that may be obtained. The royalty termination provision pursuant to (3) described above is shorter than 20 years and is the least likely cause of termination of royalty payments.

The Onxeo license agreement does not have a pre-determined term, but expires on a product-by-product and country-by-country basis; that is, the agreement expires with respect to a given product in a given country whenever our royalty payment obligations with respect to such product have expired. The agreement may also be terminated early for cause if either we or Onxeo materially breach the agreement, or if either we or Onxeo become insolvent. We may also choose to terminate the agreement, either in its entirety or as to a certain product and a certain country, by providing Onxeo with advance notice.

Grupo Español de Investigación en Sarcomas (“GEIS”)

In June 2019, we executed a clinical collaboration with GEIS for the development of camsirubicin in patients with ASTS. Following completion of the Phase 1b clinical trial in the U.S. that we initiated in the third quarter of 2021 with the first patient dosed in October 2021, we continue to expect that GEIS will sponsor and lead a multi-country, randomized, open-label Phase 2 clinical trial to evaluate camsirubicin head-to-head against doxorubicin, the current first-line treatment for ASTS. We will provide study drug and supplemental financial support for the clinical trial. For the three months ended March 31, 2021, we incurred \$0.3 million in expenses related to the GEIS collaboration including clinical material manufacturing-related expense, clinical consulting, database management expenses and intellectual property expenses. We can terminate the agreement by providing GEIS with advance notice, and without affecting our rights and ownership to any related intellectual property or clinical data. In the second quarter of 2021, due to regulatory delays in Spain, we decided to conduct an open-label Phase 1b clinical trial of camsirubicin in the U.S., therefore no expenses were incurred related to the GEIS collaboration beyond March 31, 2021.

XOMA Ltd.

To humanize our MNPR-101 antibody, we have taken a non-exclusive license to XOMA (US) LLC’s humanization technology and know-how. Humanization involves replacing most of the non-critical parts of the mouse sequence of an antibody with the human sequence to minimize the ability of the human immune system to recognize this antibody as foreign. As such, MNPR-101 has been engineered to be 95% human sequence using the XOMA technology. Under the terms of the license, we are to pay only upon developmental and sales milestone achievements which could reach up to \$14.925 million if we achieve all milestones. The agreement does not require the payment of sales royalties. There can be no assurance that we will reach any milestones. As of March 10, 2023, we had not reached any milestones and had not been required to pay XOMA Ltd. any funds under this license agreement. The first milestone payment is payable upon first dosing of a human patient in a Phase 2 clinical trial.

Intellectual Property Portfolio and Exclusivity

An important part of our strategy is obtaining patent protection to help preserve the proprietary nature of our product candidates, and to prevent others from developing competitive agents that are similar. Our patent portfolio includes issued patents and pending patent applications in the U.S. and in foreign countries. Our general practice is to seek patent protection in major markets worldwide.

Validive

We license all intellectual property related to Validive from Onxeo S.A., a French public company. See “Business – License, Development and Collaboration Agreements”. Validive is covered by 57 issued patents in 31 jurisdictions, including the U.S., EU, Japan, and other Asian countries, and has orphan drug designation in the EU as well as Fast Track designation from the FDA. These patents are method of use patents that cover the use of Validive to prevent and/or treat inflammation and inflammatory pain of the mucosa including cancer therapy-induced mucositis; the use of clonidine or clonidine derivatives for the prevention or treatment of adverse side effects of chemotherapy; and clonidine and/or clonidine derivatives for use in the prevention of skin injury resulting from radiotherapy, and have been assigned to us pursuant to our license agreement with Onxeo. The latest patent expires in 2035 not accounting for possible extensions.

In November 2020, we announced a series of recently issued patents for Validive (clonidine HCl mucobuccal tablet). These patents, including U.S. Patent No. 10,675,271, provide claims covering “Clonidine and/or clonidine derivatives for use in the prevention and/or treatment of adverse side effects of chemotherapy”. These patents expand the potential use of Validive in cancer patients, beyond the earlier allowed claims for the prevention of oral mucositis in patients receiving CRT. Specifically, they provide protection for the potential ability of Validive to prevent or treat common chemotherapy-associated side effects such as asthenia and fatigue and would provide protection should we determine in the future to conduct additional Validive development activities related to adverse side effects of chemotherapy beyond oropharyngeal cancer.

Camsirubicin

Camsirubicin (GPX-150) is covered by manufacturing process patents. We have a patent for chemical synthesis technology that efficiently converts cardiotoxic “13-keto” anthracyclines such as doxorubicin, daunorubicin, epirubicin, and idarubicin into novel, patentable, and most likely less-cardiotoxic “5-imino-13-deoxy” analogs. A novel chemical composition of an intermediate for this synthesis is also patented. In addition, we have a patent covering the combination of camsirubicin with paclitaxel for the treatment of cancer, plus covering the method of use of these two drugs for this purpose. Our camsirubicin patent portfolio contains eight issued U.S. patents (two of which have expired) and one U.S. pending patent application. We have certain corresponding patents and applications in twenty-nine foreign jurisdictions, including the U.S., EU, Japan, and other Asian countries. The process patents for the synthesis of camsirubicin intermediates will expire in 2024 and the patents covering the combination use of camsirubicin and its analogs with taxanes will expire in 2026. The patent covering novel, potentially more potent analogs of camsirubicin expires in 2038. We may pursue patent term extensions where appropriate. We have obtained patent protection around the intermediates and process used to manufacture camsirubicin and we expect to obtain Hatch-Waxman exclusivity (applicable to new chemical entities) for 5 years that will prevent generic competition. We have also obtained U.S. and EU orphan drug status in soft tissue sarcoma with additional orphan cancer indications expected to follow.

In December 2020, we announced the issuance of a U.S. patent (US 10,450,340) covering compositions of matter (2-pyrrilino camsirubicin) for a novel family of camsirubicin analogs. This patent, which expands the Company's camsirubicin intellectual property portfolio, is expected to expire in 2038 not including any patent term extensions. The patent broadens our camsirubicin portfolio and creates a pipeline that has been designed to retain the potentially favorable non-cardiotoxic chemical backbone of camsirubicin and the potent broad-spectrum antitumor activity of doxorubicin. Further, preclinical evidence suggests that this new family of 2-pyrrilino camsirubicin analogs could be active in doxorubicin-resistant tumor cells which may enable use in cancer types beyond those possible with camsirubicin.

MNPR-101

Our patent portfolio for our MNPR-101 antibody (huATN-658), as well as its epitope, consists of two issued U.S. composition of matter and their methods of use patents and corresponding (granted and pending) patents and patent applications in twenty-two foreign jurisdictions, including the European Union, Japan, and other Asian countries. These patents are owned by us. The patents covering the composition of matter of MNPR-101 will expire in 2025 and the patents covering the MNPR-101 epitope will expire in 2027. Being a novel biologic, it is eligible for 12 years of exclusivity in the U.S. under the Biologics Price Competition and Innovation Act ("BPCI Act"), and it will benefit from varying durations of similar exclusivity in numerous other countries. The Radio-Immuno-Therapeutic derivative of MNPR-101 (uPRIT) patent, if granted expires in 2041.

Patent life determination depends on the date of filing of the application and other factors as promulgated under the patent laws. In most countries, including the U.S., the patent term is generally 20 years from the earliest claimed filing date (the priority date) of a non-provisional patent application in the applicable country, not taking into consideration any potential patent term adjustment that may be filed in the future or any regulatory extensions that may be obtained. Some of our patents are currently near expiration and we may pursue patent term extensions for these where appropriate. See "Risk Factors – Risks Related to our Intellectual Property".

MNPR-101 for Radiopharmaceutical Use

In collaboration with NorthStar, we filed a provisional patent application entitled "Precision Radioimmunotherapeutic Targeting of the Urokinase Plasminogen Activator Receptor (uPAR) for Treatment of Severe COVID-19 Disease" with the USPTO on June 15, 2020. A full international application (International Application Number PCT/US2021/037416) that claims priority to the provisional filing date was filed under the Patent Cooperation Treaty ("PCT") on June 15, 2021. This application covers novel compositions and uses of cytotoxic radioisotopes attached to antibodies that bind to uPAR, thereby creating precision targeted radiotherapeutics, also known as uPRITs, for the treatment of severe COVID-19 and other respiratory diseases. Advanced COVID-19 patients frequently develop severe, life-threatening, pulmonary inflammation as a result of a viral induced cytokine storm. The development of this cytokine storm is associated with a high rate of mortality in severe COVID-19 patients, even when oxygen support and mechanical ventilation are utilized. uPRITs have been designed with the goal of selectively eradicating the aberrantly activated immune cells responsible for causing cytokine storm and its harmful systemic effects. The co-inventors of the provisional patent application are James Harvey, Chief Scientific Officer of NorthStar, and Andrew P. Mazar, former Monopar Chief Scientific Officer.

In May 2021, we and NorthStar filed a provisional patent application with the USPTO titled "Bio-Targeted Radiopharmaceutical Compositions Containing Ac-225 and Methods of Preparation." Radiopharmaceutical therapy is a promising approach to treat cancer and other diseases using radioactive isotopes bound with proteins/antibodies to target and kill cells. If validated through further evaluation, it could potentially improve efficacy and safety and enhance manufacturing efficiency of actinium-based radiopharmaceuticals, the full potential of which are presently constrained by the price and scarcity of Ac-225.

Also in May 2021, we and NorthStar filed a provisional composition of matter patent application titled "Urokinase Plasminogen Activator Receptor-Targeted Radiopharmaceutical" covering a radiotherapeutic consisting of our proprietary antibody MNPR-101 bound to Ac-225 via the isotope binding agent PCTA. This RIT demonstrated 98% radiochemical purity and high stability and has the potential to be a highly selective, potent treatment for a variety of cancers, severe COVID-19, and other diseases characterized by aberrant uPA receptor expression.

Manufacturing

We do not currently own or operate manufacturing facilities for the production or testing of Validive, camsirubicin, MNPR-101, MNPR-101-Zr, MPNR-101 RITs or MNPR-202, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We presently depend on third-party contract manufacturers for all our required raw materials, Active Pharmaceutical Ingredients (“API”), and finished drug products for our preclinical and clinical studies. Both COVID-19 and the Russia-Ukraine war, and related impacts on inflation and supply chain logistics, may impact the cost and delay shipping of supplies for our clinical materials manufacturing due to the rising cost of fuel and sanctions that may delay global shipping. We have completed manufacturing of the clinical batches of drug product for Validive that are currently being utilized in our ongoing Phase 2b/3 VOICE clinical trial and for camsirubicin which are being used in our ongoing Phase 1b dose-escalation camsirubicin clinical trial. We are in the midst of manufacturing more camsirubicin for the clinical trials. We continue to develop MNPR-101-Zr, MNPR-101 RIT and MNPR-202 for potential scale-up.

Sales and Marketing

In light of our stage of corporate development, we have not yet established a commercial organization or distribution capabilities. We have retained worldwide commercial rights for our product candidates. If our product candidates receive marketing approval, we plan to commercialize them in the U.S. and potentially in Europe with our own focused, specialty sales force to be developed. We would expect to conduct most of the buildout of this organization following approval in the U.S. or following similar marketing authorizations in Europe of any of our product candidates. We expect to explore commercialization of Validive and potentially other product candidates in certain markets outside the U.S., including the EU, utilizing a variety of collaboration, distribution and other sales and marketing arrangements with one or more third parties.

Oncology Market Competition

The pharmaceutical industry in general, and the oncology therapeutics sector in particular, are characterized by intense competition. We face competition from pharmaceutical and biotechnology companies, many of which are larger and better financed than us. We also face competition in our efforts to develop and commercialize new oncology therapeutics from academic and government laboratories. The therapeutics that we are developing, if successfully commercialized, will have to compete with existing therapeutics already on the market and novel therapeutics currently in development, as well as new therapeutics that may be discovered and developed in the future. Our product candidates will also have to compete with alternate treatment modalities, such as improvements in radiation treatments, which are also subject to continual innovation and improvement. Additional information can be found in the section entitled “Risk Factors – Risks Related to Our Business Operations and Industry.”

Validive

There is no effective standard of care or FDA approved preventive or therapeutic treatment for patients that develop chemoradiation-induced SOM. Only symptomatic treatments such as opioids and palliative mouthwashes are available but have no effect on the occurrence, time to onset, or duration of SOM. Our primary competitor is a dismutase mimetic which recently completed its Phase 3 clinical development including submission to the FDA for marketing approval. The dismutase mimetic is administered through a daily 60-minute intravenous (“IV”) infusion to be completed within an hour before each radiation treatment. Validive, in comparison, is an easy to use, once daily self-administered oral/buccal tablet that acts locally at the sites of SOM.

Camsirubicin

We believe our camsirubicin program, if approved, could replace doxorubicin as the first-line treatment for ASTS. In addition, we believe that camsirubicin would compete with a number of currently available anthracycline-based drugs on the market for other cancer indications. These are largely derivatives of doxorubicin, or reformulations of doxorubicin such as liposomal doxorubicin (e.g., Doxil, sold by Johnson & Johnson). All of these have the issue of cardiotoxicity. In addition to approved products, there are a number of product candidates in development, largely as new formulations or derivatives of doxorubicin.

MNPR-101 for Radiopharmaceutical Use and MNPR-202

Our MNPR-101-Zr, MNPR-101 RIT and MNPR-202 programs are in the early stages of development and the most susceptible to all of the competitive factors listed in the first paragraph of this section on Oncology Market Competition.

Government Regulation and Product Approval

Government authorities in the U.S., at the federal, state and local level, and in 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. The pharmaceutical product candidates that we develop must be approved by the FDA before they may be legally marketed in the U.S. See “Risk Factors – Risks Related to Clinical Development and Regulatory Approval”.

U.S. Pharmaceutical Product Development Process

In the U.S., the FDA regulates pharmaceutical products under the Federal Food, Drug and Cosmetic Act (“FDCA”) and implementing regulations. Pharmaceutical products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial enforcement. FDA enforcement could result in refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a non-biological pharmaceutical product may be marketed in the U.S. generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices (“GLP”), and other applicable regulations;
- Submission to the FDA of an Investigational New Drug application (“IND”), which must become effective before human clinical studies may begin;
- Performance of adequate and well-controlled human clinical studies according to the FDA’s current Good Clinical Practices (“GCP”), to establish the safety, efficacy and optimum dose of the proposed pharmaceutical product for its intended use;
- Submission to the FDA of a New Drug Application (“NDA”) or Biologics License Application (“BLA”), for a new pharmaceutical product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the pharmaceutical product is produced to assess compliance with the FDA’s current Good Manufacturing Practice standards (“cGMP:”), to assure that the facilities, methods and controls are adequate to preserve the pharmaceutical product’s identity, strength, quality and purity;
- FDA audits of the preclinical and clinical study sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA; and
- Fulfillment of FDA post-marketing requirements, if any.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources, and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the pharmaceutical product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as in-vitro and animal studies to assess the potential safety and activity of the pharmaceutical product candidate. These early proof-of-principle studies are done using sound scientific procedures and thorough documentation. The conduct of single and repeat dose toxicology and toxicokinetic studies in animals must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA has concerns and notifies the sponsor. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. If resolution cannot be reached within the 30-day review period, either the FDA places the IND on clinical hold, or the sponsor withdraws the application. The FDA may also impose clinical holds on a pharmaceutical product candidate at any time before or during clinical studies due to safety concerns or non-compliance. Accordingly, it is not certain that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such clinical studies.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA or BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the sponsor to ask specific questions to the FDA, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical (registration) trial(s) that they believe will support approval of the new drug. A sponsor may be able to request a Special Protocol Assessment (“SPA”), the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analyses that will form the primary basis of an efficacy claim.

According to FDA guidance for industry on the SPA process, a sponsor which meets the prerequisites may make a specific request for a SPA and provide information regarding the design and size of the proposed clinical trial. The FDA’s goal is to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. A SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the IND record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began.

Clinical studies involve the administration of the pharmaceutical product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the clinical study sponsor’s control. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, how the results will be analyzed and presented and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical studies must be conducted in accordance with Good Clinical Practice (“GCP”) guidelines. Further, each clinical study must be reviewed and approved by an independent institutional review board (“IRB”), at, or servicing, each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and is tasked with considering such items as whether the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

Human clinical studies are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The pharmaceutical product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.
- Phase 2. The pharmaceutical product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases, to determine dosage tolerance, optimal dosage and dosing schedule and to identify patient populations with specific characteristics where the pharmaceutical product may be more effective.
- Phase 3. Clinical studies are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. The studies must be well-controlled and usually include a control arm for comparison. One or two Phase 3 studies are required by the FDA for an NDA or BLA approval, depending on the disease severity and other available treatment options.
- Post-approval studies, or Phase 4 clinical studies, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.
- Progress reports detailing the results of the clinical studies must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB’s requirements or if the pharmaceutical product has been associated with unexpected serious harm to patients.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the pharmaceutical product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the pharmaceutical product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final pharmaceutical product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the pharmaceutical product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the pharmaceutical product, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act (“PREA”), an NDA, BLA or a supplement thereof must contain data to assess the safety and effectiveness of the pharmaceutical product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any pharmaceutical product for an indication for which orphan designation has been granted.

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA or BLA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act (“PDUFA”), the FDA has 10 months in which to complete its initial review of a standard NDA or BLA and respond to the applicant, and six months for a priority NDA or BLA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the NDA or BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

After the NDA or BLA submission is accepted for filing, the FDA reviews the NDA or BLA application to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product’s identity, strength, quality and purity. The FDA may refer applications for novel pharmaceutical products or pharmaceutical products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the 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. During the pharmaceutical product approval process, the FDA also will determine whether a risk evaluation and mitigation strategy (“REMS”), is necessary to assure the safe use of the pharmaceutical product. If the FDA concludes that a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the NDA or BLA without a REMS, if required.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product 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 as well as the site where the pharmaceutical product is manufactured to assure compliance with GCP and cGMP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. In addition, the FDA will require the review and approval of product labeling.

The NDA and BLA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than the sponsor interprets the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA or BLA. The complete response letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing which involves clinical studies designed to further assess pharmaceutical product safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new pharmaceutical products that meet certain criteria. Validive has Fast Track designation. New pharmaceutical products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. The Fast Track designation must be requested by the sponsor. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. With a Fast Track designated product, the FDA may consider for review sections of the NDA or BLA 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 or BLA, if the FDA agrees to accept sections of the NDA or BLA and determines that the schedule is acceptable and if the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

Any product submitted to the FDA for marketing approval, including a Fast Track program, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new pharmaceutical product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Pharmaceutical products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that the products 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 a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a pharmaceutical product receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Breakthrough Therapy Designation

The FDA is also required to expedite the development and review of the application for approval of drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new product candidate may request that the FDA designate the product candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. Validive, camsirubicin and MNPR-101 may all be eligible for breakthrough therapy designation pending additional data.

European Union Drug Review and Approval

In the European Economic Area ("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 ("MA"). There are two types of MA:

The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the CHMP, or Committee for Medicinal Products for Human Use, of the European Medicines Agency ("EMA"), is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes and auto-immune and viral diseases. 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 EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. 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.

PRIME Designation

The EMA launched its PRIME regulatory initiative to enhance support for the development of therapies that target an unmet medical need. The initiative focuses on drugs that may offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options. These therapies are considered priority medicines within the EU. Through PRIME, the EMA offers early, proactive and enhanced support to drug developers to optimize the generation of robust data on a therapy's benefits and risks and enable accelerated assessment of drug applications. MNPR-101 may be eligible for PRIME designation.

Post-Approval Requirements

Any pharmaceutical products for which a sponsor receives FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA and FTC promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, prohibitions on promoting pharmaceutical products for uses or in patient populations that are not described in the pharmaceutical product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, actions by the U.S. Department of Justice and/or U.S. Department of Health and Human Services Office of Inspector General, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available pharmaceutical products for off-label uses, manufacturers may not directly or indirectly market or promote such off-label uses.

Manufacturers of FDA approved products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance, as well as the corresponding maintenance of records and documentation. Pharmaceutical product manufacturers and other entities involved in the manufacture and distribution of approved pharmaceutical products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical product candidates for which we obtain regulatory approval. In the U.S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part upon the availability of reimbursement from third-party payers. Third-party payers include government payers such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a pharmaceutical product may be separate from the process for setting the price or reimbursement rate that the payer will pay for the pharmaceutical product. Third-party payers may limit coverage to specific pharmaceutical products on an approved list, or formulary, which might not include all of the FDA-approved pharmaceutical products for a particular indication. Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. A payer's decision to provide coverage for a pharmaceutical product does not imply that an adequate reimbursement rate will be approved.

In 2003, the federal government enacted legislation providing a partial prescription drug benefit for Medicare recipients, which became effective at the beginning of 2006. However, to obtain payments under this program, a company would be required to sell products to Medicare recipients through prescription drug plans operating pursuant to this legislation. As part of their participation in the Medicare prescription drug program, these plans negotiate discounted prices for prescription drugs. Federal, state and local governments in the U.S. continue to consider legislation to limit the growth of health care costs, including the requirement to reduce the price of certain prescription drugs. Future legislation and regulations could limit payments for pharmaceuticals such as the product candidates that we are developing.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical studies that compare the cost-effectiveness of a particular pharmaceutical product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

International Regulation

In addition to regulations in the U.S., there are a variety of foreign regulations governing clinical studies and commercial sales and distribution of our future product candidates. Whether or not FDA approval is obtained for a product, approval of a product must be obtained by the comparable regulatory authorities of foreign countries before clinical studies or marketing of the product can commence in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary greatly from country to country. In addition, certain regulatory authorities in select countries may require us to repeat previously conducted preclinical and/or clinical studies under specific criteria for approval in their respective country which may delay and/or greatly increase the cost of approval in certain markets targeted for approval by us.

Under E.U. regulatory systems, marketing applications for pharmaceutical products must be submitted under a centralized procedure to the EMA. The centralized procedure provides for the granting of a single marketing authorization that is valid for all E.U. member states. The EMA also has designations for Orphan Drugs, which, if applicable, can provide for faster review, lower fees and more access to advice during drug development. While the marketing authorization in the European Union is centralized, the system for clinical studies (application, review and requirements) is handled by each individual country. Approval to run a clinical study in one country does not guarantee approval in any other country. The pharmaceutical industry in Canada is regulated by Health Canada. A New Drug Submission (“NDS”) is the equivalent of a U.S. NDA and must be filed to obtain approval to market a pharmaceutical product in Canada. Marketing regulations and reimbursement are subject to national and provincial laws. In Japan, applications for approval to manufacture and market new drugs must be approved by the Ministry of Health, Labor and Welfare. Nonclinical and clinical studies must meet the requirements of Japanese laws. Results from clinical studies conducted outside of Japan must be supplemented with at least a bridging clinical study conducted in Japanese patients.

In addition to regulations in Europe, Canada, Japan and the U.S., there are a variety of foreign regulations governing clinical studies, commercial distribution and reimbursement of future product candidates which we may be subject to as we pursue regulatory approval and commercialization of Validive, camsirubicin, MNPR-101, or any future product candidates internationally.

Compliance with Environmental Laws

Since we do not have our own laboratory or manufacturing facilities, we do not estimate any annual costs of compliance with environmental laws.

Employees

Our operations are currently managed by five individuals (including our executive chairman and our Acting Chief Medical Officer), of whom two have a PhD, two have an MD, two have an MBA, one has an MSc in health economics and policy, one has an MS from Stanford University, and one is a former CPA. They have worked at industry leading companies such as BioMarin Pharmaceutical Inc., Raptor Pharmaceuticals, and Onyx Pharmaceuticals. As of March 10, 2023, we had twelve employees; eleven of whom were full-time. We anticipate hiring additional employees in clinical operations, regulatory affairs and other departments, to help manage our clinical studies, regulatory submissions, and manufacturing to support Validive and camsirubicin program development, business development and corporate strategy. In addition, to complement our internal expertise, we have contracts with medical and scientific consultants, manufacturers, laboratories, and contract research organizations that specialize in various aspects of drug development including clinical development, preclinical development, manufacturing, quality assurance, and regulatory affairs.

Corporate Information

We were formed as a Delaware limited liability company in December 2014, with the name Monopar Therapeutics, LLC. In December 2015, we converted to a Delaware C corporation. Our principal executive offices are located at 1000 Skokie Blvd, Suite 350, Wilmette, IL 60091. Our telephone number is (847) 388-0349. Our corporate website is located at www.monopartx.com. Any information contained in, or that can be accessed through our website, is not incorporated by reference in this Annual Report on Form 10-K.

Trademark Notice

We have a registered trademark with the USPTO for “Validive”. All other trademarks, service marks and trade names in this Annual Report on Form 10-K are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks used herein.

Available Information

Our corporate website is located at www.monopartx.com. The reference to these website addresses does not constitute incorporation by reference of the information contained on the websites and should not be considered part of this Annual Report on Form 10-K.

We intend to satisfy any disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics by posting such information on our website as specified above.

Item 1A. Risk Factors

RISK FACTORS

An investment in our common stock involves a high degree of risk. A prospective investor should carefully consider the following information about these risks, together with other information appearing elsewhere in this Annual Report on Form 10-K, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future prospects and prospective investors could lose all or part of their investment. The risk factors discussed below and elsewhere in this Annual Report on Form 10-K are not exhaustive; other significant risks may exist that are not identified in this Annual Report on Form 10-K, but that might still materially and adversely affect our business, prospects, financial condition, and results of operations were any of such risks to occur.

Risks Related to Our Financial Condition and Capital Requirements

We have a limited operating history, expect to incur significant operating losses, and have a high risk of never being profitable.

We commenced operations in December 2014 and have an operating history of approximately eight years. Therefore, there is limited historical financial or operational information upon which to evaluate our performance. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by companies in their early clinical stages of operations. Many, if not most, companies in our industry at our stage of development never become profitable and are acquired, merge, sell major product assets or go out of business before successfully developing any product that generates revenue from commercial sales and enables profitability.

From inception in December 2014 through December 31, 2022, we have incurred losses of approximately \$51.8 million, which includes \$13.5 million of non-cash in-process research and development, which was incurred in connection with our 2017 acquisition of camsirubicin. We expect to continue to incur substantial operating losses over the next several years for the clinical development of our current and future licensed or purchased product candidates and will continue to incur losses for the foreseeable future. We expect that our R&D and G&A expenses will increase to enable the execution of our strategic plan. As a result, we anticipate that we will seek to raise additional capital within the next 12 months to fund our future operations. We will seek to obtain needed capital through a combination of equity offerings, including the usage of our Capital on Demand™ Sales Agreement with JonesTrading, debt financings, strategic collaborations and grant funding. To date, we have funded our operations through net proceeds from the initial public offering of our common stock, net proceeds from sales of our common stock through an at-the-market sales program, private placements of our preferred and common stock, and the net receipt of funds related to our acquisition of camsirubicin and related assets.

The amount of future losses and when, if ever, we will become profitable are uncertain. We do not have any products that have generated revenues from commercial sales, and do not expect to generate revenues from the commercial sale of products in the near future, if ever. Our ability to generate revenue and achieve profitability will depend on, among other things, successful completion of the development of our product candidates; obtaining necessary regulatory approvals from the FDA and international regulatory agencies; establishing manufacturing/quality, sales, and marketing and distribution arrangements with third parties; obtaining adequate reimbursement by third-party payers; and raising sufficient funds to finance our activities. If we are unsuccessful at some or all of these undertakings, our business, financial condition, and results of operations are expected to be materially and adversely affected.

We will need to raise substantial additional funding or find a suitable pharmaceutical partner to continue to advance our clinical programs and support our preclinical activities.

In order to be commercially viable, we must successfully research, develop, test, obtain regulatory approval for, manufacture, introduce, market and distribute Validive, camsirubicin, MNPR-101-Zr, MNPR-101 RIT, MNPR-202, and, if applicable, any current and future product candidates we may develop. The estimated required capital and time-frames necessary to achieve these developmental milestones as described in this Annual Report on Form 10-K or as we may state from time to time is subject to inherent risks, which are beyond our control. Clinical development of Validive, camsirubicin, MNPR-101-Zr, MNPR-101 RIT, and MNPR-202 will require significant funds. Proceeds to-date from the sales of our common stock we believe could be sufficient for us to complete our ongoing open-label Phase 1b camsirubicin clinical trial (but this may not be the case if camsirubicin reaches even higher dose levels than we are anticipating) and, assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, continue enrolling the Phase 3 portion of our ongoing Validive Phase 2b/3 (VOICE) clinical program, but will not be sufficient for us to complete our VOICE clinical program, including if we need to run a second confirmatory Phase 3 clinical trial and support further development through and beyond our ongoing Phase 1b camsirubicin clinical trial. To complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will need to raise additional funding in the millions or tens of millions of dollars. Therefore, we will need to raise significant additional funds or find a suitable pharmaceutical partner within the next 12 months to complete the VOICE clinical program, as well as support further development of camsirubicin through and beyond our ongoing Phase 1b, to support MNPR-101-Zr, MNPR-101 RIT and MNPR-202 and related compounds in various indications and generally to support our current and any future product candidates through completion of clinical trials, approval processes and, if applicable, commercialization. If we are able to raise financing, it may be on terms that are unfavorable to us and if we are unable to raise sufficient funds or find a suitable pharmaceutical partner, we may have to discontinue or delay clinical development of Validive and/or any other of our current or future product candidates.

If the interim analysis for our ongoing Validive Phase 2b/3 clinical program yields a no-go decision, our business would be adversely impacted.

This interim analysis for our ongoing Validive Phase 2b/3 clinical program, and the resulting go/no-go decision about whether to proceed to the Phase 3 portion of the trial, is expected by the end of March 2023. Because the interim analysis is being performed by an independent data monitoring committee, we do not know what the results will be as of the date of this Annual Report. If the interim analysis results in a no-go decision, we would need to reconsider our efforts with respect to Validive and refocus our development efforts on our other product candidates. Validive has been our lead product candidate to date and is the most clinically advanced, and if we had to reconsider or abandon our efforts, it would likely materially adversely impact our financing prospects, as well as the price of our common stock.

Our operations and financial results could be adversely impacted by COVID-19, which may negatively impact our ability to manufacture our product candidates for our clinical trials, our ability to accrue and conduct our clinical trials, and may delay regulatory agency responses. Any such impact will negatively impact our financial condition and could require us to delay our clinical development programs.

In response to COVID-19 and its effects on clinical trials, we modified the original adaptive design Phase 3 clinical trial for our lead product candidate, Validive, in 2020 to be a Phase 2b/3 VOICE clinical trial to better fit the types of trials which can enroll patients in the current environment. We have activated sites and commenced dosing in our VOICE clinical program. We completed enrollment of the Phase 2b portion of the trial and commenced enrollment of the Phase 3 portion of the VOICE trial. To complete VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will need to raise additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive), or find a suitable pharmaceutical partner, both of which we are planning to pursue within the next 12 months. There can be no assurance that any such events will occur, and the long-term effects of COVID-19 continue to create uncertainties and challenges to our ability to seek additional funding and explore collaborations and partnerships.

While we are currently continuing our ongoing clinical trials, COVID-19 and related precautions have directly or indirectly impacted the timeline for certain of our clinical trials. We are continuing to monitor the impact of COVID-19 on our operations and ongoing clinical development activity, generally. As a result of COVID-19, we may experience further disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- Delays in receiving approval from the FDA and foreign regulatory authorities to initiate our planned clinical trials;
- Delays or difficulties in enrolling and monitoring patients in our clinical trials;
- Delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- Delays in trial drug shipments due to COVID-19 vaccine shipments tying up available pharmaceutical product shipping lanes and increasing their cost;
- Diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- Risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- Interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- Interruption or delays in the operations of the FDA and foreign regulatory agencies, which may impact approval timelines;
- Interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing or supply shortages, production slowdowns, global shipping delays or stoppages and disruptions in delivery systems;
- Limitation on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of our employees or their families or the desire of employees to avoid contact with large groups of people.
- Refusal of the FDA to accept data from clinical trials in affected geographies; and
- Impacts from prolonged remote work arrangements, such as increased cybersecurity risks.

The extent to which the long-term effects of COVID-19 further impacts our business, including our preclinical studies and clinical trials, results of operations and financial condition will depend on future developments which remain highly uncertain and cannot be predicted with confidence. Such factors include but are not limited to the global availability and acceptability of available vaccinations, the continued efficacy of available vaccines and treatments, the potential and duration of another major outbreak and the impacts of new variations of the virus, continued or reimplemented travel restrictions, local states of emergency requiring quarantines and shelter-in-place orders, adherence to social distancing and mask-wearing recommendations in the U.S. and other countries and the availability of effective global therapeutics to treat COVID-19.

The Russia-Ukraine war will likely have continuing global effects on fuel costs and shipping and broader impacts on economic, trade and financial market conditions, which could delay the shipping of supplies for our clinical material manufacturing, potentially resulting in increased manufacturing expenses, delays to our clinical programs and adverse effects on our financing activities and financial condition.

The Russia-Ukraine war is a volatile situation, resulting in financial services and banking instability in the region. The U.S. and other countries' sanctions against Russia and Russian entities, together with existing inflationary conditions and supply chain challenges arising in the wake of COVID-19, are affecting fuel costs and shipping, resulting in higher costs and delays for various types of supplies. These cost increases and delays may affect our clinical material manufacturing which will likely have an adverse effect on our financial condition. In addition, at this stage, we are unable to predict whether the war will have broader adverse impacts to European, U.S. or global economic, trade and financial market conditions, which could adversely affect our operations and financial condition in a variety of ways. In particular, financial market instability or volatility may make it more difficult to raise required financing.

If we continue to incur operating losses and fail to obtain the capital necessary to fund our operations, we will be unable to advance our development programs, complete our clinical trials, or bring products to market, or may be forced to reduce or cease operations entirely. In addition, any capital obtained by us may be obtained on terms that are unfavorable to us, our investors, or both.

While we believe adequate cash is currently available to operate for the next twelve months, developing a new drug and conducting clinical trials and the regulatory review processes for one or more disease indications involves substantial costs. We have projected cash requirements for the near term based on a variety of assumptions, but some or all of such assumptions are likely to be incorrect and/or incomplete, possibly materially in an adverse direction. Our actual cash needs may deviate materially from those projections, changes in market conditions or other factors may increase our cash requirements, or we may not be successful even in raising the amount of cash we currently project will be required for the near term. We will need to raise additional capital in the future; the amount of additional capital needed will vary as a result of a number of factors, including without limitation the following:

- receiving less funding than we require;
- higher than expected costs to manufacture and ship our active pharmaceutical ingredient and our product candidates;
- higher than expected costs for preclinical testing;
- an increase in the number, size, duration, and/or complexity of our clinical trials;
- slower than expected progress in developing Validive, camsirubicin, MNPR-101-Zr, MNPR-101 RIT, MNPR-202 or other product candidates, including without limitation, additional costs caused by program delays;
- higher than expected costs associated with attempting to obtain regulatory approvals, including without limitation additional costs caused by additional regulatory requirements or larger clinical trial requirements;
- higher than expected personnel, consulting or other costs, such as adding personnel or industry expert consultants or pursuing the licensing/acquisition of additional assets; and
- higher than expected costs to protect our intellectual property portfolio or otherwise pursue our intellectual property strategy.

When we attempt to raise additional financing, there can be no assurance that we will be able to secure such additional financing in sufficient quantities or at all. We may be unable to raise additional capital for reasons including, without limitation, our operational and/or financial performance, investor confidence in us and the biopharmaceutical industry, credit availability from banks and other financial institutions, the status of current projects, and our prospects for obtaining any necessary regulatory approvals. General economic and financial market conditions, which have recently been impacted by inflation, bank instability and other factors, can also adversely impact our ability to raise additional financing. Potential investors' capital investments may have shifted to other opportunities with perceived greater returns and/or lower risk, thereby reducing capital available to us, if available at all.

In addition, any additional financing might not be available, and even if available, may not be available on terms acceptable to us or our then-existing investors. We will seek to raise funds through public or private equity offerings, including the usage of our Capital on DemandTM Sales Agreement with JonesTrading, debt financings, corporate collaboration or licensing arrangements, mergers, acquisitions, sales of intellectual property, or other financing vehicles or arrangements. To the extent that we raise additional capital by issuing equity securities or other securities, our then-existing investors will experience dilution. If we raise funds through debt financings or bank loans, we may become subject to restrictive covenants, our assets may be pledged as collateral for the debt, and the interests of our then-existing investors would be subordinated to the debt holders or banks. In addition, our use of and ability to exploit assets pledged as collateral for debt or loans may be restricted or forfeited. To the extent that we raise additional funds through collaboration or licensing arrangements, we may be required to relinquish significant rights (including without limitation intellectual property rights) to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are not able to raise needed funding under acceptable terms or at all, then we will have to reduce expenses, including the possible options of curtailing operations, abandoning opportunities, licensing or selling off assets, reducing costs to a point where clinical development or other progress is impaired, or ceasing operations entirely.

Market variables, such as inflation of product costs, labor rates and fuel, freight and energy costs, as well as geopolitical events could likely cause us to suffer significant increases in our operating and administrative expenses.

In the wake of the COVID-19 pandemic, the Russia-Ukraine war and other geopolitical factors, economic conditions have become strained, with inflation and supply chain challenges impacting businesses worldwide. These conditions affect fuel costs and shipping, resulting in higher costs and delays for various types of supplies. These cost increases and delays may affect our clinical material manufacturing which will likely have an adverse effect on our financial condition. In addition, the effects of responses to inflationary conditions, such as significantly increased interest rates, on the economy and market conditions are difficult to predict. If U.S. or global economic, trade and financial market conditions continue to be challenged or volatile, or we do not effectively manage our response to these conditions, our operations and financial condition could be adversely affected in a variety of ways.

Unstable market and economic conditions may have serious adverse consequences on our ability to raise funds, which may cause us to delay, restructure or cease our operations.

From time to time, global and domestic credit and financial markets have experienced extreme disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. Recently, COVID-19 and the Russia-Ukraine war have created volatility and uncertainty. Recent instability in the banking industry has added to the volatility and uncertainty. Our financing strategy will be adversely affected by any such economic downturn, volatile business environment and continued unpredictable and unstable market conditions. If the equity and credit markets deteriorate, it may make a debt or equity financing more difficult to complete, costlier, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms will have a material adverse effect on our business strategy and financial performance, and could require us to cease or delay our operations.

Risks Related to Clinical Development and Regulatory Approval

We do not have and may never have any approved products on the market. Our business is highly dependent upon receiving approvals from various U.S. and international governmental agencies and will be severely harmed if we are not granted approval to manufacture and sell our product candidates.

In order for us to commercialize any treatment for chemoradiation-induced SOM, cancer or any other disease indication, we must obtain regulatory approvals of such treatment for that indication. Satisfying regulatory requirements is an expensive process that takes many years and involves compliance with requirements covering research and development, testing, manufacturing, quality control, labeling and promotion of drugs for human use. To obtain necessary regulatory approvals, we must, among other requirements, complete clinical trials demonstrating that our products are safe and effective for a particular indication. There can be no assurance that our products will prove to be safe and effective, that our clinical trials will demonstrate the necessary safety and effectiveness of our product candidates, or that we will succeed in obtaining regulatory approval for any treatment we develop even if such safety and effectiveness are demonstrated.

Any delays or difficulties we encounter in our clinical trials may delay or preclude regulatory approval from the FDA or from international regulatory organizations. Any delay or preclusion of regulatory approval would be expected to delay or preclude the commercialization of our products. Examples of delays or difficulties that we may encounter in our clinical trials include without limitation the following:

- Clinical trials may not yield sufficiently conclusive results for regulatory agencies to approve the use of our products.
- Our products may fail to be more effective than current therapies, or to be effective at all.
- We may discover that our products have adverse side effects, which could cause our products to be delayed or precluded from receiving regulatory approval or reduce the effective size of our target patient population or otherwise expose us to significant commercial and legal risks.
- It may take longer than expected to determine whether or not a treatment is safe and effective.
- Patients involved in our clinical trials may suffer severe adverse side effects even up to death, whether as a result of treatment with our products, the withholding of such treatment, or other reasons which may not include the effects of our treatment (whether within or outside of our control).
- We may fail to be able to enroll a sufficient number of patients in our clinical trials to meet trial statistical plans and gain statistical significance, or it may take longer than expected to enroll.

- Patients enrolled in our clinical trials may not have the safety or efficacy characteristics necessary to obtain regulatory approval for a particular indication or patient population.
- We may be unable to produce sufficient quantities of product to complete the clinical trials.
- Even if we are successful in our clinical trials, required governmental approvals may still not be obtained or, if obtained, may not be maintained.
- If approval for commercialization is granted, it is possible the authorized use will be more limited than is necessary for commercial success, or that approval may be conditioned on completion of further clinical trials or other activities, which will cause a substantial increase in costs and which we might not succeed in performing or completing.
- If granted, approval may be withdrawn or limited if problems with our products emerge or are suggested by the data arising from their use or if there is a change in law or regulation.

Any success we may achieve at a given stage of our clinical trials does not guarantee that we will achieve success at any subsequent stage, including without limitation final FDA or other regulatory organizations' approval.

We may encounter delays or rejections in the regulatory approval process because of additional government regulation resulting from future legislation or administrative action, or from changes in the policies of the FDA or other regulatory bodies during the period of product development, clinical trials, or regulatory review. Failure to comply with applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production, or an injunction preventing certain activity, as well as other regulatory action against our product candidates or us. As a company, we have no experience in successfully obtaining regulatory approval for a product and thus may be poorly equipped to gauge, and may prove unable to manage, risks relating to obtaining such approval.

Outside the U.S., our ability to market a product is contingent upon receiving clearances from appropriate non-U.S. regulatory authorities. Non-U.S. regulatory approval typically includes all of the risks associated with FDA clearance discussed above as well as geopolitical uncertainties and the additional uncertainties and potential prejudices faced by U.S. pharmaceutical companies conducting business abroad. In certain cases, governmental pricing restrictions and practices can make achieving even limited profitability very difficult.

Even if we complete the clinical trials we discussed with the FDA, there is no guarantee that at the time of submission the FDA will accept our new drug application ("NDA") based on the trials discussed.

The FDA provided guidance on our proposed VOICE trial, but the FDA is not bound by the guidance they give, and can change their position in the future. Any future decision by the FDA will be driven largely by the data generated from the VOICE clinical program. However, the FDA and other regulatory organizations will learn from their total experience in the review of multiple drugs in multiple indications and they will apply the knowledge of broad and diverse experience even if less than a perfect match with our product.

As a company, we have never completed a clinical trial and have limited experience in completing regulatory filings and any delays in regulatory filings could materially affect our financial condition.

While members of our team have conducted numerous clinical trials at previous companies, and have launched and marketed innovative pharmaceutical products in the U.S. and internationally, as a company, we have not yet completed any clinical trials of our product candidates, nor have we demonstrated the ability to obtain marketing approvals, manufacture product candidates at a commercial scale, or conduct sales and marketing activities necessary for the successful commercialization of a product. Consequently, we have no historical basis as a company by which one can evaluate or predict reliably our future success or viability.

Additionally, while our team has experience at prior companies with regulatory filings, as a company, we have limited experience with regulatory filings with agencies such as the FDA or EMA. Any delay in our regulatory filings for our product candidates, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including, without limitation, the FDA's issuance of a "refuse to file" letter or a request for additional information, could materially affect our financial condition.

We may seek fast track designation for one or more of our current and future product candidates, but we might not receive such designation, and even if we do, such designation may not actually lead to a faster development or regulatory review or approval process.

Our lead product candidate, Validive, has been given fast track designation from the FDA. Fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development, regulatory review or approval process with fast track designation compared to conventional FDA procedures. Additionally, the FDA may withdraw fast track designation, for reasons such as it comes to believe a drug candidate no longer adequately addresses an unmet medical need. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures. If we seek fast track designation for other product candidates, we may not receive such a designation from the FDA.

We, or any future collaborators, may not be able to obtain and maintain orphan drug exclusivity for our product candidates in the U.S. and Europe.

Validive has been granted orphan drug designation for the treatment of SOM in the EU. Camsirubicin has been granted orphan drug designation for the treatment of soft tissue sarcoma in the U.S. and in the EU. We may seek additional orphan drug designations or regulatory incentives for our pipeline product candidates, for other indications or for future product candidates. There can be no assurances that we will be able to obtain such designations.

Even if we obtain orphan drug designation for a product candidate, we may not be able to maintain orphan drug exclusivity for that drug. For example, orphan drug designation may be removed if the prevalence of an indication increases beyond the patient number limit required to maintain designation. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product in the same indication for that time period. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity at the specified quality of the product to meet the needs of patients with the rare disease or condition. Moreover, even after an orphan drug is approved, the FDA can subsequently approve a different drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared to our product.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies, and similarly the EMA may reevaluate its policies and regulations. We do not know if, when, or how the FDA or EMA may change their orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA and/or EMA may make to their orphan drug regulations and policies, our business could be adversely impacted.

If serious adverse or undesirable side effects are identified during the development of our product candidates, we may abandon or limit our development or commercialization of such product candidates.

If our product candidates are associated with undesirable side effects or have unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

If we elect to or are forced to suspend or terminate any clinical trial with one of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate revenue from such product candidate will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

With regard to our lead product candidate, unforeseen side effects from Validive could arise either during clinical development or, if approved, after Validive has been marketed. This could cause regulatory approvals for, or market acceptance of, Validive to be harder and costlier to obtain.

To date, no difference in the frequency of serious adverse events ("SAEs") has been observed in patients treated with Validive compared to placebo. In the Phase 2 clinical trial, two patients in the placebo group and 2 patients in the Validive 50 µg group experienced SAEs that were assessed as treatment related. No patients in the Validive treated cohorts were discontinued due to the study drug. Clonidine, the active ingredient of Validive, has been used for over 50 years as an orally swallowed systemic treatment for high blood pressure. Validive administration leads to very low, but still detectable exposure of clonidine outside the oral cavity. Thus, there is some risk that patients may experience side effects due to this systemic exposure, which could include a reduction in blood pressure, irregular heartbeat, drowsiness or dry mouth.

The results of our current or any future clinical trials may show that the side effects of Validive are unacceptable or intolerable, which would interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA or EMA and other regulatory authorities, or result in marketing approval from the FDA or EMA and other regulatory authorities with restrictive label warnings.

If Validive receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by the use of Validive:

- regulatory authorities may withdraw their approval of the product, which would force us to remove Validive from the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication, or field alerts to physicians and pharmacies;
- we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or our potential future collaborators from achieving or maintaining market acceptance of Validive and/or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of Validive.

As with any clinical trial, our VOICE clinical program entails significant risk of not meeting clinical endpoints. If the results of VOICE are not statistically significant, the FDA will likely not approve Validive for marketing which will result in a decrease in our stock price and market value.

The VOICE clinical program has been designed based on an analysis of the 64 oropharyngeal cancer (“OPC”) patients included in the Phase 2 trial (n= 24 in the placebo group, n= 21 Validive 50 µg group, and n= 19 Validive 100 µg group). While a dose response was observed in the Validive treated OPC cohorts compared to placebo across multiple clinically meaningful endpoints, the ability to establish statistical significance was limited by the relatively small sample size. This increases the risk that the VOICE trial may not achieve its prospectively defined endpoints. VOICE includes an interim analysis after the 2b portion that allows for an assessment of the primary (and only) endpoint, incidence of SOM, before proceeding to the Phase 3 portion of the trial. This interim analysis, and the resulting go/no-go decision about whether to proceed to the Phase 3 portion of the trial, is expected by the end of March 2023. If the interim analysis results in a no-go decision, we would need to reconsider our efforts with respect to Validive and refocus our development efforts on our other product candidates. Validive has been our lead product candidate to date and is the most clinically advanced, and if we had to reconsider or abandon our efforts, it would likely materially adversely impact our financing prospects, as well as the price of our common stock. Because the interim analysis is being performed by an independent data monitoring committee, we do not know what the results will be as of the date of this Annual Report. Assuming positive results from the interim analysis and that we fully proceed to the Phase 3 portion of the trial, we may also be required by the FDA to conduct a second Phase 3 confirmatory clinical trial which may not yield the same results. If our VOICE clinical trial results are not statistically significant, the FDA will likely not approve Validive for marketing, which will result in a decrease in our stock price and market value.

If we experience delays or difficulties in the enrollment of subjects to our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented, which could materially affect our financial condition.

Identifying, screening and enrolling patients to participate in clinical trials of our product candidates is critical to our success, and we may not be able to identify, recruit, enroll and dose a sufficient number of patients with the required or desired characteristics to complete our clinical trials in a timely manner. The timing of our clinical trials depends on our ability to recruit patients to participate as well as to subsequently dose these patients and complete required follow-up periods. In particular, because our current clinical trials of Validive and camsirubicin are focused on indications with relatively small patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

In addition, we may experience enrollment delays related to increased or unforeseen regulatory, legal and logistical requirements and COVID-19-related issues at certain clinical trial sites. These delays could be caused by reviews by regulatory authorities and contractual discussions with individual clinical trial sites. Any delays in enrolling and/or dosing patients in our current clinical trials could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or in termination of the clinical trials altogether.

Patient enrollment may be affected if our competitors have ongoing clinical trials with products for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in our competitors' clinical trials. Patient enrollment may also be affected by other factors, including:

- delays in U.S. or foreign regulatory approvals to start the clinical trial;
- coordination with clinical research organizations to enroll and administer the clinical trials;
- coordination and recruitment of collaborators and investigators at individual sites;
- size of the patient population and the effectiveness of the process for identifying patients;
- design of the clinical trial protocol;
- eligibility and exclusion criteria;
- perceived therapeutic risks and benefits of the product candidates under study;
- availability of competing commercially available therapies and other competing products' clinical trials;
- time of year in which the trials are initiated or conducted;
- severity and prognosis of the diseases under investigation;
- ability to obtain and maintain subject consents;
- ability to enroll and treat patients in a timely manner;
- risk that enrolled subjects will drop out before completion of the trials;
- proximity and availability of clinical trial sites for prospective patients;
- ability to monitor subjects adequately during and after treatment;
- patient referral practices of physicians; and
- potential long-term effects of COVID-19.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which could materially affect our financial condition.

If we or our licensees, development collaborators, or suppliers are unable to manufacture our products in sufficient quantities or at defined quality specifications, or are unable to obtain regulatory approvals for the manufacturing facility, we may be unable to develop and/or meet demand for our products and lose time to market and potential revenues.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We will utilize third parties to manufacture Validive, camsirubicin, and MNPR-101. We currently have manufacturing arrangements for Validive and camsirubicin. We have not yet secured manufacturing agreements for MNPR-101-Zr, MNPR-101 RIT or MNPR-202.

In the future we may become unable, for various reasons, to rely on our sources for the manufacture of our product candidates, either for clinical trials or, at some future date, for commercial distribution. We may not be successful in identifying additional or replacement third-party manufacturers, or in negotiating acceptable terms with any we do identify. We may face competition for access to these manufacturers' facilities and may be subject to manufacturing delays if the manufacturers give other clients higher priority than they give to us. Even if we are able to identify an additional or replacement third-party manufacturer, the delays and costs associated with establishing and maintaining a relationship with such manufacturer may have a material adverse effect on us.

Before we can begin to commercially manufacture Validive, camsirubicin, MNPR-101-Zr, MNPR-101 RIT, MNPR-202 or any other product candidate, we must obtain regulatory approval of the manufacturing facility and process. Manufacturing of drugs for clinical and commercial purposes must comply with current Good Manufacturing Practices requirements, commonly known as "cGMP." The cGMP requirements govern quality control and documentation policies and procedures. Complying with cGMP and non-U.S. regulatory requirements will require that we expend time, money, and effort in production, recordkeeping, and quality control to ensure that the product meets applicable specifications and other requirements. We, or our contracted manufacturing facility, must also pass a pre-approval inspection prior to FDA approval. Failure to pass a pre-approval inspection will likely significantly delay or prevent FDA approval of our products. If we fail to comply with these requirements, we would be subject to possible regulatory action and may be limited in the jurisdictions in which we are permitted to sell our products and will lose time to market and potential revenues.

It is uncertain whether product liability insurance will be adequate to address product liability claims, or that insurance against such claims will be affordable or available on acceptable terms in the future.

Clinical research involves the testing of new drugs on human volunteers pursuant to a clinical trial protocol. Such testing involves a risk of liability for personal injury to or death of patients due to, among other causes, adverse side effects, improper administration of the new drug, or improper volunteer behavior. Claims may arise from patients, clinical trial volunteers, consumers, physicians, hospitals, companies, institutions, researchers, or others using, selling, or buying our products, as well as from governmental bodies including a possibility in some states for product liability claims being made based on generic copies of our drugs. In addition, product liability and related risks are likely to increase over time, in particular upon the commercialization or marketing of any products by us or parties with which we enter into development, marketing, or distribution collaborations. Although we have obtained product liability insurance in connection with our clinical trials, there can be no assurance that the amount and scope of such insurance coverage will be appropriate and sufficient in the event any claims arise, that we will be able to secure additional coverage should we attempt to do so, or that our insurers would not contest or refuse any attempt by us to collect on such insurance policies. Regardless of their merit or eventual outcome, product liability claims may result in:

- withdrawal of clinical trial volunteers;
- decreased demand for our products when approved;
- injury to our reputation and significant, adverse media attention; and
- potentially significant litigation costs, including without limitation, any damages awarded to the plaintiffs if we lose or settle claims.

If the market opportunities for our current and potential future drug candidates are smaller than we believe they are, our ability to generate product revenues will be adversely affected and our business may suffer.

Our understanding of the number of people who suffer from SOM resulting from CRT for the treatment of OPC, whom Validive may have the potential to treat, is based upon estimates and on various reports from governments or medical institutions. These estimates or reports may prove to be incorrect, and new studies may demonstrate or suggest a lower estimated incidence or prevalence of this condition. The number of patients in the U.S. or elsewhere may turn out to be lower than expected, may not be otherwise amenable to Validive treatment, or treatment-amenable patients may become increasingly difficult to identify and access, all of which would adversely affect our business prospects and financial condition. In particular, the treatable population for Validive may further be reduced if our estimates of addressable populations are erroneous or sub-populations of patients within the addressable population do not derive benefit from Validive.

Risks Related to Our Reliance on Third Parties

Corporate, non-profit, and academic collaborators may take actions (including lack of effective actions) to delay, prevent, or undermine the success of our products.

Our operating and financial strategy for the development, clinical testing, manufacture, and commercialization of product candidates is heavily dependent on us entering into collaborations with corporations, non-profit organizations, academic institutions, licensors, licensees, and other parties. There can be no assurance that we will be successful in establishing such collaborations. Current and future collaborations are and may be terminable at the sole discretion of the collaborator. The activities of any collaborator will not be within our direct control and may not be in our power to influence. There can be no assurance that any collaborator will perform its obligations to our satisfaction or at all; that we will derive any revenue, profits, or benefit from such collaborations; or that any collaborator will not compete with us. If any collaboration is not pursued, we may require substantially greater capital to undertake development and commercialization of our proposed products, and may not be able to develop and commercialize such products effectively, if at all. In addition, a lack of development and commercialization collaborations may lead to significant delays in introducing proposed products into certain markets and/or reduced sales of proposed products in such markets. Furthermore, current and future collaborators may act deliberately or inadvertently in ways detrimental to our interests.

The termination of third-party licenses could adversely affect our rights to important compounds or technologies.

We have exercised our option to license Validive; as such, Onxeo has the ability to terminate the license if we breach our obligations under the license agreement. A termination of the license agreement might force us to cease developing and/or selling Validive, if it gets to market. We rely on certain rights to MNPR-101 that we have secured through a non-exclusive license agreement with XOMA. XOMA, as licensor, has the ability to terminate the license if we breach our obligations under the license agreement and do not remedy any such breach within a set time after receiving written notice of such breach from XOMA. A termination of the license agreement might force us to cease developing and/or selling MNPR-101-Zr or MNPR-101 RIT, if it gets to market.

Data provided by collaborators and other parties upon which we rely have not been independently verified and could turn out to be inaccurate, misleading, or incomplete.

We rely on third-party vendors, scientists, and collaborators to provide us with significant data and other information related to our projects, clinical trials, and business. We do not independently verify or audit all of such data (including possibly material portions thereof). As a result, such data may be inaccurate, misleading, or incomplete.

In certain cases, we may need to rely on a single supplier for a particular manufacturing material or service, and any interruption in or termination of service by such supplier could delay or disrupt the commercialization of our products.

We rely on third-party suppliers for the materials used to manufacture our compounds. Some of these materials may at times only be available from one supplier. Any interruption in or termination of service by such single source suppliers could result in a delay or disruption in manufacturing until we locate an alternative source of supply. There can be no assurance that we would be successful in locating an alternative source of supply or in negotiating acceptable terms with such prospective supplier.

Our Validive manufacturer is in the United Kingdom (“UK”), and it is unknown in the long-term how they will be impacted by Brexit; however, if they are negatively impacted, this could increase our manufacturing costs, delivery schedules, and adversely impact our financial condition.

The UK left the European Union (“EU”) on January 31, 2020, which is commonly referred to as “Brexit.” The full long-term impact of Brexit, however, remains uncertain. Our Validive manufacturer may be negatively affected by interest rate, exchange rate and other market and economic volatility, as well as regulatory and political uncertainty. The tax consequences of the UK’s withdrawal from the EU are uncertain as well. If Brexit has a detrimental effect on our Validive manufacturer, it could, in turn, adversely impact our manufacturing costs and financial condition.

We rely on a limited number of contracted manufacturing plants. If we need to enlist new contract manufacturers, it will delay our camsirubicin clinical program and may increase our cost for our Phase 1b and future camsirubicin clinical trials.

Our contracted camsirubicin active pharmaceutical ingredient manufacturing plant and our contracted raw materials manufacturing plant are in countries in Asia and Europe, either of which may be affected by imposed tariffs and regional geopolitical factors outside of their control, including the Russia-Ukraine war, which may affect the supply of camsirubicin active pharmaceutical ingredient and raw materials. If we need to enlist new contract manufacturers, it will delay our camsirubicin clinical program and may increase our cost for our Phase 1b and future camsirubicin clinical trials.

We rely on third parties to conduct our non-clinical studies and our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize our current product candidates or any future products, on a timely and efficient basis or at all, and our financial condition will be adversely affected.

We do not have the capacity to independently conduct non-clinical studies and clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, collaborative partners and other third parties, such as contract research organizations or clinical research organizations, to conduct non-clinical studies and clinical trials on our product candidates. The third parties with whom we contract for execution of our non-clinical studies and clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our programs.

Although we rely on third parties to conduct our non-clinical studies and clinical trials, we remain responsible for ensuring that each of our non-clinical studies and clinical trials is conducted in accordance with its investigational plan and protocol. Moreover, the FDA, EMA and other foreign regulatory authorities require us to comply with regulations and standards, including some regulations commonly referred to as good clinical practices (“GCPs”), for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial subjects are adequately informed of the potential risks of participating in clinical trials.

In addition, the execution of non-clinical studies and clinical trials, and the subsequent compilation and analyses of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. Moreover, these third parties may also have relationships with other commercial entities, some of which may compete with us. Under certain circumstances, these third parties may be able to terminate their agreements with us upon short notice. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial protocols or GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated or may need to be repeated. If any of the foregoing were to occur, we may not be able to obtain, on a timely and efficient basis or at all, regulatory approval for or to commercialize the product candidate being tested in such trials, and as a result, our financial condition will be adversely affected.

Risks Related to Commercialization of Our Product Candidates

We have no experience as a company in commercializing any product. If we fail to obtain commercial expertise, upon product approval by regulatory agencies, our product launch and revenues could be delayed.

As a company, we have never obtained regulatory approval for, or commercialized, any product. Accordingly, we have not yet begun to build out any sales or marketing or distribution capabilities. If we are unable to establish, or contract for, effective sales and marketing and distribution capabilities, or if we are unable to enter into agreements with third parties to commercialize our product candidates on favorable terms or on any reasonable terms at all, we may not be able to effectively generate product revenues once our product candidates are approved for marketing. If we fail to obtain commercial expertise or capabilities, upon drug approval, our product launch and subsequent revenues could be delayed and /or fail to reach their commercial potential.

Our product development efforts are at an early stage. We have not yet undertaken any marketing efforts, and there can be no assurance that future anticipated market testing and analyses will validate our marketing strategy. We may need to modify the products, or we may not be successful in either developing or marketing those products.

As a company, we have not completed the development or clinical trials of any product candidates and, accordingly, have not yet begun to market or generate revenue from the commercialization of any products. Obtaining approvals of these product candidates will require substantial additional research and development as well as costly clinical trials. There can be no assurance that we will successfully complete development of our product candidates or successfully market them. We may encounter problems and delays relating to research and development, regulatory approval, intellectual property rights of product candidates, or other factors. There can be no assurance that our development programs will be successful, that our product candidates will prove to be safe and effective in or after clinical trials, that the necessary regulatory approvals for any product candidates will be obtained, or, even if obtained, will be as broad as sought or will be maintained for any period thereafter, that patents will issue on our patent applications, that any intellectual property protections we secure will be adequate, or that our collaboration arrangements will not diminish the value of our intellectual property through licensing or other arrangements. Furthermore, there can be no assurance that any product we might market will be received favorably by customers (whether physicians, payers, patients, or all three), adequately reimbursed by third-party payers, or that competitive products will not perform better and/or be marketed more successfully. Additionally, there can be no assurances that any future market testing and analyses will validate our marketing strategies. We may need to seek to modify the product labels through additional studies in order to be able to market them successfully to reach their commercial potential.

If we are unable to establish relationships with licensees or collaborators to carry out sales, marketing, and distribution functions or to create effective marketing, sales, and distribution capabilities, we will be unable to market our products successfully.

Our business strategy may include out-licensing product candidates to or collaborating with larger firms with experience in marketing and selling pharmaceutical products. There can be no assurance that we will successfully be able to establish marketing, sales, or distribution relationships with any third-party, that such relationships, if established, will be successful, or that we will be successful in gaining market acceptance for any products we might develop. To the extent that we enter into any marketing, sales, or distribution arrangements with third parties, our product revenues per unit sold are expected to be lower than if we marketed, sold, and distributed our products directly, and any revenues we receive will depend upon the efforts of such third parties.

If we are unable to establish such third-party marketing and sales relationships, or choose not to do so, we would have to establish in-house marketing and sales capabilities. We have no experience in marketing or selling oncology pharmaceutical products, and currently have no marketing, sales, or distribution infrastructure and no experience developing or managing such infrastructure for an oncology related product. To market any products directly, we would have to establish a marketing, sales, and distribution force that has technical expertise and could support a distribution capability. Competition in the biopharmaceutical industry for technically proficient marketing, sales, and distribution personnel is intense and attracting and retaining such personnel may significantly increase our costs. There can be no assurance that we will be able to establish internal marketing, sales, or distribution capabilities or that these capabilities will be sufficient to meet our needs.

Commercial success of our product candidates will depend on the acceptance of these products by physicians, payers, and patients.

Any product candidate that we may develop may not gain market acceptance among physicians, payers and patients. Market acceptance of and demand for any product that we may develop will depend on many factors, including without limitation:

- Comparative superiority of the efficacy and safety in the treatment of the disease indication compared to alternative treatments;
- Less incidence, less prevalence and more severity of adverse side effects;
- Potential advantages over alternative treatments;
- Cost effectiveness;
- Convenience and ease of administration, stability and shelf life, for distributor, physician and patient;
- Sufficient third-party coverage and/or reimbursement;
- Strength of sales, marketing and distribution support; and
- Our ability to provide acceptable and compelling evidence of safety and efficacy.

If any product candidate developed by us receives regulatory approval but does not achieve an adequate level of market acceptance by physicians, payers, and patients, we may generate insufficient, little, or no product revenue to earn appropriate returns on the investment of product development costs and may not become profitable at sufficient product sales volumes to earn sustainable profitability.

Our products may not be accepted for reimbursement or adequately reimbursed by third-party payers.

The successful commercialization of any products we might develop will depend substantially on whether the costs of our products and related treatments are reimbursed at acceptable levels by government authorities, private healthcare insurers, and other third-party payers, such as health maintenance organizations. Reimbursement rates may vary, depending upon the third-party payer, the type of insurance plan, and other similar or dissimilar factors. If our products do not achieve adequate reimbursement, then the number of physician prescriptions of our products may not be sufficient to make our products profitable, and to earn a sufficient profit to earn a reasonable return on our investment and a provide a cash flow to finance future investments on the next generation of products and investments in new technological platforms.

Comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of our product candidates. If third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis sufficient for our Company to remain competitive and thrive.

Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in the product development of that product. In addition, in the U.S. there is a growing emphasis on comparative effectiveness research, both by private payers and by government agencies. To the extent other drugs or therapies are found to be more effective than our products, payers may elect to cover such therapies in lieu of our products or reimburse our products at a lower rate.

The effects of economic and political pressure to lower pharmaceutical prices are a major threat to the economic viability of new research-based pharmaceutical products, and any significant decrease in drug prices could materially and adversely affect our prospects.

Emphasis on managed care and government price controls in the U.S. has increased and we expect this will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Any development along these lines could materially and adversely affect our prospects. We are unable to predict what political, legislative or regulatory changes relating to the healthcare industry, including without limitation any changes affecting governmental and/or private or third-party coverage and reimbursement, may be enacted in the future, or what effect such legislative or regulatory changes would have on our business. However, if governmental price management does not provide for the very high price of pharmaceutical research, it could create very demanding challenges for our industry and our prospects or require breakthroughs in research productivity, of which there can be no assurance.

If we obtain FDA approval for any of our product candidates, we will be subject to various federal and state fraud and abuse laws; these laws may impact, among other things, our proposed sales, marketing and education programs. Fraud and abuse laws are expected to increase in breadth and in detail, which will likely increase our operating costs and the complexity of our programs to ensure compliance with such enhanced laws.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our customers, distributors, or other business partners, subject to various federal and state fraud and abuse laws, including, without limitation, anti-kickback statutes and false claims statutes which may increase our operating costs. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct business.

If our operations are found to be in violation of any of the federal and state fraud and abuse laws or any other governmental regulations that apply to us, we may be subject to criminal actions and significant civil monetary penalties, which would adversely affect our ability to operate our business and our results of operations.

If our operations are found to be in violation, even inadvertently, of any of the federal and state fraud and abuse laws, including, without limitation, anti-kickback statutes and false claims statutes or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Negotiated prices for our products covered by a Part D prescription drug plan and other government programs will be lower than the prices we might otherwise obtain.

Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval; however, any negotiated prices for our products covered by a Part D prescription drug plan and other government programs will be lower than the prices we might otherwise obtain. We anticipate that the number and type of products that will be subject to federal pricing will increase substantially over time. There may be rules to demand that the government and medical institutions, which are in part supported by government funding, will be granted access to medicines at the same highly favorable prices given to the governmental direct medical care programs.

Risks Related to Our Intellectual Property

If we and our third-party licensors do not obtain and preserve protection for our respective intellectual property rights, our competitors may be able to take advantage of our (and our licensors') development efforts to develop competing drugs.

Our commercial success will depend in part on obtaining patent protection for any products and other technologies we might develop, and successfully defending any patents we obtain against third-party challenges. We have licensed all intellectual property related to Validive from Onxeo S.A., a French public company. See “Business – License, Development and Collaboration Agreements”. The assignment and transfer of the camsirubicin (formerly GPX-150) patent portfolio from TacticGem, LLC (“TacticGem”) to us has been completed. We filed and have been granted in the U.S. and various countries around the world patents for antibodies that target uPAR for our MNPR-101 program. We have also been granted in the U.S. and various countries around the world patents to a specific sequence of amino acids on uPAR, to which our MNPR-101 antibody binds. We are currently prosecuting this patent in other countries around the world to further protect MNPR-101. We also have jointly applied for patents with our collaborator, NorthStar, for MNPR-101-Zr and MNPR-101 RIT conjugates. The patent process is subject to numerous risks and uncertainties, and there can be no assurance that we will be successful in obtaining and defending patents. See “Business - Intellectual Property Portfolio and Exclusivity”. These risks and uncertainties include without limitation the following:

- Patents that may be issued or licensed may be challenged, invalidated, or circumvented; or may not provide any competitive advantage for other reasons.
- Our licensors may terminate or breach our existing or future license agreements, thereby reducing or preventing our ability to exclude competition; termination of such license agreements may also subject us to risk of patent infringement of patents to which we no longer have a license.

- Our competitors, many of which have substantially greater resources than us and 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 either in the U.S. or in international markets.
- As a matter of public policy regarding worldwide health concerns, there may be significant pressure on the U.S. government and other international governmental bodies to limit the scope of domestic and international patent protection for cancer treatments that prove successful.
- Countries other than the U.S. may have less restrictive patent laws than those upheld by the U.S. courts; therefore, non-U.S. competitors could exploit these laws to create, develop, and market competing products. In some countries, the legal compliance with pharmaceutical patents, patent applications and other intellectual property regulations is very weak or actively evaded in some cases with government aid.

In addition, the U.S. Patent and Trademark Office (“USPTO”) and patent offices in other jurisdictions have often required that patent applications concerning pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting their scope of protection against competitive challenges. Thus, even if we or our licensors are able to obtain patents, the scope of the patents may be substantially narrower than anticipated.

If we permit our patents to lapse or expire, we will not be protected and will have less of a competitive advantage. The value of our products may be greatly reduced if this occurs. Our patents expire at different times and are subject to the laws of multiple countries. Some of our patents are currently near expiration and we may pursue patent term extensions for these where appropriate. See “Business - Intellectual Property Portfolio and Exclusivity”.

In addition to patents, we also rely on trade secrets and proprietary know-how. While we take measures to protect this information by entering into confidentiality and invention agreements with our employees, consultants and collaborators, we cannot provide any assurances that these agreements will be fully enforceable and will not be breached, that we will be able to protect ourselves from the harmful effects of disclosure if they are not fully enforceable or are breached, that any remedy for a breach will adequately compensate us, that these agreements will achieve their intended aims, or that our trade secrets will not otherwise become known or be independently discovered by competitors. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U.S., are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed, and the value of the trade secrets may be greatly reduced.

The patent protection we obtain and preserve for our product candidates may not be sufficient to provide us with any material competitive advantage.

We may be subject to competition despite the existence of intellectual property we license or own. We can give no assurances that our intellectual property claims will be sufficient to prevent third parties from designing around patents we own or license and developing and commercializing competitive products. The existence of competitive products that avoid our intellectual property could materially adversely affect our operating results and financial condition. Furthermore, limitations, or perceived limitations, in our intellectual property may limit the interest of third parties to partner, collaborate or otherwise transact with us, if third parties perceive a higher than acceptable risk to commercialization of our products or future products. When looking at our Validive patents’ ability to block competition, the protection offered by our patents may be, to some extent, more limited than the protection provided by patents claiming the composition of matter of entirely new chemical structures previously unknown. If a competitor were able to successfully design around any method of use and formulation patents we may have now or in the future, it is highly likely that our business and competitive advantage would be adversely affected.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. If this occurs, our competitive position, business, financial condition, results of operations, and prospects would be materially harmed.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for the applicable product candidate will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our competitive position, business, financial condition, results of operations, and prospects would be materially harmed.

Intellectual property disputes could require us to spend time and money to address such disputes and could limit our intellectual property rights.

The biopharmaceutical industry has been characterized by extensive litigation regarding patents and other intellectual property rights, and companies have employed intellectual property litigation and USPTO post-grant proceedings to gain a competitive advantage. We may become subject to infringement claims or litigation arising out of patents and pending applications of our competitors, or additional interference proceedings declared by the USPTO to determine the priority and patentability of inventions. The defense and prosecution of intellectual property suits, USPTO proceedings, and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain. Litigation may be necessary to enforce our issued patents, to protect our trade secrets and know-how, or to determine the enforceability, scope, and validity of the proprietary rights of others. An adverse determination in litigation or USPTO post-grant and interference proceedings to which we may become a party could subject us to significant liabilities, require us to obtain licenses from third parties, or restrict or prevent us from selling our products in certain markets. Even if a given patent or intellectual property dispute were settled through licensing or similar arrangements, our costs associated with such arrangements may be substantial and could include the payment by us of large, fixed payments and ongoing royalties. Furthermore, the necessary licenses may not be available on satisfactory terms or at all. Even where we have meritorious claims or defenses, the costs of litigation may prevent us from pursuing these claims or defenses and/or may require extensive financial and personnel resources to pursue these claims or defenses. In addition, it is possible there may be defects of form in our current and future patents that could result in our inability to defend the intended claims. Intellectual property disputes arising from the aforementioned factors, or other factors, may materially harm our business.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market Validive or any future products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the U.S. and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our products and technology.

Changes to the patent law in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal diligence and complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, the U.S. has recently enacted and is currently implementing wide ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, as well as other jurisdictions around the world, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance due to issues beyond our control, 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. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

If we fail to comply with our obligations under any license, collaboration or other intellectual property-related agreements, we may be required to pay damages and could lose intellectual property rights that may be necessary for developing, commercializing and protecting our current or future technologies or drug candidates or we could lose certain rights to grant sublicenses.

Any license, collaboration or other intellectual property-related agreements impose, and any future license, collaboration or other intellectual property-related agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license. In spite of our best efforts, any of our future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technologies covered by these license agreements. Any license agreements we enter into may be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may seek to obtain licenses from licensors in the future, however, we may be unable to obtain any such licenses at a reasonable cost or on reasonable terms, if at all. In addition, if any of our future licensors terminate any such license agreements, such license termination could result in our inability to develop, manufacture and sell products that are covered by the licensed technology or could enable a competitor to gain access to the licensed technology. Any of these events could have a material adverse effect on our competitive position, business, financial condition, results of operations, and ability to achieve profitability.

Furthermore, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our future licensors fail to prosecute, maintain, enforce and defend patents we may in-license, or lose rights to licensed patents or patent applications, our license rights may be reduced or eliminated. In such circumstances, our right to develop and commercialize any of our products or drug candidates that is the subject of such licensed rights could be materially adversely affected. In certain circumstances, our licensed patent rights are subject to our reimbursing our licensors for their patent prosecution and maintenance costs.

Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing, misappropriating or otherwise violating the licensor's intellectual property rights and the amount of any damages or future royalty obligations that would result, if any such claims were successful, would depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, due to such obligations, we may be unable to achieve or maintain profitability.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse impact on the success of our business.

Our commercial success depends, in part, upon our ability or the ability of any of our future collaborators to develop, manufacture, market and sell our current or any future drug candidates and to use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary and intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights.

We or any of our future licensors or strategic partners, may be party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current or any potential future drug candidates and technologies, including derivation, reexamination, inter partes review, post-grant review or interference proceedings before the USPTO and similar proceedings in jurisdictions outside of the U.S. such as opposition proceedings. If we or our licensors or strategic partners are unsuccessful in any interference proceedings or other priority or validity disputes (including through any patent oppositions) to which we or they are subject, we may lose valuable intellectual property rights through the loss of one or more patents or our patent claims may be narrowed, invalidated, or held unenforceable. In some instances, we may be required to indemnify our licensors or strategic partners for the costs associated with any such adversarial proceedings or litigation. Third parties may also assert infringement, misappropriation or other claims against us, our licensors or our strategic partners based on existing patents or patents that may be granted in the future, as well as other intellectual property rights, regardless of their merit. There is a risk that third parties may choose to engage in litigation or other adversarial proceedings with us, our licensors or our strategic partners to enforce or otherwise assert their patent rights or other intellectual property rights. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents and other intellectual property rights are valid, enforceable and infringed, which could have a material adverse impact on our ability to utilize our developed technologies or to commercialize our current or any future drug candidates deemed to be infringing. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity by presenting clear and convincing evidence of invalidity. There is no assurance that a court of competent jurisdiction, even if presented with evidence we believe to be clear and convincing, would invalidate the claims of any such U.S. patent.

Further, we cannot guarantee that we will be able to successfully settle or otherwise resolve such adversarial proceedings or litigation. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or to continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our drug candidates. If we or any of our licensors or strategic partners are found to infringe, misappropriate or violate a third-party patent or other intellectual property rights, we could be required to pay damages, including treble damages and attorney's fees, if we are found to have willfully infringed. In addition, we, or any of our licensors or strategic partners may choose to seek, or be required to seek, a license from a third-party, which may not be available on commercially reasonable terms, if at all. Even if a license can be obtained on commercially reasonable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us, and we could be required to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease utilizing, developing, manufacturing and commercializing our developed technologies or drug candidates deemed to be infringing. We may be forced to redesign current or future technologies or products. Any of the foregoing could have a material adverse effect on our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

In addition, we or our licensors or strategic partners may find it necessary to pursue claims or to initiate lawsuits to protect or enforce our patent or other intellectual property rights. If we or our licensors or strategic partners were to initiate legal proceedings against a third-party to enforce a patent covering one of our drug candidates or our developed technology, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, claiming patent-ineligible subject matter, lack of novelty, indefiniteness, lack of written description, non-enablement, anticipation or obviousness. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcome of such invalidity and unenforceability claims is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we or our licensors or strategic partners and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection for one or more of our drug candidates. The narrowing or loss of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technologies and products. All of these events could have a material adverse effect on our business, financial condition, results of operations and prospects. Patent and other intellectual property rights also will not protect our drug candidates and technologies if competitors or third parties design around such drug candidates and technologies without legally infringing, misappropriating or violating our patent or other intellectual property rights.

The cost to us in defending or initiating any litigation or other proceedings relating to our patent or other intellectual property rights, even if resolved in our favor, could be substantial, and any litigation or other proceedings would divert our management's attention and distract our personnel from their normal responsibilities. Such litigation or other proceedings could materially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to more effectively sustain the costs of complex patent litigation because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and materially limit our ability to continue our operations. Furthermore, because of the substantial amount of discovery required in connection with certain such proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, such announcements could have a material adverse effect on the price of our common stock.

Intellectual property rights of third parties could adversely affect our ability to commercialize our current or future technologies or drug candidates, and we might be required to litigate or obtain licenses from third parties to develop or market our current or future technologies or drug candidates, which may not be available on commercially reasonable terms, or at all.

There are numerous companies that have pending patent applications and issued patents broadly covering immune-therapies generally or covering small molecules directed against the same targets as, or targets similar to, those we are pursuing. Our competitive position may materially suffer if patents issued to third parties or other third-party intellectual property rights cover our current or future technologies, drug candidates or elements thereof, or our manufacture or uses relevant to our development plans. In such cases, we may not be in a position to develop or commercialize current or future technologies or drug candidates unless we successfully pursue litigation to nullify or invalidate the third-party intellectual property rights concerned or enter into a license agreement with the intellectual property rights holder, if available on commercially reasonable terms. There may be issued patents of which we are not aware, held by third parties that, if found to be valid and enforceable, could be alleged to be infringed by our current or future technologies or drug candidates. There also may be pending patent applications of which we are not aware that may result in issued patents, which could be alleged to be infringed by our current or future technologies or drug candidates. Should such an infringement claim be successfully brought, we may be required to pay substantial damages or be forced to abandon our current or future technologies or drug candidates or to seek a license from any patent holders. No assurances can be given that a license will be available on commercially reasonable terms, if at all.

Third-party intellectual property rights holders may also actively bring infringement, misappropriation or other claims alleging violations of intellectual property rights against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or to continue costly, unpredictable and time-consuming litigation and may be prevented from, or experience substantial delays in, marketing our drug candidates. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our current or future technologies or drug candidates that are held to be infringing, misappropriating or otherwise violating third-party intellectual property rights. We might, if possible, also be forced to redesign current or future technologies or drug candidates so that we no longer infringe, misappropriate or violate the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business, which could have a material adverse effect on our financial condition and results of operations.

Risks Related to Our Business Operations and Industry

We have a limited operating history.

To date, we have engaged exclusively in acquiring pharmaceutical product candidates, licensing rights to product candidates, entering into collaboration agreements with respect to key services or technologies for our drug product development, and commenced clinical trials, but have not yet completed any clinical trials, received any governmental approvals, brought any product to market, manufactured products in commercial quantities or sold any pharmaceutical products. As a company we have limited experience in negotiating, establishing, and maintaining strategic relationships, conducting clinical trials, and managing the regulatory approval process, all of which will be necessary if we are to be successful. Our lack of experience in these critical areas makes it difficult for a prospective investor to evaluate our abilities and increases the risk that we will fail to successfully execute our strategies.

Furthermore, if our business grows rapidly, our operational, managerial, legal, and financial resources will be strained. Our development will require continued improvement and expansion of our management team and our operational, managerial, legal, and financial systems and controls.

In the normal course of business, we have evaluated and expect to evaluate potential acquisitions and/or licenses of patents, compounds, and technologies that our management believes could complement or expand our business. In the event that we identify an acquisition or license candidate we find attractive, there is no assurance that we will be successful in negotiating an agreement to acquire or license, or in financing or profitably exploiting, such patents, compounds, or technologies. Furthermore, such an acquisition or license could divert management time and resources away from other activities that would further our current business development.

If we lose key management leadership, and/or scientific personnel, and if we cannot recruit qualified employees, managers, directors, officers, or other significant personnel, it is highly likely that we will experience program delays and increases in compensation costs, and our business will be materially disrupted.

Our future success is highly dependent on the continued service of principal members of our management, leadership, and scientific personnel, who are able to terminate their employment with us at any time and may be able to compete with us. The loss of any of our key management, leadership, or scientific personnel including, in particular, Christopher M. Starr, our Executive Chairman of the Board of Directors (referred to as the “Board”), and Chandler D. Robinson, our President and CEO, could materially disrupt our business and materially delay or prevent the successful product development and commercialization of our product candidates. We have an employment agreement with Dr. Robinson which has no term but is for at-will employment, meaning the executive has the ability to terminate his employment at any time. We have a consulting agreement with Dr. Starr that is terminable with 30-days’ notice by Dr. Starr or us.

Our future success will also depend on our continuing ability to identify, hire, and retain highly skilled personnel for all areas of the organization. Competition in the biopharmaceutical industry for scientifically and technically qualified personnel is intense, and we may be unsuccessful in identifying, hiring, and retaining qualified personnel. Our continued requirement to identify, hire, and retain highly competent personnel may cause our compensation costs to increase materially.

We incur costs as a result of operating as a public company, and our management is required to devote substantial time to investor relations, information and communication to the public, and related compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our Board. However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Despite ongoing compliance training and periodic education, our employees and consultants may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in delays or terminations of our development programs and adversely affect our business.

Although we regularly train our employees on compliance and we are aware of no misconduct or improper activities to date, we are exposed to the risk of employee or consultant fraud or other misconduct. Misconduct by our employees or consultants could include intentional failures to: comply with FDA regulations; provide accurate information to the FDA; comply with manufacturing standards; comply with federal and state healthcare fraud and abuse laws and regulations; report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, 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. 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, including the imposition of significant fines or other sanctions. Such actions could adversely affect our business including delaying or terminating one or more of our development programs.

We are an emerging growth company and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company. Under the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”), emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected to opt out of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

For as long as we continue to be an emerging growth company, we also intend to take advantage of certain other exemptions from various reporting requirements that are applicable to other public companies including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory stockholder vote on executive compensation and any golden parachute payments not previously approved, exemption from the requirement of auditor attestation in the assessment of our internal control over financial reporting and exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements (auditor discussion and analysis). If we do take advantage of these exemptions, the information that we provide stockholders will be different than what is available with respect to other public companies. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If investors find our common stock less attractive as a result of our status as an emerging growth company, there may be less liquidity for our common stock and our stock price may be more volatile.

We will remain an emerging growth company until the earliest of (1) the last day of the year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least \$1.235 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. We anticipate this will be December 31, 2024.

Competition and technological change may make our product candidates less competitive or obsolete.

The biopharmaceutical industry is subject to rapid technological change. We have many potential competitors, including major drug and chemical companies, specialized biopharmaceutical firms, universities and other research institutions. These companies, firms, and other institutions may develop products that are more effective than our product candidates or that would make our product candidates less competitive or obsolete. Many of these companies, firms, and other institutions have greater financial resources than us and may be better able to withstand and respond to adverse market conditions within the biopharmaceutical industry, including without limitation the lengthy product development and regulatory approval processes for product candidates.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe we have significant competitive advantages with our expertise in small molecules and biologics, and rare disease clinical development, along with a strong intellectual property portfolio, we currently face and will continue to face competition for our drug development programs from companies that target SOM, are developing doxorubicin analogs/replacement, or are targeting uPAR. The competition is likely to come from multiple sources, including larger pharmaceutical companies, biotechnology companies and academia. Accordingly, our competitors may have more resources and be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, we will have to compete with new therapies that may become available in the future.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases, and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction will require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown technologies, product candidates, medical conditions and indications, product manufacturing challenges and uncertainties, and other unknown factors of potential high risk;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher-than-expected acquisition and integration costs;
- write-downs of assets, goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses or for our current business based on changed circumstances.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks, and could have a material adverse effect on our business, results of operations, financial condition and prospects.

Our business and operations are vulnerable to computer system failures, cyber-attacks or deficiencies in our cyber-security, which could increase our expenses, divert the attention of our management and key personnel away from our business operations and adversely affect our results of operations.

Despite the implementation of security measures, our internal computer systems, and those of 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. 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. 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. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, and damage to our reputation, and the further development of our product candidates could be delayed. We could be forced to expend significant resources in response to a cyber security breach, including repairing system damage, increasing cyber security protection costs by deploying additional personnel and protection technologies, paying regulatory fines and resolving legal claims and regulatory actions, all of which would increase our expenses, divert the attention of our management and key personnel away from our business operations and adversely affect our results of operations.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business.

We and our current and any of our future collaborators may be subject to federal, state and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws (e.g., the Health Insurance Portability and Accountability Act (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”)), state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH, or other privacy and data security laws. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

International data protection laws, including Regulation 2016/679, known as the General Data Protection Regulation (“GDPR”) may also apply to health-related and other personal information obtained outside of the U.S. The GDPR went into effect on May 25, 2018. The GDPR introduced new data protection requirements in the EU, as well as potential fines for non-compliant companies of up to the greater of €20 million or 4% of annual global revenue. The regulation imposes numerous new requirements for the collection, use, storage and disclosure of personal information, including more stringent requirements relating to consent and the information that must be shared with data subjects about how their personal information is used, the obligation to notify regulators and affected individuals of personal data breaches, extensive new internal privacy governance obligations and obligations to honor expanded rights of individuals in relation to their personal information (e.g., the right to access, correct and delete their data). In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Further Brexit has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

In addition, California recently enacted the California Consumer Privacy Act (“CCPA”), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide new disclosure to consumers about such companies’ data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA was amended on September 23, 2018, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business.

If we, our contract research organizations (“CROs”) or our IT vendors experience security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of personal data, we may face costs, significant liabilities, harm to our brand and business disruption.

In connection with our drug research and development efforts, we or our CROs may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. Although we have extensive measures in place to prevent the sharing and loss of patient data in our clinical trial processes associated with our developed technologies and drug candidates, any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients’ personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., HIPAA, as amended by HITECH), and international laws (e.g., the GDPR). Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients’ personal data may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business. We may also rely on third-party IT vendors to host or otherwise process some of our data and that of users, and any failure by such IT vendor to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development and drug candidates and future commercial manufacturing may involve the use of hazardous materials and various chemicals. We currently do not maintain a research laboratory, but we engage third-party research organizations and manufacturers to conduct our preclinical studies, clinical trials and manufacturing. These third-party laboratories and manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We must rely on the third parties' procedures for storing, handling and disposing of these materials in their facilities to comply with the relevant guidelines of the states in which they operate and the Occupational Safety and Health Administration of the U.S. Department of Labor. Although we believe that their safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, this could result in significant delays in our development. We are also subject to numerous environmental, health and workplace safety laws and regulations. Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees, this insurance may not provide adequate coverage against potential liabilities. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

We have limited the liability of and indemnified our directors and officers.

Although our directors and officers are accountable to us and must exercise good faith, good business judgement, and integrity in handling our affairs, our Second Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") and indemnification agreements executed by all of our non-employee directors and officers provides that our non-employee directors and officers will be indemnified to the fullest extent permitted under Delaware law. As a result, our stockholders may have fewer rights against our non-employee directors and officers than they would have absent such provisions in our Certificate of Incorporation and indemnification agreements, and a stockholder's ability to seek and recover damages for a breach of fiduciary duties may be reduced or restricted. Delaware law allows indemnification of our non-employee directors and officer, if they (a) have acted in good faith, in a manner the non-employee director or officer reasonably believes to be in or not opposed to our best interests, and (b) with respect to any criminal action or proceeding, if the non-employee director or officer had no reasonable cause to believe the conduct was unlawful.

Pursuant to the Certificate of Incorporation and indemnification agreement, each non-employee director and officer who is made a party to a legal proceeding because he or she is or was a non-employee director or officer, is indemnified by us from and against any and all liability, except that we may not indemnify a non-employee director or officer: (a) for any liability incurred in a proceeding in which such person is adjudged liable to Monopar or is subjected to injunctive relief in favor of Monopar; (b) for acts or omissions that involve intentional misconduct or a knowing violation of law, fraud or gross negligence; (c) for unlawful distributions; (d) for any transaction for which such non-employee director or officer received a personal benefit or as otherwise prohibited by or as may be disallowed under Delaware law; or (e) with respect to any dispute or proceeding between us and such non-employee director or officer unless such indemnification has been approved by a disinterested majority of the Board or by a majority in interest of disinterested stockholders. We are required to pay or reimburse attorney's fees and expenses of a non-employee director or officer seeking indemnification as they are incurred, provided the non-employee director or officer executes an agreement to repay the amount to be paid or reimbursed if there is a final determination by a court of competent jurisdiction that such person is not entitled to indemnification.

Future legislation or executive or private sector actions may increase the difficulty and cost for us to commercialize our products and adversely affect the prices obtained for such products.

In the U.S., there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Affordable Care Act (the "ACA"), was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the US Supreme Court; the Trump Administration signed various executive orders and other directives that eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The US Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in 2021. The American Rescue Plan Act of 2021 which was recently enacted into law includes provisions which further the ACA, including expansion of marketplace subsidies and credits to reduce or eliminate premiums in the federal exchange for persons with certain income levels and providing subsidies for state exchanges. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

In addition, government price reporting and payment regulations are complex, and we will be required to continually assess the methods by which we plan to calculate and report any future pricing in accordance with these obligations. Our methodologies for calculations are inherently subjective and may be subject to review and challenge by various government agencies, which may disagree with our interpretation. If the government disagrees with our reported calculations, we may need to restate the previously reported data and could be subject to additional financial and legal liability.

Further, the increasing cost of healthcare as a percentage of GDP and the massive and increasing deferred liabilities behind most governmental healthcare programs (such as Medicare and Medicaid and state and local healthcare programs especially for retirement benefits) continue to be an economic challenge which threatens the overall economic health of the U.S. High cost healthcare products and therapies that are early in their life cycle are attractive targets for parties that believe that the cost of healthcare must be better controlled and significantly reduced. Pharmaceutical prices and healthcare reform have been debated and acted upon by legislators for many years. Future legislation or executive or private sector actions related to healthcare reform could materially and adversely affect our business by reducing our ability to generate revenue at prices sufficient to reward for the risks and costs of pharmaceutical development, to raise capital, and to market our products.

There is no assurance that federal or state healthcare reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform and third-party payers will affect the pharmaceutical industry in general and our business in particular.

Even if we are able to commercialize any drug candidate, such drug candidate may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

Our ability to commercialize any products successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, such as government authorities, private healthcare insurers and health maintenance organizations. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from government healthcare programs, such as Medicare and Medicaid, and private healthcare insurers are critical to new product acceptance. Patients are unlikely to use our future products, if any, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost.

Cost-containment is a priority in the U.S. healthcare industry and elsewhere. As a result, government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors also may request additional clinical evidence beyond the data required to obtain marketing approval, requiring a company to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of its products. Commercial third-party payors often rely upon Medicare coverage policy and payment limitations in setting their reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement for pharmaceutical products in the U.S. can differ significantly from payor to payor. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, that the level of reimbursement will be adequate. Coverage and reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

Additionally, the regulations that govern regulatory approvals, pricing and reimbursement for new drugs and therapeutic biologics vary widely from country to country. Some countries require approval of the sale price of a drug or therapeutic biologic before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain regulatory approval.

Politically divided governmental actions and related political actions outside of government can impact the FDA's role in the timely and effective review of new pharmaceutical products in the U.S. and our business may be adversely impacted.

A relevant example of dysfunctional government was the 35-day government shutdown that ended February 15, 2019, which limited the FDA to activities necessary to address imminent threats to human life and to activities funded by carry-over user fees. Future government shutdowns or other activities which limit the financial resources available to the FDA (and in particular to the Center for Drug Evaluation and Research) will delay the processing of new product drug development submissions, reviews, and approvals and other required regulatory actions. Such delays will adversely impact our business and financial condition.

Effective collaboration with the FDA's Center for Drug Evaluation and Research ("CDER") for the approval of drug candidates is a highly demanding process which can result in increased time and expense to gain approvals.

Our lead drug development program, Validive, will be reviewed by CDER. Efficient and professional collaboration with the FDA's CDER is essential for the timely clinical testing, test evaluations, analysis and approval of our drug candidates. CDER has an outstanding record of drug approvals and substantial funds to operate a highly professional organization but is also very demanding as to the quality of clinical research and applications for marketing approvals for drug candidates.

Our Company has in-house expertise and experience in the management of drug approvals. Qualified consultants and drug research organizations are also available to aid in our drug approval process; however, there is a meaningful risk that discussions and interactions inherent in the drug approval process and future developments or new improvements will result in delays, added expenses and new scientific/medical requirements which will cause adverse financial results and will likely impact the price of the Company's stock.

Future tax reform measures may negatively impact our financial position.

Tax reform measures are unpredictable and can change as the U.S. Congress and executive leadership changes. For example, on December 22, 2017, the Tax Cuts and Jobs Act of 2017 was signed into law that significantly revised the Internal Revenue Code of 1986, as amended (the "Code"). It is difficult to predict what future tax reform measures, if any, could be implemented and the extent to which they will impact our financial condition and our business.

Foreign currency exchange rates may adversely affect our consolidated financial statements.

Sales and purchases in currencies other than the U.S. Dollar expose us to fluctuations in foreign currencies relative to the U.S. Dollar and may adversely affect our consolidated financial statements. Increased strength of the U.S. Dollar increases the effective price of our future drug products sold in U.S. Dollars into other countries, which may require us to lower our prices or adversely affect sales to the extent we do not increase local currency prices. Decreased strength of the U.S. Dollar could adversely affect the cost of materials, products and services we purchase overseas. Sales and expenses of our non-U.S. businesses are also translated into U.S. Dollars for reporting purposes and the strengthening or weakening of the U.S. Dollar could result in unfavorable foreign currency translation and transaction effects. In addition, certain of our businesses may in the future invoice customers in a currency other than the business' functional currency, and movements in the invoiced currency relative to the functional currency could also result in unfavorable foreign currency translation and transaction effects. We also face exchange rate risk from our investments in subsidiaries owned and operated in foreign countries.

Our anticipated operating expenses and capital expenditures over the next year are based upon our management's estimates of possible future events. Actual amounts and the cost of new conditions could differ materially from those estimated by our management.

Development of pharmaceuticals and cancer drugs is extremely risky and unpredictable. We have estimated operating expenses and capital expenditures over the next year based on certain assumptions. Any change in the assumptions could cause the actual results to vary substantially from the anticipated expenses and expenditures and could result in material differences in actual versus forecasted expenses or expenditures. Furthermore, all of the factors are subject to the effect of unforeseeable future events. The estimates of capital expenditures and operating expenses represent forward-looking statements within the meaning of the federal securities laws. Prospective investors are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties. Actual events or results may differ materially from those discussed in the forward-looking statements as a result of various factors, including the risk factors set forth under this "Risk Factors" section in this Annual Report on Form 10-K.

The financial and operational projections that we may make from time to time are subject to inherent risks.

The projections that we provide herein or our management may provide from time to time (including, but not limited to, our success in raising strategic and substantial financial resources, the cost and timing of our clinical trials, clinical and regulatory timelines, production and supply matters, commercial launch dates, and other financial or operational matters) reflect numerous assumptions made by our management, including assumptions with respect to our specific as well as general business, regulatory, economic, market and financial conditions and other matters, all of which are difficult to predict and many of which are beyond our control. Accordingly, there is a risk that the assumptions made in preparing the projections, or the projections themselves, will prove inaccurate. There may be differences between actual and projected results, and actual results may be materially different from those contained in the projections. The inclusion of the projections in this Annual Report on Form 10-K should not be regarded as an indication that our management considered or consider the projections to be a guaranteed prediction of future events, and the projections should not be relied upon as such. See “Cautionary Statement Concerning Forward-Looking Statements.”

Our present and potential future international operations may expose us to business, political, operational, and financial risks associated with doing business outside of the U.S.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and clinical research organizations and clinical trial sites are located outside of the U.S. Furthermore, if we or any future collaborator succeeds in developing any products, we anticipate marketing them in the EU, the United Kingdom and other jurisdictions in addition to the U.S. If approved, we or our collaborator may hire sales representatives and conduct physician and patient association outreach activities outside of the U.S. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits and licenses which can vary jurisdictions to jurisdiction with different degrees of review and enforcement;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- rejection or qualification of foreign clinical trial data by the competent authorities of other countries;
- additional potentially relevant third-party patent and other intellectual property rights that may be necessary to develop and commercialize our products and drug candidates;
- complexities and difficulties in obtaining, maintaining, enforcing and defending our patent and other intellectual property rights;
- difficulties in staffing and managing foreign operations by a small-scale organization;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- limits, as a U.S.-based company, in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions, implementation of tariffs;
- certain expenses including, among others, expenses for travel, translation and insurance; and
- regulatory and compliance risks that relate to anti-corruption compliance and record-keeping that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its accounting provisions or its anti-bribery provisions or provisions of anti-corruption or anti-bribery laws in other countries.

Any of these factors could harm our ongoing international clinical operations and supply chain, as well as any future international expansion and operations and, consequently, our business, financial condition, prospects and results of operations.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended (“the FCPA”), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We interact with officials and employees of government agencies and government-affiliated hospitals, universities and other organizations. In addition, we may engage third-party intermediaries to promote our clinical research activities abroad or to obtain necessary permits, licenses and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have a Code of Business Conduct and Ethics which mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. However, we cannot assure you that our employees and third-party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. If any subpoenas, investigations or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management’s attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Risks Associated with our Common Stock

Existing and new investors will experience dilution as a result of future sales or issuances of our common stock and future option exercises under our 2016 Stock Incentive Plan and any amendments to the plan.

Our non-employee directors, employees, and certain of our consultants have been and will be issued equity and/or granted options that vest with the passage of time. Up to a total of 5,100,000 shares of our common stock may be issued as stock options or restricted stock units under the Amended and Restated Monopar Therapeutics Inc. 2016 Stock Incentive Plan, and stock options for the purchase of up to 2,147,790 shares of our common stock have already been granted (1,215,724 stock options are exercisable) and are outstanding along with 633,042 restricted stock units that have been granted to non-employee directors and employees as of March 10, 2023. The issuance of such equity upon vesting of restricted stock units and/or the exercise of such options will dilute both our existing and our new investors. As of March 10, 2023, 189,346 stock options have been exercised.

Our existing and our new investors will also experience substantial dilution resulting from the issuance by us of equity securities in connection with certain transactions, including without limitation, future offering of shares in future fundraising efforts, intellectual property licensing, acquisition, or commercialization arrangements.

Holders of the shares of our common stock will have no control of our operations or of decisions on major transactions.

Our business and affairs are managed by or under the direction of our Board. Our stockholders are entitled to vote only on actions that require a stockholder vote under federal or state law. Stockholder approval requires the consent and approval of holders of a majority or more of our outstanding stock. Shares of stock do not have cumulative voting rights and therefore, holders of a majority of the shares of our outstanding stock will be able to elect all Board members. TacticGem, LLC (“TacticGem”) owns 7,166,667 shares of common stock (54.34%). The limited liability company agreement requires TacticGem to pass through votes (including the vote for the election of directors) to its members in proportion to their membership percentages in TacticGem (57.367% owned by Tactic Pharma and 42.633% owned by Gem). As a result, Tactic Pharma, our initial investor, holds an approximately 32.4% beneficial interest in us and together with Gem’s beneficial ownership of approximately 23.2%, the two entities control a majority of our stock and will be able to elect all Board members and control our affairs. Some of our Board members and executive officers own and control Tactic Pharma. Although no single person has a controlling interest in Tactic Pharma, acting together, they are able to control Tactic Pharma and a large voting block of our common stock and together with Gem can elect a majority of our Board.

Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a de-listing of our common stock.

If we fail to satisfy the continued listing requirements of The Nasdaq Capital Market, such as the corporate governance requirements or the minimum closing bid price requirement, the Nasdaq Stock Market (“Nasdaq”) may take steps to de-list our common stock. Such a de-listing or the announcement of such de-listing will have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a de-listing, we would take actions to restore our compliance with the Nasdaq listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with the Nasdaq listing requirements.

The stock price of our common stock may be volatile or may decline regardless of our operating performance.

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has from time-to-time experienced significant price and volume fluctuations that appear to be unrelated to the operating performance of particular companies. Our common stock has only been trading on the Nasdaq Capital Market since December 19, 2019, and has experienced significant volatility in market prices through March 10, 2023, ranging from a low of \$1.39 to a high of \$48.00. Our small public float and relatively low and inconsistent trading volumes exacerbate volatility.

The market price of our common stock is likely to remain highly volatile and may fluctuate substantially due to many factors, including:

- announcements concerning the progress and success of our clinical trials, our ability to obtain regulatory approval for and commercialize our product candidates, including any requests we receive from the FDA for additional studies or data that result in delays in obtaining regulatory approval or launching our product candidates, if approved;
- unstable market conditions in the pharmaceutical and biotechnology sectors or the economy as a whole;
- price and volume fluctuations in the overall stock market;
- the failure of our product candidates, if approved, to achieve anticipated commercial success; in the time projected by securities analysts and others;
- announcements of the clinical success, NDA approval or introduction of new products by us or our direct competitors;
- announcements of developments concerning product development results or intellectual property rights of others;
- litigation or public concern about the safety and/or efficacy of our potential or approved products;
- actual fluctuations in our quarterly or annual operating results, and concerns by investors that such fluctuations may occur in the future and are indicative of internal problems;
- deviations in our operating results from the estimates of securities analysts or other analyst comments;
- additions or departures of key personnel;
- healthcare reform legislation, including measures directed at controlling the pricing of pharmaceutical products, and third-party coverage and reimbursement policies;
- announcements or publicity concerning current or future strategic collaborations;
- discussion of our Company, our stock price or our potential future market value by the financial and scientific press and online investor communities; and
- market responses to the fluctuating conditions of COVID-19 or to the Russia-Ukraine war.

We may become involved in securities class action litigation that could divert management’s attention and harm our business.

The stock markets have from time-to-time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and pharmaceutical companies. Our stock price has experienced such fluctuations since our initial public offering. These broad market fluctuations may cause the market price of our stock to advance or decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management’s attention and resources, which could adversely affect our business.

Substantial amounts of our outstanding shares may be sold into the market. If there are substantial sales of shares of our common stock, the price of our common stock could decline.

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our non-employee directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. We have 13,193,172 outstanding shares of our common stock as of March 10, 2023. A majority of our outstanding shares of common stock are currently held by non-employee directors, executive officers and other affiliates and are subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended (Securities Act).

Our largest stockholders have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or our stockholders. We have also registered shares of common stock that we have issued and may issue under our employee equity incentive plans. These shares are able to be sold freely in the public market upon issuance, subject to existing internal practices which prohibit sales under certain circumstances. The market price of the shares of our common stock could decline as a result of the sale of a substantial number of our shares of common stock in the public market or the perception in the market that the holders of a large number of shares intend to sell their shares.

Our ability to use our net operating loss carry-forwards and certain other tax attributes may be limited.

Under Section 382 of the Code, if a corporation undergoes an “ownership change” (generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period), the corporation’s ability to use its pre-change net operating loss carry-forwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We believe that additional fundraising efforts in the next three years, may trigger an “ownership change” limitation in the near future. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carry-forwards to offset U.S. federal taxable income will be subject to limitations, which could result in increased future tax liability to us had we not been subject to such limitations.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our Company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We do not intend to pay dividends for the foreseeable future and, as a result, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividends on our capital stock, and we do not intend to pay any cash dividends in the foreseeable future. Any determination to pay dividends in the future will be at the discretion of our Board. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains as a return on their investments.

There can be no assurance that we will ever provide liquidity to our investors through a sale of our Company.

While acquisitions of pharmaceutical companies like ours are not uncommon, potential investors are cautioned that no assurances can be given that any form of merger, combination, or sale of our Company will take place or that any merger, combination, or sale, even if consummated, would provide liquidity or a profit for our investors. You should not invest in our Company with the expectation that we will be able to sell the business in order to provide liquidity or a profit for our investors.

Delaware law and provisions in our amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the potential trading price of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management or Board and adversely affect our stock price.

Provisions of our amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, our amended and restated bylaws:

- provide that all vacancies on our Board may only be filled by our Board and not by stockholders;
- allow the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose; and
- provide that special meetings of our stockholders may be called only by our Board.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any “interested” stockholder for a period of three years following the date on which the stockholder became an “interested” stockholder.

Item 2. Properties

We are currently leasing office space for our executive headquarters at 1000 Skokie Blvd in the Village of Wilmette, Illinois for our corporate offices. We believe that we will lease additional office space within the next 12 months as we continue to hire additional personnel.

Item 3. Legal Proceedings

We are currently not, and to date have never been, a party to any adverse material legal proceedings.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is listed under the symbol “MNPR” on the Nasdaq Capital Market.

Holdings

As of March 10, 2023, there were 13,193,172 shares of our common stock outstanding held by 30 holders of record and approximately 2,700 beneficial stockholders.

Dividends

We have never paid cash dividends on any of our capital stock and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

Registration Rights

We are subject to an agreement with TacticGem, LLC (“TacticGem”), our largest stockholder, which obligates us to file a Form S-3 or other appropriate form of registration statement covering the resale of any of our common stock by TacticGem, or its members Gem Pharmaceuticals, LLC, or Tactic Pharma, LLC, upon direction by TacticGem. We are required to use our best efforts to have such registration statement declared effective as soon as practical after it is filed. In the event that such registration statement for resale is not approved by the SEC, and TacticGem submits a written request, we are required to prepare and file a registration statement on Form S-1 registering such common stock for resale and to use our best efforts to have such registration statement declared effective as soon as practical thereafter. Additionally, if we propose to register our common stock for sale for cash, TacticGem and its members have the right to include some of their shares in such registration. After registration, pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act other than pursuant to restrictions on affiliates under Rule 144.

Recent Sales of Unregistered Securities.

There were no securities issuances that were not registered under the Securities Act during the reporting period.

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing activities, includes forward-looking statements that involve risks and uncertainties. You should read the “Risk Factors” section of this Annual Report on Form 10-K, Item 1A, for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical stage biopharmaceutical company focused on developing proprietary therapeutics designed to extend life or improve quality of life for cancer patients. We are building a drug development pipeline through the licensing and acquisition of therapeutics in late preclinical or in clinical development stages. We leverage our scientific and clinical experience to help reduce the risk of and accelerate the clinical development of our drug product candidates.

Financial Status

Our cash, cash equivalents and investments as of December 31, 2022, was \$13.1 million. As discussed further below and elsewhere in this Annual Report, we expect that our current funds will be sufficient for us to obtain topline results from our ongoing open-label Phase 1b camsirubicin clinical trial as planned by the end of 2023 (but as discussed below, this may not be the case if camsirubicin reaches even higher dose levels than we are anticipating and topline results are deferred as dosing continues beyond 2023) and, assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, the continued enrollment in the Phase 3 portion of our ongoing Validive Phase 2b/3 (VOICE) clinical program. We will require additional funding to advance our clinical and preclinical programs and we anticipate that we will seek to raise additional capital within the next 12 months to fund our future operations.

Our primary funding source over the past three years was sales of shares of our common stock under at-the-market sales programs through Capital on Demand™ Sales Agreements with JonesTrading Institutional Services LLC (“Jones Trading”). During 2020 and the first quarter of 2021, we sold 1,964,724 shares of our common stock at an average gross price of \$10.02 per share for net proceeds of \$19,100,603, after fees and commissions of \$591,188. The maximum aggregate offering price under the prior agreement was reached during the first quarter of 2021 and there were no further sales under that agreement. In April 2022, we entered into a new at-the-market sales agreement. Pursuant to that agreement, during 2022, the Company sold 64,573 shares of its common stock at an average gross price per share of \$2.71 for net proceeds of \$170,552, after fees and commissions of \$4,377. In addition, the Company incurred legal, accounting and other fees totaling \$83,234 for net proceeds after fees, commissions and expenses of \$87,318. From January 1, 2023 to March 10, 2023, the Company sold 241,475 shares of its common stock at an average gross price per share of \$3.47 for net proceeds of \$836,836, after fees and commissions of \$20,940.

Validive Clinical Update

In February 2021, we dosed the first patient in our Phase 2b/3 VOICE trial of Validive® for the prevention of chemoradiation treatment (“CRT”)-induced severe oral mucositis (“SOM”) in patients with oropharyngeal cancer (“VOICE”). In August 2021, we successfully reached our original target of 20 activated clinical trial sites for the Phase 2b portion of the 2b/3 Validive® VOICE trial and in September 2021, we received authorization to proceed with the VOICE clinical trial in multiple countries in Europe. In 2022, we completed enrollment of the Phase 2b portion of the VOICE trial and commenced enrollment in the Phase 3 portion. As of March 10, 2023, we have 81 clinical sites activated and enrolling patients in the U.S. and Europe. To be prepared for a potential positive go/no-go decision based on the interim analysis, we continue to activate additional sites globally. This interim analysis, and the resulting go/no-go decision about whether to proceed to the Phase 3 portion of the trial, is expected by the end of March 2023. If the interim analysis results in a no-go decision, we would need to reconsider our efforts with respect to Validive and refocus our development efforts on our other product candidates. Validive has been our lead product candidate to date and is the most clinically advanced, and if we had to reconsider or abandon our efforts, it would likely materially adversely impact our financing prospects, as well as the price of our common stock. Because the interim analysis is being performed by an independent data monitoring committee, we do not know what the results will be as of the date of this Annual Report.

To complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will require additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive), which we are planning to pursue within the next 12 months.

Camsirubicin Clinical Update

In August 2021, we announced clearance from the U.S. Food and Drug Administration (“FDA”) to proceed with an open-label Phase 1b dose-escalation clinical trial evaluating camsirubicin plus growth factor support (pegfilgrastim/G-CSF) in patients with advanced soft tissue sarcoma (“ASTS”). In September 2021, we initiated the Phase 1b clinical trial, and in October 2021 we dosed the first patients. In February 2022, we announced that the first dose level of camsirubicin had been completed in November 2021, with a positive recommendation from the trial safety review committee to proceed to next higher dose level and that three patients had already been dosed at the second dose level. That dose level was successfully cleared, as was the third and fourth dose levels, and we are presently enrolling patients at the fifth dose level. The fifth dose level is over twice the highest dose administered in any prior camsirubicin clinical trial (650 mg/m² versus 265 mg/m²) and no drug-related cardiotoxicity has been observed to date up to the current dose-level. The open-label Phase 1b camsirubicin dose-escalation trial is planning to enroll additional cohorts until the maximum tolerable dose is reached.

In November 2022, we presented an abstract and poster of the Phase 1b clinical trial data at the Connective Tissue Oncology Society Annual Meeting in Vancouver, BC. Following completion of the Phase 1b clinical trial, we continue to expect that Grupo Español de Investigación en Sarcomas (“GEIS”) will sponsor and lead a multi-country, randomized, open-label Phase 2 clinical trial to evaluate camsirubicin head-to-head against doxorubicin, the current first-line treatment for ASTS. We currently anticipate topline results in the camsirubicin Phase 1b clinical trial by the end of 2023 and believe we have sufficient funds to advance the trial through that date. However, if camsirubicin reaches higher dose levels than we are anticipating, the Phase 1b clinical trial may still be dosing patients beyond the end of 2023 and topline results may be deferred. Although we would likely consider this a positive development, it is possible that we would require additional funding to complete an extended Phase 1b clinical trial in this situation. Regardless, additional funding is expected to be required to support further development through and beyond our ongoing Phase 1b clinical trial.

MNPR-101 for Radiopharmaceutical Use Development Update

Pursuant to our 50/50 collaboration development agreement with NorthStar Medical Radioisotopes, LLC (“NorthStar”) to develop potential radioimmunotherapeutics based on MNPR-101 (“MNPR-101 RITs”), we have coupled MNPR-101 to imaging and therapeutic radioisotopes. The resulting conjugates, MNPR-101-Zr and MNPR-101-PCTA-Ac225, are designed to be highly selective agents that have the potential to image and kill certain cancer cells. By eradicating these cancer cells with a uPAR-targeted RIT (“uPRIT”), the therapeutic goal is to spare healthy cells while quickly killing the cancer cells.

Based on promising recently generated preclinical imaging results with MNPR-101-Zr showing high uptake across multiple tumor types, the companies committed to additional funding with the aim of initiating a first-in-human imaging study with MNPR-101-Zr as early as the end of this year. MNPR-101-Zr is a zirconium-89 labeled version of MNPR-101, a highly selective antibody against the urokinase plasminogen activator receptor (“uPAR”). Positron emission tomography (“PET”) imaging of preclinical mouse models for triple-negative breast, colorectal, and pancreatic tumors displayed high and selective uptake of MNPR-101-Zr in these uPAR-expressing tumors. These proof-of-concept studies provide support for a first-in-human PET imaging study with MNPR-101-Zr and a future therapeutic study using the previously announced actinium-225 labeled MNPR-101 RIT. Overall, the imaging results demonstrate the potential utility of MNPR-101 as a precision targeting agent for both imaging and therapy in multiple cancer indications.

MNPR-202 and Related Analogs Updates

In June 2021, we entered into a collaboration agreement with the Cancer Science Institute of Singapore (“CSI Singapore”), one of Asia’s premier cancer research centers, at the National University of Singapore (“NUS”) (consistently ranked as one of the world’s top universities) to evaluate the activity of MNPR-202 and related analogs in multiple types of cancer. MNPR-202 was designed to retain the same potentially non-cardiotoxic backbone as camsirubicin but is modified at other positions which may enable it to work in certain cancers that are resistant to camsirubicin and doxorubicin. In December 2020, we announced the issuance of our composition of matter U.S. patent (US10,450,340) covering MNPR-202 and related analogs. CSI Singapore has tested MNPR-202 in preclinical cancer models with promising results. In December 2022, in collaboration with Dr. Anand Jeyasekharan of CSI Singapore, we presented an abstract and poster of the preclinical data of MNPR-202 at the American Society of Hematology 64th Annual Meeting in New Orleans, LA.

Our Strategy

Our management team has extensive experience in developing therapeutics and medical technologies through global regulatory approval and commercialization. In aggregate, companies they co-founded have achieved four drug approvals and three diagnostic medical imaging device approvals in the U.S. and the EU, successfully sold an asset

developed by management which is currently in Phase 3 clinical trials, sold two oncology-focused diagnostic imaging businesses to Fortune Global 1000 firms, and completed the clinical and commercial development and ultimately the sale of a commercial biopharmaceutical company for over \$800 million in cash. In addition, the team has supported multiple regulatory submissions with the FDA and EMA and launched multiple drugs in the U.S and the EU. Understanding the preclinical, clinical, regulatory and commercial development processes and hurdles are key factors in successful drug development and the expertise demonstrated by our management team across all of these areas increases the probability of success in advancing the product candidates in our product pipeline. Our strategic goal is to acquire, develop and commercialize promising oncology product candidates that address important unmet medical needs of cancer patients. Seven key elements of our strategy to achieve this goal are to:

- **Leverage data generated from the Phase 2 Validive clinical trial to complete the execution of a hopefully successful VOICE clinical program for Validive for SOM in oropharyngeal cancer (“OPC”).** In the prior Phase 2 clinical trial the absolute incidence of SOM in OPC patients was reduced by 26.3%, the time to SOM onset was delayed, and the duration of disease in patients that developed SOM was decreased by 15.5 days in the Validive 100 µg cohort versus placebo. In addition to the data from the Phase 2 clinical trial, we believe the guidance from our key opinion leaders (“KOLs”) as well as from the FDA and EMA, and our own internal clinical trial design expertise, help position us well for an effective VOICE clinical trial program.
- **Obtain FDA and EMA approval of Validive to maximize the commercial potential of Validive in both the U.S. and the EU, and seek marketing partnerships outside these markets.** If the VOICE clinical program of Validive is successful and FDA and EMA approvals are obtained, we currently intend to commercialize Validive in the U.S. and the EU ourselves, which may include establishing our own specialty sales force and seeking partnerships outside of these territories for regulatory approval and drug sales and distribution.
- **Advance the clinical development of camsirubicin, by pursuing indications where doxorubicin has demonstrated efficacy.** ASTS will be the first indication, which is anticipated to allow camsirubicin to go head-to-head against doxorubicin, the current first-line treatment. In this indication, camsirubicin previously demonstrated clinical benefit (stable disease or partial response) in 52.6% of patients evaluable for tumor progression in a single-arm Phase 2 study. Clinical benefit was proportional to dose and was consistently observed at higher cumulative doses of camsirubicin (>1000 mg/m²). Camsirubicin was very well tolerated in this Phase 2 study and underscored the ability to potentially administer camsirubicin without restriction as to cumulative dose (doxorubicin is limited due to heart toxicity to 450 mg/m² cumulative dose). Our current ongoing Phase 1b clinical trial continues towards establishing a new, higher recommended dose for the next Phase 2 ASTS clinical trial.
- **Continue the development of MNPR-101-Zr, MNPR-101 RIT and related molecules as therapeutic, diagnostic and imaging agents.** We plan to continue the development of MNPR-101-Zr, MNPR-101 RIT and related molecules for diagnostic, imaging, and therapeutic use in cancer.
- **Continue the development of MNPR-202 and related analogs in multiple types of cancers.** The 2-pyrrilino camsirubicin analog (MNPR-202) and related analogs represent proprietary compositions of matter designed to retain the non-cardiotoxic backbone of camsirubicin yet exhibit novel features in terms of antitumor activity and mechanism that distinguish these analogs from camsirubicin as well as from doxorubicin, **potentially addressing camsirubicin- and doxorubicin-resistant cancers.**
- **Expand our drug development pipeline through advancing current assets, in-licensing, and acquisition of oncology product candidates.** We plan to continue the expansion of our drug development pipeline through acquiring or in-licensing additional oncology product candidates, particularly those that leverage existing scientific and clinical data that helps reduce the risks of the next steps in clinical development.
- **Utilize the expertise and prior experience of our team in the areas of asset acquisition, drug development and commercialization to establish ourselves as a leading biopharmaceutical company.** Our senior executive team has relevant experience in biopharmaceutical in-licensing and acquisitions as well as developing product candidates through approval and commercialization. In aggregate, our team has co-founded BioMarin Pharmaceutical (Nasdaq: BMRN), Sensant Corp (acquired by Siemens), American BioOptics (assets acquired by Olympus), Raptor Pharmaceuticals (\$800 million sale to Horizon Therapeutics), and Tactic Pharma, LLC (“Tactic Pharma”) (sale of lead asset, choline tetrathiomolybdate, was ultimately acquired by Alexion in June 2018 for \$764 million; Alexion was subsequently acquired by AstraZeneca).

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”). An emerging growth company may take advantage of specified reduced reporting burdens that are otherwise applicable generally to public companies. These provisions include, but are not limited to:

- inclusion of only two years, as compared to three years, of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced “Management’s discussion and analysis of financial condition and results of operations” disclosures;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002 (“Sarbanes-Oxley Act”);
- an exemption from compliance with any new requirements adopted by the Public Company Accounting Oversight Board (“PCAOB”) requiring mandatory audit firm rotation;
- reduced disclosure about executive compensation arrangements; and
- an exemption from the requirement to seek non-binding advisory votes on executive compensation or golden parachute arrangements.

We expect to take advantage of these provisions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (1) the last day of the year (a) following the fifth anniversary of the completion of our initial public offering which is December 2024, (b) in which we have total annual gross revenue of at least \$1.235 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in this Annual Report on Form 10-K, and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be reduced and/or less detailed than what you might find from other public reporting companies.

The JOBS Act also permits an emerging growth company such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to opt out of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies. In addition, we are also a “smaller reporting company” as defined in Rule 12b-2 of the Exchange Act and have elected to take advantage of certain of the scaled back disclosure requirements available to smaller reporting companies such as avoiding the extensive narrative disclosure required of other reporting companies, particularly in the description of executive compensation.

Revenues

We are an emerging growth company. We have no approved drugs and have not generated any revenues. To date, we have engaged in acquiring or in-licensing drug product candidates, entering into collaboration agreements for testing and clinical development of our drug product candidates and providing the infrastructure to support the clinical development of our drug product candidates. We do not anticipate commercial revenues from operations until we complete testing and development of one of our drug product candidates and obtain marketing approval or we sell, enter into a collaborative marketing arrangement, or out-license one of our drug product candidates to another party. See “Liquidity and Capital Resources”.

Recently Issued and Adopted Accounting Pronouncements

During the year ended December 31, 2022, there were no relevant recently issued accounting pronouncements that would impact our financial position and our consolidated results of operations and comprehensive loss or cashflows.

Critical Accounting Policies and Use of Estimates

While our significant accounting policies are described in more detail in Note 2 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Clinical Trials Accruals

We accrue and expense the costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with contract research organizations, service providers, and clinical trial sites. We estimate the amounts to accrue based upon discussions with internal clinical personnel and external service providers as to progress or stage of completion of trials or services and the agreed upon fee to be paid for such services. Costs of setting up clinical trial sites for participation in

the trials are expensed immediately as R&D expenses. Clinical trial site costs related to patient screening and enrollment are accrued as patients are screened/entered into the trial.

Stock-Based Compensation

We account for stock-based compensation arrangements with employees, non-employee directors and consultants using a fair value method, which requires the recognition of compensation expense for costs related to all stock-based compensation grants, including stock option and restricted stock unit (“RSU”) grants. The fair value method requires us to estimate the fair value of stock-based payment awards on the date of grant using an option pricing model or the closing stock price on the date of grant in the case of RSUs.

Stock-based compensation costs for stock awards granted to our employees, non-employee directors and consultants are based on the fair value of the underlying instruments calculated using the Black-Scholes option-pricing model on the date of grant for stock options and using the closing stock price on the date of grant for RSUs and recognized as expense on a straight-line basis over the requisite service period, which is the vesting period. Determining the appropriate fair value model and related assumptions requires judgment, including selecting methods for estimating our future stock price volatility and expected holding term. The expected volatility rates are estimated based on our actual historical volatility over the two-year period from our initial public offering on December 18, 2019, through December 31, 2021. The expected term for stock options granted during the years ended December 31, 2022, and 2021, was estimated using the simplified method. Forfeitures only include actual forfeitures to-date as the Company accounts for forfeitures as they occur due to a limited history of forfeitures. We have not paid dividends and do not anticipate paying a cash dividend in future vesting periods and, accordingly, use an expected dividend yield of zero. The risk-free interest rate is based on the rate of U.S. Treasury securities with maturities consistent with the estimated expected term of the awards.

Results of Operations

Comparison of the Years Ended December 31, 2022, and December 31, 2021

The following table summarizes the results of our operations for the years ended December 31, 2022, and 2021:

(in thousands)	Years Ended December 31,		Variance
	2022	2021	
Research and development expenses	\$ 7,592	\$ 6,493	\$ 1,099
General and administrative expenses	2,945	2,634	311
Total operating expenses	10,537	9,127	1,410
Operating loss	(10,537)	(9,127)	(1,410)
Interest income	21	24	(3)
Net loss	<u>\$ (10,516)</u>	<u>\$ (9,103)</u>	<u>\$ (1,413)</u>

Research and Development (“R&D”) Expenses

R&D expenses for the year ended December 31, 2022 were \$7,592,000, compared to \$6,493,000 for the year ended December 31, 2021. This represents an increase of \$1,099,000 primarily attributed to (1) a \$1,044,000 increase for Validive clinical trial planning and execution including manufacturing costs, (2) a \$460,000 increase due to camsirubicin clinical trial planning and execution including manufacturing costs, (3) a \$193,000 increase in R&D consulting, partially offset by (1) a \$534,000 decrease for R&D personnel salaries, bonuses, benefits and annual (non-cash) equity grants and (2) a \$64,000 net decrease in other R&D expenses.

General and Administrative (“G&A”) Expenses

G&A expenses for the year ended December 31, 2022, were \$2,945,000, compared to \$2,634,000 for the year ended December 31, 2021. This represents an increase of \$311,000 primarily attributed to (1) a \$349,000 increase in G&A personnel salaries, bonuses, benefits and stock-based compensation for annual (non-cash) equity grants, and (2) a \$27,000 net increase in other G&A expenses partially offset by a \$65,000 decrease in patent costs.

Interest Income

Interest income for the year ended December 31, 2022, decreased by \$3,000 versus the year ended December 31, 2021. The decrease was caused by lower bank balances offset by an increase in interest rates in 2022.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred losses and cumulative negative cash flows from operations since we commenced operations resulting in an accumulated deficit of approximately \$51.8 million as of December 31, 2022. We anticipate that we will continue to incur losses for the foreseeable future. We expect that our R&D and G&A expenses will increase to enable the execution of our strategic plan. As a result, we anticipate that we will seek to raise additional capital within the next 12 months to fund our future operations. We will seek to obtain needed capital through a combination of equity offerings, including the usage of our Capital on Demand™ Sales Agreement with JonesTrading, debt financings, strategic collaborations and grant funding. To date, we have funded our operations through net proceeds from the initial public offering of our common stock, net proceeds from sales of our common stock through at-the-market sales programs, private placements of our preferred and common stock, and the net receipt of funds related to the acquisition of camsirubicin. We anticipate that the currently available funds as of March 10, 2023, will fund our planned operations at least through March 31, 2024.

We invest our cash equivalents in two money market accounts and U.S. Treasury Bills.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2022, and 2021.

(in thousands)	Years Ended December 31,		Variance
	2022	2021	
Net cash used in operating activities.....	\$ (7,228)	\$ (7,317)	\$ 89
Net cash used in investing activities	(4,919)	-	(4,919)
Net cash provided by financing activities	33	10,879	(10,846)
Effect of exchange rates	(4)	5	(9)
Net increase (decrease) in cash and cash equivalents	<u>\$ (12,118)</u>	<u>\$ 3,567</u>	<u>\$ (15,685)</u>

During 2022, the Company began investing its idle cash due to the rising interest rates and at December 31, 2022, the Company holds short term liquid investments of \$4,934,000 which can be readily converted to cash. During the years ended December 31, 2022 and 2021, we had net cash outflows of \$12,118,000 and net cash inflows of \$3,567,000, respectively, a decrease of \$15,685,000. During 2022, we had higher net cash used investing activities and less funds raised from sales of our common stock under an at-the-market sales program compared to 2021.

Cash Flow Used in Operating Activities

The cash flow used in operating activities during the year ended December 31, 2022, compared to the year ended December 31, 2021 was essentially flat.

Cash Flow Used in Investing Activities

The increase to cash flow used in investing activities during the year ended December 31, 2022, compared to the year ended December 31, 2021 of approximately \$4,919,000 was a result of our investment in U.S. Treasury Bills at the end of 2022. Prior to 2022, idle cash was invested in money market accounts and recorded as cash equivalents.

Cash Flow Provided by Financing Activities

The decrease in cash flow provided by financing activities during the year ended December 31, 2022, compared to the year ended December 31, 2021, of approximately \$10,846,000 was primarily due to higher net proceeds from sales of our common stock through an at-the-market sales program in 2021.

Future Funding Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate any revenue from product sales or royalties unless and until we obtain regulatory approval of and commercialize any of our current or future drug product candidates or we out-license or sell a drug product candidate to another party. At the same time, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the research, development, future preclinical studies and clinical trials of, and seek regulatory approval for, our current and future drug product candidates.

If we obtain regulatory approval of any of our current or future drug product candidates, we will need substantial additional funding for commercialization requirements and our continuing drug product development operations.

As a company, we have not completed development through marketing approvals of any therapeutic products. We expect to continue to incur significant increases in expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- advance the clinical development and execute the regulatory strategy for Validive, assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023;
- advance the clinical development and execute the regulatory strategy for camsirubicin;
- continue the preclinical activities and potentially enter clinical development of an MNPR-101-derived radioimmunotherapeutics (MNPR-101 RIT) and companion diagnostics (MNPR-101-Zr), to treat cancer;
- continue the preclinical activities, and potentially later-on enter clinical development, of MNPR-202 (and related analogs) for various cancer indications;
- acquire and/or license additional pipeline drug product candidates and pursue the future preclinical and/or clinical development of such drug product candidates;
- seek regulatory approvals for any of our current and future drug product candidates that successfully complete registration clinical trials;
- establish or purchase the services of a sales, marketing and distribution infrastructure to commercialize any products for which we obtain marketing approval;
- develop or contract for manufacturing/quality capabilities or establish a reliable, high quality supply chain sufficient to support our clinical requirements and to provide sufficient capacity to launch and supply the market for any product for which we obtain marketing approval; and
- add or contract for required operational, financial and management information systems and capabilities and other specialized expert personnel to support our drug product candidate development and planned commercialization efforts.

We anticipate that the funds available as of March 10, 2023, will fund our obligations at least through March 31, 2024. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug product candidates, and the extent to which we enter into collaborations with third parties to participate in the development and commercialization of our drug product candidates, we are unable to accurately estimate with high reliability the amounts and timing required for increased capital outlays and operating expenditures associated with our current and anticipated drug product candidate development programs.

Our future capital requirements will depend on many factors, including:

- the progress of clinical development and regulatory interactions and approvals of Validive;
- the progress of clinical development and regulatory interactions and approvals of camsirubicin;
- the costs, timing and outcomes of seeking, obtaining, and maintaining FDA and international regulatory approvals;
- the progress of preclinical and clinical development of MNPR-101-derived radioimmunotherapeutics and companion diagnostics, to treat cancer, including activities through our collaboration with NorthStar;
- the progress of preclinical and potentially clinical development of MNPR-202 (and related analogs);
- the number and characteristics of other drug product candidates that we may license, acquire, invent or otherwise pursue;
- the scope, progress, timing, cost and results of research, preclinical development and clinical trials and regulatory requirements for future drug product candidates;
- the costs associated with manufacturing/quality requirements and establishing or contracting for sales, marketing and distribution capabilities;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make in connection with the licensing, filing, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to hire or contract for additional management, administrative, scientific, medical, sales and marketing, and manufacturing/quality and other specialized personnel or external expertise;

- the effect and timing of entry of competing products or new therapies that may limit market penetration or prevent the introduction of our drug product candidates or reduce the commercial potential of our product portfolio;
- our need to implement additional required internal management, operational, record keeping and other systems and infrastructure; and
- the economic and other terms, timing and success of our existing collaboration and licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future, including the timing of receipt of or payment to or from others of any license, milestone or royalty payments under these arrangements.

Expenditures are expected to increase in 2023 and onward for:

- assuming a positive result of the go/no go interim analysis decision anticipated by the end of March 2023, clinical research services and clinical site fees for our Phase 3 VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial;
- process development, manufacturing costs, clinical trial expenses and clinical database management of camsirubicin in connection with the Phase 1b dose escalation clinical trial and other future clinical development;
- support of the development of MNPR-101-derived radioimmunotherapeutics (MNPR-101 RIT) and companion diagnostics (MNPR-101-Zr) to treat cancer, including activities through our collaboration with NorthStar;
- preclinical studies (and if successful, clinical studies) of MNPR-202 (and related analogs); and
- employee compensation and consulting fees to support the increased scope of activities required for the progress of our product candidate programs including Validive, camsirubicin, MNPR-101 RIT (uPRIT and related compounds) and companion diagnostics (MNPR-101-Zr) and MNPR-202 (and related analogs).

We have activated clinical trial sites and are dosing patients in our VOICE clinical trial. In order to complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, we will require additional funding in the millions or tens of millions of dollars (depending on if we have consummated a collaboration or partnership or neither for Validive), or find a suitable pharmaceutical partner, both of which we are planning to pursue within the next 12 months. There can be no assurance that any such events will occur. We have also initiated and commenced dosing in our Phase 1b camsirubicin clinical trial. We intend to continue evaluating drug product candidates for the purpose of growing our pipeline. Identifying and securing high-quality compounds usually takes time and related expenses; however, our spending could be significantly accelerated in 2023 and onward if additional drug product candidates are acquired and enter clinical development. In this event, we may be required to expand our management team, and pay higher contract manufacturing costs, contract research organization fees, other clinical development costs and insurance costs that are not currently projected. Beyond our need to raise additional funding within the next 12 months to complete the VOICE clinical program, additional long-term funding is needed to commercialize Validive, if approved, and otherwise generally to support our current and future product candidates through clinical trials, approval processes and, if applicable, commercialization.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, we expect to finance our future cash needs primarily through a combination of equity offerings, including the usage of our Capital on Demand™ Sales Agreement with JonesTrading, debt financings, strategic collaborations and grant funding. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our current stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our current stockholders' rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with other parties, we likely will have to share or relinquish valuable rights to our technologies, future revenue streams, research programs or drug product candidates or grant licenses on terms that may not be favorable to us, which will reduce our future returns and affect our future operating flexibility. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our pipeline product development or commercialization efforts or grant rights to others to develop and market drug product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

License, Development and Collaboration Agreements

Onxeo S.A.

In June 2016, we executed an agreement with Onxeo S.A., a French public company, which gave us the exclusive option to license (on a world-wide exclusive basis) Validive (clonidine hydrochloride mucobuccal tablet; clonidine HCl MBT a mucoadhesive tablet of clonidine based on the Lauriad mucoadhesive technology. The agreement includes clinical, regulatory, developmental and sales milestones that could reach up to \$108 million if we achieve all milestones, and escalating royalties from 5% to 10% on net sales. In September 2017, we exercised the option to license Validive from Onxeo for \$1 million, but as of March 10, 2023, we have not been required to pay Onxeo any other funds under the agreement. We will need to raise significant funds or enter into a collaboration partnership to support the completion of clinical development and marketing approval of Validive.

Under the agreement, we are required to pay royalties to Onxeo on a product-by-product and country-by-country basis until the later of (1) the date when a given product is no longer within the scope of a patent claim in the country of sale or manufacture, (2) the expiry of any extended exclusivity period in the relevant country (such as orphan drug exclusivity, pediatric exclusivity, new chemical entity exclusivity, or other exclusivity granted beyond the expiry of the relevant patent), or (3) a specific time period after the first commercial sale of the product in such country. In most countries, including the U.S., the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country, not taking into consideration any potential patent term adjustment that may be filed in the future or any regulatory extensions that may be obtained. The royalty termination provision pursuant to (3) described above is shorter than 20 years and is the least likely cause of termination of royalty payments.

The Onxeo license agreement does not have a pre-determined term, but expires on a product-by-product and country-by-country basis; that is, the agreement expires with respect to a given product in a given country whenever our royalty payment obligations with respect to such product have expired. The agreement may also be terminated early for cause if either we or Onxeo materially breach the agreement, or if either we or Onxeo become insolvent. We may also choose to terminate the agreement, either in its entirety or as to a certain product and a certain country, by providing Onxeo with advance notice.

Grupo Español de Investigación en Sarcomas (“GEIS”)

In June 2019, we executed a clinical collaboration with GEIS for the development of camsirubicin in patients with advanced soft tissue sarcoma (“ASTS”). Following completion of the Phase 1b clinical trial in the U.S. that we initiated in the third quarter of 2021 with the first patient dosed in October 2021, we continue to expect that GEIS will sponsor and lead a multi-country, randomized, open-label Phase 2 clinical trial to evaluate camsirubicin head-to-head against doxorubicin, the current first-line treatment for ASTS. We will provide study drug and supplemental financial support for the clinical trial. For quarter ended March 31, 2021, we incurred \$0.3 million in expenses under the GEIS agreement and other clinical-related expenses including clinical material manufacturing and database management expenses in support of the then-planned GEIS Phase 2 camsirubicin clinical trial. We can terminate the agreement by providing GEIS with advance notice, and without affecting our rights and ownership to any related intellectual property or clinical data. In the second quarter of 2021, due to regulatory delays in Spain, we decided to conduct an open-label Phase 1b clinical trial of camsirubicin in the U.S., therefore no expenses were incurred related to the GEIS collaboration beyond March 31, 2021.

XOMA Ltd.

Pursuant to a non-exclusive license agreement with XOMA Ltd. for the humanization technology used in the development of MNPR-101, we are obligated to pay XOMA Ltd. clinical, regulatory and sales milestones which could reach up to \$14.925 million if we achieve all milestones for MNPR-101. The agreement does not require the payment of sales royalties. There can be no assurance that we will achieve any milestones. As of March 10, 2023, we had not reached any milestones and had not been required to pay XOMA Ltd. any funds under this license agreement.

Service Providers

In the normal course of business, we contract with service providers to assist in the performance of R&D, including drug product manufacturing, process development, clinical and preclinical development, and G&A including financial strategy, audit, tax and legal support. We can elect to discontinue the work under these agreements at any time. We could also enter into collaborative research and development, contract research, manufacturing and supplier agreements in the future, which may require upfront payments and/or long-term commitments of cash.

Office Lease

We are currently leasing office space for our executive headquarters at 1000 Skokie Blvd., in the Village of Wilmette, Illinois for \$4,238 per month through February 2024, and we anticipate that we will lease additional space in the future as we hire additional personnel.

Legal Contingencies

We are currently not, and to date have never been, a party to any adverse material legal proceedings.

Indemnification

In the normal course of business, we enter into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. Our exposure under these agreements is unknown because it involves claims that may be made against us in the future, but that have not yet been made. To date, we have not paid any claims or been required to defend any action related to our indemnification obligations. However, we may record charges in the future as a result of these indemnification obligations.

In accordance with our Second Amended and Restated Certificate of Incorporation, Amended and Restated Bylaws and the indemnification agreements entered into with each officer and non-employee director, we have indemnification obligations to our officers and non-employee directors for certain events or occurrences, subject to certain limits, while they are serving at our request in such capacity. There have been no claims to date. See Item 1A - "Risk Factors - We have limited the liability of and indemnified our directors and officers."

Item 8. Financial Statements and Supplementary Data

The information required to be filed in this item appears on pages F-1 to F-25 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Our Chief Executive Officer and Chief Financial Officer have provided certifications filed as Exhibits 31.1 and 32.1, and 31.2, respectively. Such certifications should be read in conjunction with the information contained in this Item 9A for a more complete understanding of the matters covered by those certifications.

(a) 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 defined in Rule 13a15(f) of the Securities Exchange Act of 1934 (the "Exchange Act"). Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of the financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. This process includes those policies and procedures (i) that pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets, (ii) that receipts and expenditures are being made only in accordance with authorizations of our management and non-employee directors, (iii) that provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on our financial statements, and (iv) that provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the internal control over financial reporting to future periods are subject to risk that the internal control may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. Management based this assessment on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control – Integrated Framework (2013). Management's assessment included an evaluation of the design of our internal control over financial reporting and testing of the operational effectiveness of our internal control over financial reporting. Based on management's assessment, management has concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

(b) Disclosure Controls and Procedures

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures as of December 31, 2022, pursuant to Rules 13a15(e) and 15d15(e) under the Exchange Act. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures, as of such date, were effective.

(c) Changes in Internal Control over Financial Reporting

We have concluded that the consolidated financial statements and other financial information included in this Annual Report on Form 10-K fairly present in all material respects our financial condition, results of operations and comprehensive loss and cash flows as of, and for, the periods presented.

There have been no changes in our internal control over financial reporting during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On March 20, 2023, our Board of Directors (“Board”) increased the size of our Board from five to six members. Simultaneously, upon recommendation from our Corporate Governance & Nominating Committee, our Board appointed Kim R. Tsuchimoto to serve on our Board until our next annual meeting of stockholders. Ms. Tsuchimoto is our Chief Financial Officer and brings over 25 years of experience in the biopharma industry.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item regarding our directors, executive officers and corporate governance is incorporated into this section by reference to the sections captioned “Election of Directors” and “Executive Officers” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

Item 11. Executive Compensation

The information required by this Item regarding executive compensation is incorporated into this section by reference to the section captioned “Executive Compensation” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item regarding security ownership of our beneficial owners, management and related stockholder matters is incorporated into this section by reference to the section captioned “Security Ownership of Certain Beneficial Owners and Management” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

The information required by this Item regarding the securities authorized for issuance under our equity compensation plans is incorporated into this section by reference to the section captioned “Equity Compensation Plan Information” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this Item regarding certain relationships, related transactions and director independence is incorporated into this section by reference to the sections captioned “Transactions with Related Persons, Promoters and Certain Control Persons,” “Review, Approval and Ratification of Transactions with Related Parties” and “Director Independence” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

Item 14. Principal Accounting Fees and Services

The information required by this Item regarding our principal accountant fees and services is incorporated into this section by reference to the section captioned “Independent Registered Public Accounting Firm” in the proxy statement for our 2023 annual meeting of stockholders, which will be filed with the SEC pursuant to Regulation 14A not later than 120 days after December 31, 2022.

PART IV

Item 15. Exhibits, Financial Statement Schedule

1. Financial Statements

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2. Financial Statements Schedules

Other financial statements schedules are not included because they are not required, or the information is otherwise shown in the Consolidated Financial Statements or notes thereto.

(b) Exhibits

The following exhibits are filed as part of this Annual Report on Form 10-K.

Exhibit	Document	Incorporated by Reference From:
3.1	Second Amended and Restated Certificate of Incorporation	Form 10-K filed on March 26, 2018
3.2	Amended and Restated Bylaws	Form 10-Q filed on May 12, 2022
4.1	Description of Registered Securities	Filed herewith as Exhibit 4.1
10.1*	License Agreement with XOMA Ltd.	Form 10-K filed on March 26, 2018
10.2*	Option and License Agreement with Onxeo S.A.	Form 10-K filed on March 26, 2018
10.3*	Contribution Agreement (351) – Containing Registration Rights with TacticGem	Form 10-K filed on March 26, 2018
10.4	2016 Stock Incentive Plan, as amended	Form DEF14A filed on April 29, 2022
10.5	Form of Incentive Stock Option Agreement	Form 10-K filed on March 24, 2022
10.6	Form of Non-qualified Stock Option Agreement	Form 10-K filed on March 24, 2022
10.7	Form of Restricted Stock Unit Grant Notice	Form 10-K filed on March 24, 2022
10.8	Employment Agreement of Chandler D. Robinson – effective November 1, 2017	Form 10-K filed on March 26, 2018
10.9	Employment Agreement of Kim R. Tsuchimoto – effective November 1, 2017	Form 10-K filed on March 26, 2018
10.10	Amendment One to Employment Agreement of Kim R. Tsuchimoto – effective March 1, 2018	Form 10-K filed on March 26, 2018
10.11	Consulting Agreement of pRx Consulting (Patrice Rioux) – effective January 1, 2021	Form 10-K filed on March 24, 2022
10.12	Consulting Agreement of pRx Consulting (Patrice Rioux) – effective October 1, 2021	Form 10-K filed on March 24, 2022
10.13	Amendment No 1 to Consulting Agreement of pRx Consulting (Patrice Rioux) – effective October 1, 2021	Form 10-K filed on March 24, 2022
10.14	Consulting Agreement of pRx Consulting (Patrice Rioux) – effective January 1, 2022	Filed herewith as Exhibit 10.2
10.15	Consulting Agreement of Christopher M. Starr – effective January 1, 2022	Form 10-K filed on March 24, 2022
10.16	Capital on Demand TM Sales Agreement with JonesTrading Institutional Services, LLC	Form 8-K filed on April 20, 2022
21.1	Subsidiaries of Monopar Therapeutics Inc. as of December 31, 2022	Filed herewith as Exhibit 21.1
23.1	Consent of Independent Registered Public Accounting Firm	Filed herewith as Exhibit 23.1
24.1	Power of Attorney (included in the signature page hereto)	
31.1	Certification of Chandler D. Robinson, Chief Executive Officer	Filed herewith as Exhibit 31.1
31.2	Certification of Kim R. Tsuchimoto, Chief Financial Officer	Filed herewith as Exhibit 31.2
32.1	Certification of Chandler D. Robinson, Chief Executive Officer and Kim R. Tsuchimoto, Chief Financial Officer	Filed herewith as Exhibit 32.1
101.INS	Inline XBRL Taxonomy Extension Schema	
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)	

Confidential Information has been omitted and filed separately with the SEC on exhibits marked with (*). Confidential treatment has been approved with respect to the omitted information, pursuant to an Order dated January 8, 2018.

SIGNATURES

Pursuant to the requirements of 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, thereunto duly authorized.

MONOPAR THERAPEUTICS INC

Dated: March 23, 2023

By: /s/ Kim R. Tsuchimoto

Name: Kim Tsuchimoto
Title: Chief Financial Officer
(Principal Financial Officer)

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Chandler D. Robinson and Kim R. Tsuchimoto, his attorney-in-fact, with the power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

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

<u>Signatures</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Chandler D. Robinson</u> Chandler Robinson	Chief Executive Officer and Director (Principal Executive Officer)	March 23, 2023
<u>/s/ Kim R. Tsuchimoto</u> Kim Tsuchimoto	Chief Financial Officer and Director (Principal Financial Officer and Principal Accounting Officer)	March 23, 2023
<u>/s/ Christopher M. Starr</u> Christopher Starr	Executive Chairman of the Board and Director	March 23, 2023
<u>/s/ Raymond W. Anderson</u> Raymond W. Anderson	Director	March 23, 2023
<u>/s/ Michael J. Brown</u> Michael Brown	Director	March 23, 2023
<u>/s/ Arthur J. Klausner</u> Arthur Klausner	Director	March 23, 2023

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of Monopar Therapeutics Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Monopar Therapeutics Inc. and its subsidiaries (the “Company”) as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive loss, stockholders’ equity and cash flows, for each of the two years in the period ended December 31, 2022, 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 financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

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 Company 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 its 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.

/s/ BPM LLP

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

Walnut Creek, California
March 22, 2023

Monopar Therapeutics Inc.

Consolidated Balance Sheets

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 8,186,194	\$ 20,303,869
Investments	4,933,550	-
Other current assets	45,982	217,745
Total current assets	13,165,726	20,521,614
Operating lease right-of-use asset	61,228	-
Total assets	\$ 13,226,954	\$ 20,521,614
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable, accrued expenses and other current liabilities	\$ 3,128,894	\$ 1,580,543
Total current liabilities	3,128,894	1,580,543
Non- current operating lease liability	8,408	-
Total liabilities	3,137,302	1,580,543
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Common stock, par value of \$0.001 per share, 40,000,000 shares authorized, 12,946,573 and 12,598,125 shares issued and outstanding at December 31, 2022, and December 31, 2021, respectively	12,947	12,598
Additional paid-in capital	61,871,784	60,220,016
Accumulated other comprehensive income (loss)	8,942	(3,160)
Accumulated deficit	(51,804,021)	(41,288,383)
Total stockholders' equity	10,089,652	18,941,071
Total liabilities and stockholders' equity	\$ 13,226,954	\$ 20,521,614

The accompanying notes are an integral part of these consolidated financial statements.

Monopar Therapeutics Inc.

Consolidated Statements of Operations and Comprehensive Loss

	For the Years Ended December 31,	
	2022	2021
Operating expenses:		
Research and development	\$ 7,591,601	\$ 6,493,208
General and administrative	2,945,276	2,634,040
Total operating expenses	<u>10,536,877</u>	<u>9,127,248</u>
Loss from operations	(10,536,877)	(9,127,248)
Interest income	21,239	24,024
Net loss	<u>(10,515,638)</u>	<u>(9,103,224)</u>
Other comprehensive income:		
Foreign currency translation gain/(loss)	(2,937)	4,713
Unrealized gain on investments	15,039	-
Comprehensive loss	<u>\$(10,503,536)</u>	<u>\$(9,098,511)</u>
Net loss per share:		
Basic and diluted	<u>\$ (0.83)</u>	<u>\$ (0.73)</u>
Weighted average shares outstanding:		
Basic and diluted	<u>12,718,166</u>	<u>12,471,217</u>

The accompanying notes are an integral part of these consolidated financial statements.

Monopar Therapeutics Inc.
Consolidated Statements of Stockholders' Equity
Years Ended December 31, 2022 and 2021

	<u>Common Stock</u>		<u>Additional Paid-in Capital</u>	<u>Accumulated Other Comprehensive Income (Loss)</u>	<u>Accumulated Deficit</u>	<u>Total Stockholders' Equity</u>
	<u>Shares</u>	<u>Amount</u>				
Balance at January 1, 2021	11,453,465	\$ 11,453	\$47,873,570	\$ (7,873)	\$ (32,185,159)	\$ 15,691,991
Issuance of common stock under a Capital on Demand™ Sales Agreement with JonesTrading Institutional Services LLC, net of commissions and fees of \$338,153.....	1,104,047	1,104	10,924,208	—	—	10,925,312
Issuance of common stock to non-employee directors pursuant to vested restricted stock units.....	12,020	12	(12)	—	—	—
Issuance of common stock to employees pursuant to vested restricted stock units, net of taxes	25,680	26	(63,279)	—	—	(63,253)
Issuance of common stock upon exercise of stock options.....	2,913	3	17,475	—	—	17,478
Stock-based compensation (non-cash).....	—	—	1,468,054	—	—	1,468,054
Net loss.....	—	—	—	—	(9,103,224)	(9,103,224)
Other comprehensive income.....	—	—	—	4,713	—	4,713
Balance at December 31, 2021	12,598,125	12,598	60,220,016	(3,160)	(41,288,383)	18,941,071
Issuance of common stock under a Capital on Demand™ Sales Agreement with JonesTrading Institutional Services LLC, net of commissions, fees and expenses of \$87,611	64,573	65	87,253	—	—	87,318
Issuance of common stock to non-employee directors pursuant to vested restricted stock units.....	45,744	45	(45)	—	—	—
Issuance of common stock to employees pursuant to vested restricted stock units, net of taxes	70,131	70	(76,703)	—	—	(76,633)
Issuance of common stock upon exercise of stock options.....	168,000	169	—	—	—	169
Stock-based compensation (non-cash).....	—	—	1,641,263	—	—	1,641,263
Net loss.....	—	—	—	—	(10,515,638)	(10,515,638)
Other comprehensive income.....	—	—	—	12,102	—	12,102
Balance at December 31, 2022	<u>12,946,573</u>	<u>\$ 12,947</u>	<u>\$61,871,784</u>	<u>\$ 8,942</u>	<u>\$ (51,804,021)</u>	<u>\$ 10,089,652</u>

The accompanying notes are an integral part of these consolidated financial statements.

Monopar Therapeutics Inc.

Consolidated Statements of Cash Flows

	For the Years	
	Ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss.....	\$(10,515,638)	\$(9,103,224)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense (non-cash).....	1,641,263	1,468,054
Changes in operating assets and liabilities, net		
Other current assets.....	171,755	(86,198)
Accounts payable, accrued expenses and other current liabilities.....	1,478,299	403,967
Operating lease right-of-use assets and liabilities, net.....	(4,238)	-
Net cash used in operating activities.....	<u>(7,228,559)</u>	<u>(7,317,401)</u>
Cash flows from investing activities:		
Purchase of investments	(4,918,511)	-
Net cash used in investing activities.....	<u>(4,918,511)</u>	<u>-</u>
Cash flows from financing activities:		
Cash proceeds from the sales of common stock under a Capital on Demand™ Sales Agreement.....	109,337	10,925,312
Taxes paid related to net share settlement of vested restricted stock units.....	(76,633)	(63,253)
Cash proceeds from the issuance of stock upon exercise of stock options.....	169	17,478
Net cash provided by financing activities.....	<u>32,873</u>	<u>10,879,537</u>
Effect of exchange rates.....	(3,478)	4,624
Net increase (decrease) in cash and cash equivalents.....	(12,117,675)	3,566,760
Cash and cash equivalents at beginning of period	<u>20,303,869</u>	<u>16,737,109</u>
Cash and cash equivalents at end of period.....	<u>\$ 8,186,194</u>	<u>\$20,303,869</u>

The accompanying notes are an integral part of these consolidated financial statements.

MONOPAR THERAPEUTICS INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2022

Note 1 - Nature of Business and Liquidity

Nature of Business

Monopar Therapeutics Inc. (“Monopar” or the “Company”) is a clinical-stage biopharmaceutical company focused on developing proprietary therapeutics designed to extend life or improve quality of life for cancer patients. Monopar currently has four compounds in development: 1) Validive® (clonidine hydrochloride mucobuccal tablet; clonidine HCl MBT), a Phase 2b/3 clinical stage, first-in-class mucoadhesive buccal tablet for the prevention of radiation induced severe oral mucositis (“SOM”) in oropharyngeal cancer patients; 2) camsirubicin (generic name for MNPR-201, GPX-150; 5-imino-13-deoxydoxorubicin), a Phase 1b clinical stage novel analog of doxorubicin engineered specifically to retain anticancer activity while minimizing toxic effects on the heart; 3) MNPR-101 RIT and MNPR-101-Zr, a preclinical stage uPAR-targeted antibody being developed as a radioimmunotherapeutic and companion diagnostic for advanced cancers; and 4) an early stage camsirubicin analog, MNPR-202, for various cancers.

Liquidity

The Company has incurred an accumulated deficit of approximately \$51.8 million as of December 31, 2022. To date, the Company has primarily funded its operations with the net proceeds from the Company’s initial public offering of its common stock on Nasdaq, sales of its common stock in the public market through at-the-market sales agreements, private placements of convertible preferred stock and of common stock and cash provided in the camsirubicin asset purchase transaction. Management estimates that currently available cash will provide sufficient funds to enable the Company to meet its obligations at least through March 2024. The Company’s ability to fund its future operations, including the continued clinical development of Validive and camsirubicin, is dependent upon its ability to execute its business strategy, to obtain additional funding and/or to execute collaborative research agreements. There can be no certainty that future financing or collaborative research agreements will occur in the amounts required or at a time needed to maintain operations, if at all.

The coronavirus disease (“COVID-19”) continues to affect economies and business around the world. In response to COVID-19 and its effects on clinical trials, in 2020 Monopar modified the original adaptive design Phase 3 clinical trial for its lead product candidate, Validive, to be a Phase 2b/3 clinical trial (“VOICE”) to better fit the types of trials which can enroll sufficient required patients in the current environment. This modification allowed the Company to activate the VOICE clinical trial without requiring near-term financing. To complete the VOICE clinical program, including, if required, completing a second Phase 3 confirmatory clinical trial, Monopar will require additional funding in the millions or tens of millions of dollars (depending on if the Company has consummated a collaboration or partnership or neither for Validive), which it is planning to pursue within the next 12 months. Due to many uncertainties, the Company is unable to estimate COVID-19’s financial impact or duration in light of global vaccine rollouts, treatment options and potential surges of new cases from current or future COVID-19 variants or its potential impact on the Company’s current clinical trials, including COVID-19’s effect on drug candidate manufacturing, shipping, patient recruitment at clinical sites and regulatory agencies around the globe.

The Russia-Ukraine war, and resulting sanctions against Russia and Russian entities or allies, have increased fuel costs and may cause shipping delays. The broader economic, trade and financial market consequences are uncertain at this time, which may increase the cost of supplies for the Company’s clinical materials, may delay the manufacture of its clinical materials, may increase costs of other goods and services, or make it more difficult or costly to raise additional financing, any of which could cause an adverse effect on the Company’s clinical programs and on the Company’s financial condition.

Market variables, such as inflation of product costs, higher capital costs, labor rates and fuel, freight and energy costs, as well as geopolitical events could likely cause the Company to suffer significant increases in its operating and administrative expenses.

MONOPAR THERAPEUTICS INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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Note 2 - Significant Accounting Policies

Basis of Presentation

These consolidated financial statements include the financial results of Monopar Therapeutics Inc., its wholly-owned French subsidiary, Monopar Therapeutics, SARL, and its wholly-owned Australian subsidiary, Monopar Therapeutics Australia Pty Ltd and have been prepared in accordance with accounting principles generally accepted in the U.S. (“GAAP”) and include all disclosures required by GAAP for financial reporting. All intercompany accounts have been eliminated. The principal accounting policies applied in the preparation of these consolidated financial statements are set out below and have been consistently applied in all periods presented. The Company has been primarily involved in performing research activities, developing product candidates, and raising capital to support and expand these activities.

The accompanying consolidated financial statements contain all normal, recurring adjustments necessary to present fairly the Company’s consolidated financial position as of December 31, 2022 and 2021, the Company’s consolidated results of operations and comprehensive loss and the Company’s consolidated cash flows for the years ended December 31, 2022 and 2021.

Functional Currency

The Company’s consolidated functional currency is the U.S. Dollar. The Company’s Australian subsidiary and French subsidiary use the Australian Dollar and European Euro, respectively, as their functional currency. At each quarter-end, each foreign subsidiary’s balance sheets are translated into U.S. Dollars based upon the quarter-end exchange rate, while their statements of operations and comprehensive loss and statements of cash flows are translated into U.S. Dollars based upon an average exchange rate during the period.

Comprehensive Loss

Comprehensive loss represents net loss plus any income or losses not reported in the consolidated statements of operations and comprehensive loss, such as foreign currency translations gains and losses and unrealized gains and losses on debt security investments that are reflected on the Company’s consolidated statements of stockholders’ equity.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities, and reported amounts of expenses in the consolidated financial statements and accompanying notes. Actual results could differ from those estimates.

Going Concern Assessment

The Company applies Accounting Standards Codification 205-40 (“ASC 205-40”), *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern*, which the Financial Accounting Standards Board (“FASB”) issued to provide guidance on determining when and how reporting companies must disclose going concern uncertainties in their financial statements. ASC 205-40 requires management to perform interim and annual assessments of an entity’s ability to continue as a going concern within one year of the date of issuance of the entity’s financial statements (or within one year after the date on which the financial statements are available to be issued, when applicable). Further, a company must provide certain disclosures if there is “substantial doubt about the entity’s ability to continue as a going concern.” In February 2023, the Company analyzed its cash requirements at least through March 2024 and has determined that, based upon the Company’s current available cash, the Company has no substantial doubt about its ability to continue as a going concern.

Cash Equivalents

The Company considers all highly liquid investments purchased with a maturity of 90 days or less on the date of purchase to be cash equivalents. Cash equivalents as of December 31, 2022 consisted of two money market accounts and U.S. Treasury Bills. Cash equivalents as of December 31, 2021 consisted of one money market account.

MONOPAR THERAPEUTICS INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2022

Investments

The Company considers all of its investments in debt securities (U.S. Government or Agencies), with maturities at the date of purchase from three months to one year to be available-for-sale securities. These investments are recorded at fair value with the unrealized gains and losses reflected in accumulated other comprehensive income (loss) on the Company's consolidated balance sheets. Realized gains and losses from the sale of investments, if any, are determined and recorded net in the consolidated statements of operations and comprehensive loss. The investments selected by the Company have a low level of inherent credit risk given they are issued by the U.S. government and any changes in their fair value are primarily attributable to changes in interest rates and market liquidity. Investments as of December 31, 2022 consisted of U.S. Treasury Bills with maturities of 91 days to one year. There were no investments as of December 31, 2021.

Prepaid Expenses

Prepayments are expenditures for goods or services before the goods are used or the services are received and are charged to operations as the benefits are realized. Prepaid expenses may include payments to development collaborators in excess of actual expenses incurred by the collaborator, measured at the end of each reporting period. Prepayments also include insurance premiums, dues and subscriptions and software costs of \$10,000 or more per year that are expensed monthly over the life of the contract, which is typically one year. Prepaid expenses are reflected on the Company's consolidated balance sheets as other current assets.

Leases

Lease agreements are evaluated to determine whether an arrangement is or contains a lease in accordance with ASC 842, *Leases*. Right-of-use lease assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use lease asset on the Company's consolidated balance sheets includes any lease payments made and excludes lease incentives. The incremental borrowing rate is determined by taking into consideration the Company's credit quality and borrowing rate for similar assets is used in determining the present value of future payments. Lease expense is recorded as general and administrative expenses on the Company's consolidated statements of operations and comprehensive loss. ASC 842 was adopted by the Company on January 1, 2019. See Note 8 for discussion of operating leases.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents. The Company maintains cash and cash equivalents at two reputable financial institutions. As of December 31, 2022, the balance at one financial institution was in excess of the \$250,000 Federal Deposit Insurance Corporation ("FDIC") insurable limit. The Company has not experienced any losses on its deposits since inception and management believes the Company is not exposed to significant risks with respect to these financial institutions.

Fair Value of Financial Instruments

For financial instruments consisting of cash and cash equivalents, investments, accounts payable, accrued expenses, and other current liabilities, the carrying amounts are reasonable estimates of fair value due to their relatively short maturities.

The Company adopted ASC 820, *Fair Value Measurements and Disclosures*, as amended, which addresses the measurement of the fair value of financial assets and financial liabilities. Under this standard, fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (i.e., the "exit price") in an orderly transaction between market participants at the measurement date.

The standard establishes a hierarchy for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs reflect assumptions market participants would use in pricing an asset or liability based on market data obtained from independent sources. Unobservable inputs reflect a reporting entity's pricing an asset or liability developed based on the best information available under the circumstances. The fair value hierarchy consists of the following three levels:

Level 1 – instrument valuations are obtained from real-time quotes for transactions in active exchange markets involving identical assets.

Level 2 – instrument valuations are obtained from readily available pricing sources for comparable instruments.

Level 3 – instrument valuations are obtained without observable market values and require a high-level of judgment to determine the fair value.

MONOPAR THERAPEUTICS INC.

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Determining which category an asset or liability falls within the hierarchy requires significant judgment. The Company evaluates its hierarchy disclosures each reporting period. There were no transfers between Level 1, 2 or 3 of the fair value hierarchy during the years ended December 31, 2022, and 2021. The following table presents the assets and liabilities recorded that are reported at fair value on our consolidated balance sheets on a recurring basis. No values were recorded in Level 2 or Level 3 at December 31, 2022, and 2021.

Assets and Liabilities Measured at Fair Value on a Recurring Basis

December 31 2022	Level 1	Total
Assets:		
Cash equivalents ⁽¹⁾	\$ 7,248,946	\$ 7,248,946
Investments ⁽²⁾	<u>4,933,550</u>	<u>4,933,550</u>
Total	<u>\$12,182,496</u>	<u>\$12,182,496</u>
December 31 2021		
Assets:		
Cash equivalents ⁽¹⁾	\$20,014,205	\$20,014,205
Total	<u>\$20,014,205</u>	<u>\$20,014,205</u>

- (1) Cash equivalents as of December 31, 2022 represent the fair value of the Company's investment in two money market accounts and U.S. Treasury Bills with maturities at the date of purchase of less than 90 days. On December 31, 2021 cash equivalents represented the fair value of the Company's investment in a money market account.
- (2) Investments represents the fair value of the Company's investment in U.S. Treasury Bills with maturities at the date of purchase from 90 days to one year.

Net Loss per Share

Net loss per share for the years ended December 31, 2022, and 2021, is calculated by dividing net loss by the weighted-average shares of common stock outstanding during the period. Diluted net loss per share for the years ended December 31, 2022, and 2021 is calculated by dividing net loss by the weighted-average shares of the sum of a) weighted average common stock outstanding (12,718,166 and 12,472,217 shares for the years ended December 31, 2022, and 2021, respectively) and b) potentially dilutive shares of common stock (such as stock options and restricted stock units) outstanding during the period. As of December 31, 2022, and 2021, potentially dilutive securities included stock-based awards to purchase up to 1,915,600 and 1,655,451 shares of the Company's common stock, respectively. For the years ended December 31, 2022, and 2021, potentially dilutive securities are excluded from the computation of fully diluted net loss per share as their effect is anti-dilutive.

Research and Development Expenses

Research and development ("R&D") costs are expensed as incurred. Major components of R&D expenses include salaries and benefits paid to the Company's R&D staff, compensation expenses of G&A personnel performing R&D, fees paid to consultants and to the entities that conduct certain R&D activities on the Company's behalf and materials and supplies which were used in R&D activities during the reporting period.

Clinical Trials Accruals

The Company accrues and expenses the costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with contract research organizations, service providers, and clinical trial sites. The Company estimates the amounts to accrue based upon discussions with internal clinical personnel and external service providers as to progress or stage of completion of trials or services and the agreed upon fee to be paid for such services. Costs of setting up clinical trial sites for participation in the trials are expensed immediately as R&D expenses. Clinical trial site costs related to patient screening and enrollment are accrued as patients are screened/entered into the trial.

Collaborative Agreements

The Company and its collaborative partners are active participants in collaborative agreements and all parties would be exposed to significant risks and rewards depending on the technical and commercial success of the activities. Contractual payments to the other parties in collaboration agreements and costs incurred by the Company when the Company is deemed to be the principal participant for a given transaction are recognized on a gross basis in R&D expenses. Royalties and license payments are recorded as earned.

During the years ended December 31, 2022, and 2021, no milestones were met, and no royalties were earned, therefore, the Company did not pay or accrue/expense any license or royalty payments.

MONOPAR THERAPEUTICS INC.

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Licensing Agreements

The Company has various agreements licensing technology utilized in the development of its product or technology programs. The licenses contain success milestone obligations and royalties on future sales. During the years ended December 31, 2022, and 2021, no milestones were met, and no royalties were earned, therefore, the Company did not pay or accrue/expense any license or royalty payments under any of its license agreements.

Patent Costs

The Company expenses costs relating to issued patents and patent applications, including costs relating to legal, renewal and application fees, as a component of general and administrative expenses in its consolidated statements of operations and comprehensive loss.

Income Taxes

The Company uses an asset and liability approach for accounting for deferred income taxes, which requires recognition of deferred income tax assets and liabilities for the expected future tax consequences of events that have been recognized in its financial statements but have not been reflected in its taxable income. Estimates and judgments are required in the calculation of certain tax liabilities and in the determination of the recoverability of certain deferred income tax assets, which arise from temporary differences and carryforwards. Deferred income tax assets and liabilities are measured using the currently enacted tax rates that apply to taxable income in effect for the years in which those tax assets and liabilities are expected to be realized or settled.

The Company regularly assesses the likelihood that its deferred income tax assets will be realized from recoverable income taxes or recovered from future taxable income. To the extent that the Company believes any amounts are not “more likely than not” to be realized, the Company records a valuation allowance to reduce the deferred income tax assets. In the event the Company determines that all or part of the net deferred tax assets are not realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period such determination is made. Similarly, if the Company subsequently determines deferred income tax assets that were previously determined to be unrealizable are now realizable, the respective valuation allowance would be reversed, resulting in an adjustment to earnings in the period such determination is made.

Internal Revenue Code Sections 382 and 383 (“Sections 382 and 383”) limit the use of net operating loss (“NOL”) carryforwards and R&D credits, after an ownership change. To date, the Company has not conducted a Section 382 or 383 study, however, because the Company will continue to raise significant amounts of equity in the coming years, the Company expects that Sections 382 and 383 will limit the Company’s usage of NOLs and R&D credits in the future.

ASC 740, *Income Taxes*, requires that the tax benefit of net operating losses, temporary differences, and credit carryforwards be recorded as an asset to the extent that management assesses that realization is “more likely than not.” Realization of the future tax benefits is dependent on the Company’s ability to generate sufficient taxable income within the carryforward period. The Company has reviewed the positive and negative evidence relating to the realizability of the deferred tax assets and has concluded that the deferred tax assets are not “more likely than not” to be realized. As a result, the Company recorded a full valuation allowance as of December 31, 2022, and 2021. U.S. Federal R&D tax credits from 2016 to 2019 were utilized to reduce payroll taxes in future periods and were recorded as other current assets (anticipated to be received within 12 months), on the Company’s consolidated balance sheets. The Company intends to maintain the valuation allowance until sufficient evidence exists to support its reversal. The Company regularly reviews its tax positions. For a tax benefit to be recognized, the related tax position must be “more likely than not” to be sustained upon examination. Any amount recognized is generally the largest benefit that is “more likely than not” to be realized upon settlement. The Company’s policy is to recognize interest and penalties related to income tax matters as an income tax expense. For the years ended December 31, 2022, and 2021, the Company did not have any interest or penalties associated with unrecognized tax benefits.

The Company is subject to U.S. Federal, Illinois and California state income taxes. In addition, the Company is subject to local tax laws of France and Australia. Tax regulations within each jurisdiction are subject to the interpretation of the related tax laws and regulations and require significant judgment to apply. Monopar was originally formed as an LLC in December 2014, then incorporated on December 16, 2015. The Company is subject to U.S. Federal, state and local tax examinations by tax authorities for the tax years 2015 through 2021. The Company does not anticipate significant changes to its current uncertain tax positions through December 31, 2022. The Company plans on filing its U.S. Federal and state tax returns for the year ended December 31, 2022, prior to the extended filing deadlines in all jurisdictions.

MONOPAR THERAPEUTICS INC.

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Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees, non-employee directors and consultants using a fair value method, which requires the recognition of compensation expense for costs related to all stock-based awards, including stock option and restricted stock unit (“RSU”) grants. The fair value method requires the Company to estimate the fair value of stock-based payment awards on the date of grant using an option pricing model or the closing stock price on the date of grant in the case of RSUs.

Stock-based compensation expense for awards granted to employees, non-employee directors and consultants are based on the fair value of the underlying instrument calculated using the Black-Scholes option-pricing model on the date of grant for stock options and using the closing stock price on the date of grant for RSUs and recognized as expense on a straight-line basis over the requisite service period, which is the vesting period. Determining the appropriate fair value model and related assumptions requires judgment, including estimating the future stock price volatility and expected terms. The expected volatility rates are estimated based on the Company’s historical actual volatility over the two-year period from its initial public offering on December 18, 2019 through December 31, 2021. Forfeitures only include known forfeitures to-date as the Company accounts for forfeitures as they occur due to a limited history of forfeitures. The expected term for options granted to date is estimated using the simplified method. The Company has not paid dividends and does not anticipate paying a cash dividend in the future vesting period and, accordingly, uses an expected dividend yield of zero. The risk-free interest rate is based on the rate of U.S. Treasury securities with maturities consistent with the estimated expected term of the awards.

Note 3 - Investments

As of December 31, 2022 the Company had two money market accounts and available-for-sale investments with contractual maturities of one year or less as follows:

As of December 31, 2022	Cost Basis	Unrealized Gains	Aggregate Fair Value
U.S. Treasury Bills.....	\$ 6,905,171	\$ 15,039	\$ 6,920,210
Money Market Funds	5,262,286	-	5,262,286
Total.....	<u>\$12,167,457</u>	<u>\$ 15,039</u>	<u>\$12,182,496</u>

As of December 31, 2022, there were no available-for-sale securities in an unrealized-loss position and there were no sales of available-for-sale securities made during 2022. U.S. Treasury Bills classified as Investments on the consolidated balance sheet as of December 31, 2022 were \$4.9 million.

See Note 2 for additional discussion regarding the Company’s fair value measurements.

Note 4 - Capital Stock

Holders of the common stock are entitled to receive such dividends as may be declared by the Board of Directors out of funds legally available therefor. To date no dividends have been declared. Upon dissolution and liquidation of the Company, holders of the common stock are entitled to a ratable share of the net assets of the Company remaining after payments to creditors of the Company. The holders of shares of common stock are entitled to one vote per share for the election of each director nominated to the Board and one vote per share on all other matters submitted to a vote of stockholders.

The Company’s amended and restated certificate of incorporation authorizes the Company to issue 40,000,000 shares of common stock with a par value of \$0.001 per share.

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Sales of Common Stock

On January 13, 2020, the Company entered into a Capital on Demand™ Sales Agreement with JonesTrading Institutional Services LLC (“JonesTrading”), as sales agent, pursuant to which Monopar could offer and sell (at its discretion), from time to time, through or to JonesTrading shares of Monopar’s common stock, having an aggregate offering price of up to \$19.7 million. Pursuant to this agreement, during the year ended December 31, 2021, the Company sold 1,104,047 shares of its common stock at an average gross price per share of \$10.20 for net proceeds of \$10,925,312 after fees and commissions of \$338,153. In aggregate pursuant to this agreement, the Company sold 1,964,724 shares of its common stock at an average gross price per share of \$10.02 for net proceeds of \$19,100,603, after fees and commissions of \$591,188. During the year ended December 31, 2022, the Company did not sell any shares of common stock under this agreement as the maximum aggregate offering price was reached during the first quarter of 2021.

On April 20, 2022, the Company executed a new Capital on Demand™ Sales Agreement with JonesTrading, pursuant to which Monopar may offer and sell, from time to time, through or to JonesTrading, as sales agent or principal, shares of Monopar’s common stock. On April 20, 2022, the Company filed a prospectus supplement with the U.S. Securities and Exchange Commission relating to the offer and sale of its common stock from time to time pursuant to the agreement up to an aggregate amount of \$4,870,000. In addition, the Company filed a Form S-3 and prospectus to increase the aggregate amount under this agreement to \$6,680,571 less \$174,929 sold within 12 months of the filing. The Form S-3 and prospectus were declared effective by the Securities and Exchange Commission on January 4, 2023. Expenses related to these financing activities were recorded as offering costs (a reduction of additional paid in capital) on the Company’s consolidated statement of stockholders’ equity for the period. During the year ended December 31, 2022, the Company sold 64,573 shares of its common stock at an average gross price per share of \$2.71 for net proceeds of \$170,552, after fees and commissions of \$4,377. In addition, the Company incurred legal, accounting and other fees totaling \$83,234 for net proceeds after fees, commissions and expenses of \$87,318.

As of December 31, 2022, the Company had 12,946,573 shares of common stock issued and outstanding.

Note 5 - Stock Incentive Plan

In April 2016, the Company’s Board of Directors and stockholders representing a majority of the Company’s outstanding stock at that time, approved the Monopar Therapeutics Inc. 2016 Stock Incentive Plan, as amended (the “Plan”), allowing the Company to grant up to an aggregate 700,000 shares of stock-based awards in the form of stock options, restricted stock units, stock appreciation rights and other stock-based awards to employees, non-employee directors and consultants. In October 2017, the Company’s Board of Directors voted to increase the stock award pool to 1,600,000 shares of common stock, which subsequently was approved by the Company’s stockholders. In April 2020, the Company’s Board of Directors voted to increase the stock award pool to 3,100,000 (an increase of 1,500,000 shares of common stock), which was approved by the Company’s stockholders in June 2020. In April 2021, the Company’s Board of Directors voted to approve an amendment to the 2016 Stock Incentive Plan to remove certain individual award limits and other provisions related to I.R.C. Section 162(m) and to update the limit on Incentive Stock Options to no more than 100% of the maximum aggregate number of shares which may be granted under the plan, which was approved by the Company’s stockholders in June 2021. In March 2022, the Company’s Board of Directors voted to increase the stock award pool to 5,100,000 (an increase of 2,000,000 shares of common stock), which was approved by the Company’s stockholders in June 2022.

During the year ended December 31, 2022, the Company’s Plan Administrator Committee (with regards to non-officer employees and consultants) and the Company’s Compensation Committee, as ratified by the Board of Directors (in the case of executive officers and non-employee directors), granted to executive officers, non-officer employees, non-employee directors and consultants aggregate stock options for the purchase of 604,064 shares of the Company’s common stock with exercise prices ranging from \$1.59 to \$3.95 per share which vest over 1 to 4 years. All stock option grants have a 10-year term. In addition, during the year ended December 31, 2022, an aggregate 403,522 restricted stock units were granted to executive officers, non-officer employees and non-employee directors which vest over 1 to 4 years.

Under the Plan, the per share exercise price for the shares to be issued upon exercise of an option shall be determined by the Plan Administrator, except that the per share exercise price shall be no less than 100% of the fair market value per share on the grant date. Fair market value is the Company’s closing price on Nasdaq. Stock options generally expire after 10 years.

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Stock option activity under the Plan was as follows:

	Options Outstanding	
	Number of Shares Subject to Options	Weighted-Average Exercise Price
Balance at January 1, 2021	1,258,577	\$ 4.47
Granted.....	403,476	6.27
Forfeited.....	(115,151)	6.49
Exercised.....	(2,913)	6.00
Balance at December 31, 2021	1,543,989	4.78
Granted ⁽¹⁾	604,064	2.83
Forfeited ⁽²⁾	(337,103)	6.13
Exercised.....	(168,000)	0.001
Balance at December 31, 2022	1,642,950	4.28
Unvested options outstanding expected to vest ⁽³⁾	<u>461,524</u>	<u>4.00</u>

- (1) 604,064 options vest as follows: options to purchase 533,552 shares of the Company's common stock vest 6/48ths on the six-month anniversary of vesting commencement date and 1/48th per month thereafter; options to purchase 60,512 shares of the Company's common stock vest quarterly over one year; and options to purchase 10,000 shares of the Company's common stock vest monthly over one year. Exercise prices range from \$1.59 to \$3.95 per share.
- (2) Forfeited options represent unvested shares and vested, expired shares related to employee terminations.
- (3) Estimated forfeitures only include known forfeitures to-date as the Company typically accounts for forfeitures as they occur due to a limited history of forfeitures.

A summary of options outstanding as of December 31, 2022, is shown below:

Exercise Prices	Number of Shares Subject to Options Outstanding	Weighted-Average Remaining Contractual Term in Years	Number of Shares Subject to Fully Vested and Exercisable	Weighted-Average Remaining Contractual Term in Years
\$0.001-\$5.00	893,939	6.79	558,142	5.36
\$5.01-\$10.00	629,216	6.39	516,336	5.97
\$10.01-\$15.00	113,670	7.05	100,823	7.05
\$15.01-\$20.00	6,125	7.09	6,125	7.09
	<u>1,642,950</u>	6.65	<u>1,181,426</u>	5.78

Restricted stock unit activity under the Plan was as follows:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value per Unit
Unvested balance at December 31, 2020	40,066	\$ 12.93
Granted.....	124,374	6.81
Vested.....	(49,758)	8.04
Forfeited.....	(3,220)	7.52
Unvested balance at December 31, 2021	111,462	8.44
Granted.....	403,522	2.80
Vested.....	(149,706)	4.07
Forfeited.....	(92,628)	4.01
Unvested Balance at December 31, 2022	<u>272,650</u>	<u>4.00</u>

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During the years ended December 31, 2022, and 2021, the Company recognized \$818,164 and \$560,317 of employee, non-employee director and consultant stock-based compensation expense as general and administrative expenses, respectively, and \$823,099 and \$907,737 as research and development expenses, respectively. The stock-based compensation expense is allocated on a departmental basis, based on the classification of the stock-based award holder. No income tax benefits have been recognized in the consolidated statements of operations and comprehensive loss for stock-based compensation arrangements.

The fair value of options granted from inception to December 31, 2022, was based on the Black-Scholes option-pricing model assuming the following factors: 4.7 to 6.2 years expected term, 55% to 92% volatility, 0.4% to 4.4% risk free interest rate and zero dividends. The expected term for options granted to date was estimated using the simplified method.

Stock option grants and fair values under the Plan were as follows:

	Years Ended December 31,	
	2022	2021
Stock options granted.....	604,064	403,476
Weighted-average grant date fair value per share.....	\$ 2.13	\$ 4.46
Fair value of shares vested.....	\$ 970,451	\$ 1,152,572

At December 31, 2022, the aggregate intrinsic value of outstanding vested stock options was \$917,798 and of outstanding unvested stock options was \$2,690 and the weighted-average exercise price in aggregate was \$4.28 which includes \$4.39 for fully vested stock options and \$4.00 for stock options expected to vest. At December 31, 2022, unamortized balance of stock-based compensation was \$2.2 million, to be amortized over the following 2.6 years.

Note 6 - Related Party Transactions

As of December 31, 2022, Tactic Pharma, LLC (“Tactic Pharma”), the Company’s initial investor, beneficially owned 33% of Monopar’s common stock and during the year ended December 31, 2022, there were no transactions between Tactic Pharma and Monopar.

None of the related parties discussed in this paragraph received compensation other than market-based salary, market-based stock-based compensation and benefits and performance-based incentive bonus or in the case of non-employee directors, market-rate Board fees and market-rate stock-based compensation. The Company considers the following individuals as related parties: Two of the Company’s board members were also Managing Members of Tactic Pharma as of December 31, 2022. Chandler D. Robinson is a Company Co-Founder, Chief Executive Officer, common stockholder, Managing Member of Tactic Pharma, former Manager of the predecessor LLC, Manager of CDR Pharma, LLC and Board member of Monopar as a C Corporation. Michael Brown is a Managing Member of Tactic Pharma (as of February 1, 2019, with no voting power as it relates to Monopar), a previous managing member of Monopar as an LLC, common stockholder and Board member of Monopar as a C Corporation.

Note 7 – Income Taxes

ASC 740, *Income Taxes*, requires that the tax benefit of net operating losses, temporary differences, and credit carryforwards be recorded as an asset to the extent that management assesses that realization is “more likely than not.” Realization of the future tax benefits is dependent on the Company’s ability to generate sufficient taxable income within the carryforward period. The Company has reviewed the positive and negative evidence relating to the realizability of the deferred tax assets and has concluded that the deferred tax assets are not “more likely than not” to be realized. The valuation allowance increased by approximately \$3,421,000 and \$2,500,000 during the years ended December 31, 2022, and 2021, respectively.

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The provision for income taxes for December 31, 2022, and 2021, consists of the following:

	As of December 31,	
	2022	2021
Current:		
Federal	\$ -	\$ -
State	-	-
Foreign	-	-
Total current:	-	-
Deferred:		
Federal	-	-
State	-	-
Foreign	-	-
Total deferred:	-	-
Total provision*	\$ -	\$ -

*Total provision for income taxes of \$800 for each of the years ended December 31, 2022 and 2021, is recorded in general and administrative expenses on the Company's consolidated statements of operations and comprehensive loss as it is not considered a material amount.

The difference between the effective tax rate and the U.S. federal tax rate is as follows (in %):

	As of December 31,	
	2022	2021
Federal income tax	21.00	21.00
State income taxes, less federal benefit	6.39	7.12
Tax credits	5.57	2.03
Permanent differences	(2.45)	(1.97)
Change in valuation allowances	(32.58)	(27.47)
Other	2.06	0.71
Effective tax rate benefit (expense)	(0.01)	0.00

Deferred tax assets and liabilities consist of the following:

	As of December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	\$ 3,548,494	\$ 3,484,229
Tax credits carryforwards	1,254,678	382,648
Stock-based compensation	630,113	700,208
Intangible asset basis differences	3,824,482	3,153,199
Accrued liabilities & allowances	96,478	-
Capitalized research and development	1,787,350	-
Gross deferred tax assets	11,141,595	7,720,284
Valuation allowance	(11,141,595)	(7,720,284)
Net deferred tax assets	\$ -	\$ -

As of December 31, 2022, Company had total federal net operating loss carryforwards of approximately \$12,428,000, which will begin to expire in 2035. Losses generated after 2017 will be carried forward indefinitely. At December 31, 2022, the Company had state net operating loss carryforwards of approximately \$12,457,000 which will begin to expire in 2027.

As of December 31, 2022, the Company had federal and state tax credits of \$1,426,000 and \$183,000, respectively. The federal credits expire beginning after the year 2035 and the state credits began to expire in 2023.

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The Tax Reform Act of 1986 limits the use of net operating carryforwards and R&D credits in certain situations where changes occur in the stock ownership of a company. In the event the Company has had a change in ownership, utilization of the carryforwards and R&D credits could be limited. The Company has not performed a net operating loss or R&D credit utilization study to date.

The Company accounts for uncertain tax positions in accordance with ASC 740-10, “Accounting for Uncertainty in Income Taxes.” ASC 740-10 prescribes a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of any uncertain tax positions that have been taken or are expected to be taken on a tax return. It is Company’s policy to include penalties and interest expense related to income taxes as an income tax expense.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	<u>2022</u>	<u>2021</u>
Beginning uncertain tax benefits.....	\$ 103,104	\$ 63,262
Current year – increases.....	150,701	46,092
Prior year - increases (decreases).....	67,370	(6,250)
Ending uncertain tax benefits.....	<u>\$ 321,175</u>	<u>\$ 103,104</u>

Included in the balance of uncertain tax benefits at December 31, 2022 are \$321,175 of tax benefits that, if recognized, would not impact the effective tax rate as it would be offset by the reversal of related deferred tax assets which are subject to a full valuation allowance. The Company anticipates that no material amounts of unrecognized tax benefits will be settled within 12 months of the reporting date. As of December 31, 2022, the Company had no accrued interest or penalties recorded related to uncertain tax positions.

The Company files U.S. federal, California and Illinois state tax returns. Company is subject to California state minimum franchise taxes. All tax returns will remain open for examination by the federal and state taxing authorities for three and four years, respectively, from the date of utilization of any net operating loss carryforwards or R&D credits. In addition, due to the operations in certain foreign countries, the Company became subject to local tax laws of such countries. Nonetheless, as of December 31, 2022, due to the insignificant expenditures in such countries, there was no material tax effect to the Company’s 2022 consolidated financial statements.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (“TCJA”) was enacted. On January 1, 2022, a provision of the TCJA went into effect which requires the capitalization of research and development costs in the year incurred and requires taxpayers to amortize such costs over five years and 15 years for domestic and foreign expense, respectively. The Company evaluated the impact of the TCJA and prepared the provision by following the treatment of research and development expenditures for tax purposes under Section 174.

Note 8 – Commitments and Contingencies

License, Development and Collaboration Agreements

Onxeo S.A.

In June 2016, the Company executed an option and license agreement with Onxeo S.A. (“Onxeo”), a public French company, which gave Monopar the exclusive option to license (on a world-wide exclusive basis) Validive to pursue treating severe oral mucositis in patients undergoing chemoradiation treatment for head and neck cancers. The pre-negotiated Onxeo license agreement for Validive as part of the option agreement includes clinical, regulatory, developmental and sales milestones that could reach up to \$108 million if the Company achieves all milestones, and escalating royalties on net sales from 5% to 10%. On September 8, 2017, the Company exercised the license option, and therefore paid Onxeo the \$1 million fee under the option and license agreement.

Under the agreement, the Company is required to pay royalties to Onxeo on a product-by-product and country-by-country basis until the later of (1) the date when a given product is no longer within the scope of a patent claim in the country of sale or manufacture, (2) the expiry of any extended exclusivity period in the relevant country (such as orphan drug exclusivity, pediatric exclusivity, new chemical entity exclusivity, or other exclusivity granted beyond the expiry of the relevant patent), or (3) a specific time period after the first commercial sale of the product in such country. In most countries, including the U.S., the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country, not taking into consideration any potential patent term adjustment that may be filed in the future or any regulatory extensions that may be obtained. The royalty termination provision pursuant to (3) described above is shorter than 20 years and is the least likely cause of termination of royalty payments.

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The Onxeo license agreement does not have a pre-determined term, but expires on a product-by-product and country-by-country basis; that is, the agreement expires with respect to a given product in a given country whenever the Company's royalty payment obligations with respect to such product have expired. The agreement may also be terminated early for cause if either the Company or Onxeo materially breach the agreement, or if either the Company or Onxeo become insolvent. The Company may also choose to terminate the agreement, either in its entirety or as to a certain product and a certain country, by providing Onxeo with advance notice.

The Company is internally developing Validive and has its ongoing VOICE clinical trial, which, if successful, may allow the Company to apply for marketing approval within the next several years. The Company will need to raise significant funds or enter into a collaboration partnership to support the further development, including potential commercialization of Validive. As of December 31, 2022, the Company had not reached any of the pre-specified milestones and has not been required to pay Onxeo any funds under this license agreement other than the \$1 million one-time license fee.

Grupo Español de Investigación en Sarcomas ("GEIS")

In June 2019, the Company executed a clinical collaboration agreement with GEIS for the development of camsirubicin in patients with advanced soft tissue sarcoma ("ASTS"). Following completion of the Phase 1b clinical trial in the U.S. that Monopar initiated in the third quarter of 2021 with the first patient dosed in October 2021, the Company continues to expect that GEIS will sponsor and lead a multi-country, randomized, open-label Phase 2 clinical trial to evaluate camsirubicin head-to-head against doxorubicin, the current first-line treatment for ASTS. The Company will provide study drug and supplemental financial support for the clinical trial. For three months ended March 31, 2021, Monopar incurred \$0.3 million in expenses under the GEIS agreement and other clinical-related expenses including clinical material manufacturing and database management expenses in support of the then-planned GEIS Phase 2 camsirubicin clinical trial. The Company can terminate the agreement by providing GEIS with advance notice, and without affecting the Company's rights and ownership to any related intellectual property or clinical data. In the second quarter of 2021, due to regulatory delays in Spain, Monopar decided to conduct an open-label Phase 1b clinical trial of camsirubicin in the U.S., therefore no expenses were incurred related to the GEIS collaboration beyond March 31, 2021.

XOMA Ltd.

The intellectual property rights contributed by Tactic Pharma to the Company included the non-exclusive license agreement with XOMA Ltd. for the humanization technology used in the development of MNPR-101. Pursuant to such license agreement, the Company is obligated to pay XOMA Ltd. clinical, regulatory and sales milestones for MNPR-101 that could reach up to \$14.925 million if the Company achieves all milestones. The agreement does not require the payment of sales royalties. There can be no assurance that the Company will reach any milestones under the XOMA agreement. As of December 31, 2022, the Company had not reached any milestones and has not been required to pay XOMA Ltd. any funds under this license agreement.

Operating Leases

The Company is currently leasing office space for its executive headquarters at 1000 Skokie Blvd., in the Village of Wilmette, Illinois for \$4,238 per month. In February 2022, the Company entered into a 24-month lease for 1,202 square feet of the office space for \$2,379 per month. In May 2022, the Company entered into a 22-month lease for 939 square feet of additional office space for \$1,859 per month.

As of December 31, 2022, in accordance with ASC 842, *Leases*, the two leases were recorded as an operating lease right-of-use ("ROU") asset and a lease liability included in accounts payable, accrued expenses and other current liabilities, and non-current operating lease liability on the Company's consolidated balance sheets. The initial ROU asset and associated liability is equal to the present value of the minimum lease payments. Since the rate implicit in the lease is rarely readily determinable, the Company applied an incremental borrowing rate taking into consideration our credit quality and borrowing rate for similar assets. The lease terms used to calculate the ROU asset and related lease liability does not include an option to extend but does include an option to terminate the lease. Lease costs for operating leases are recognized on a straight-line basis over the expected lease term and recorded as general and administrative expenses on the Company's consolidated statements of operations and comprehensive loss. Amortization of the ROU asset commenced on April 1, 2022, and June 1, 2022, for the two operating leases, respectively. No ROU asset or lease liability was recorded in 2021 as the lease obligation was less than one year.

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The components of lease expense were as follows:

	Years Ended December 31,	
	2022	2021
Total lease costs	\$ 34,424	\$ 54,960

Maturities of the lease liability as of December 31, 2022 are as follows:

Fiscal Year	Operating Leases	
December 31, 2023	\$ 50,856	
December 31, 2024	8,476	
Total lease payments	59,332	
Less: imputed interest	(2,342)	
Total lease liability as of December 31, 2022	\$ 56,990	

The following table presents the weighted average remaining lease term and the discount rate used in calculating the ROU asset and related lease liability for the periods presented:

	December 31,	
	2022	2021
Lease term:		
Operating leases	1.2 years	-
Discount rate:		
Operating lease	6.50%	-

Supplemental balance sheet information:

	As of December 31,	
	2022	2021
ROU asset - non-current	\$ 61,228	-
Total ROU asset	\$ 61,228	-
Operating lease liability – current	\$ 48,582	-
Operating lease liability - non-current	8,408	-
Total operating lease liabilities	\$ 56,990	-

Legal Contingencies

The Company may be subject to claims and assessments from time to time in the ordinary course of business. No claims have been asserted to date.

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future, but that have not yet been made. To date, the Company has not paid any claims nor been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of future claims against these indemnification obligations.

In accordance with its second amended and restated certificate of incorporation, amended and restated bylaws and the indemnification agreements entered into with each officer and non-employee director, the Company has indemnification obligations to its officers and non-employee directors for certain events or occurrences, subject to certain limits, while they are serving at the Company's request in such capacities. There have been no indemnification claims to date.