Filed pursuant to Rule 424(b)(5)
Registration No. 333-235791

PROSPECTUS SUPPLEMENT
(To Prospectus dated January 13, 2020)

$4,870,000

Common Stock

In accordance with the terms of the Capital on Demand™ Sales Agreement entered into with JonesTrading Institutional Services LLC ("JonesTrading" or the "Agent"), dated April 20, 2022, which we refer to as the Sales Agreement, we may offer and sell under this prospectus supplement and accompanying prospectus shares of our Common Stock, $0.001 par value per share, having an aggregate offering price of up to $4,870,000 from time to time through or to the Agent, acting as sales agent or principal.

Our Common Stock is listed for trading on the Nasdaq Capital Market under the symbol "MNPR." On April 18, 2022, the last reported sale price of our Common Stock was $2.3765 per share.

The aggregate market value of our outstanding Common Stock held by non-affiliates was approximately $14.6 million based on 4,285,219 shares of outstanding Common Stock held by non-affiliates and a price per share of $3.41, the closing price of our Common Stock on February 22, 2022. Pursuant to General Instruction I.B.6 of Form S-3, we may not sell securities registered on Form S-3 with a value more than one-third of the aggregate market value of our Common Stock held by non-affiliates in any 12-month period, so long as the aggregate market value of our Common Stock held by non-affiliates remains less than $75.0 million. In the event that the aggregate market value of our outstanding Common Stock held by non-affiliates equals or exceeds $75.0 million, then the one-third limitation on sales may not apply. We have not sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to, and including, the date of this prospectus supplement.

Sales of our Common Stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"). The Agent is not required to sell any specific amount of shares of our Common Stock, but will act as our sales agent using commercially reasonable efforts consistent with their normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The Agent will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share of our Common Stock sold. In connection with the sale of our Common Stock on our behalf, the Agent will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the Agent will be deemed to be underwriting commission or discount. We have also agreed to provide indemnification and contribution to the Agent with respect to certain liabilities, including liabilities under the Securities Act.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus supplement and future filings.

Investing in our Common Stock involves significant risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our Common Stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement. Any representation to the contrary is a criminal offense.

The date of this Prospectus Supplement is April 20, 2022

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is a supplement to the accompanying prospectus that is also a part of this document. This prospectus supplement and the accompanying prospectus, dated January 13, 2020, are part of a registration statement on Form S-3 (File No. 333-235791) that we filed with the Securities and Exchange Commission (the "SEC"), utilizing a "shelf" registration process. Under the shelf registration process, we may offer and sell from time to time in one or more offerings our Common Stock described in the accompanying prospectus.

This document is in two parts. The first part is this prospectus supplement, which describes our Common Stock we are offering and the terms of the offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information. Generally, when we refer to this "prospectus," we are referring to both documents combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any earlier dated document incorporated by reference therein, on the other hand, you should rely on the information in this prospectus supplement. Additional prospectus supplements or documents filed after the date hereof that are deemed incorporated by reference herein may modify and supersede the information in this prospectus supplement. We urge you to carefully read this prospectus supplement and the accompanying prospectus and any related free writing prospectus, together with the information incorporated herein and therein by reference as described under the heading "Incorporation of Information by Reference," before buying any of our Common Stock being offered.

You should rely only on the information that we have provided or incorporated by reference in this prospectus supplement and the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you. We have not, and Agent has not, authorized anyone to provide you with different information. No other dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement and the accompanying prospectus or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus supplement is an offer to sell only our Common Stock offered hereby and only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus supplement and the accompanying prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any related free writing prospectus, or any sale of our Common Stock.

This prospectus supplement contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

As used in this prospectus supplement, the terms "we", "us", "our", "Company", "Monopar Therapeutics" and "Monopar" refer to Monopar Therapeutics Inc., a Delaware corporation.

We own or have rights to trademarks or trade names that we use in conjunction with the operation of our business. Each trademark, trade name or service mark of any other company appearing in this prospectus supplement or the accompanying prospectus belongs to its holder. Use or display by us of other parties' trademarks, trade names or service marks is not intended to and does not imply a relationship with, or endorsement or sponsorship by us of, the trademark, trade name or service mark owner.

SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our Common Stock. For a more complete understanding of our Company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference into this prospectus, and the information referred to under the heading "Risk Factors" in this prospectus beginning on page S-6, and in the documents incorporated by reference into this prospectus.

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 oncology 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 2021, we made significant strides in our clinical development programs and commenced a global Phase 2b/3 clinical trial of our lead product candidate, Validive (clonidine hydrochloride mucobuccal tablet; clonidine HCI MBT), for the prevention of chemoradiotherapy ("CRT")-induced severe oral mucositis ("SOM") in patients with oropharyngeal cancer ("VOICE" trial). We also commenced a U.S.-based open-label, Phase 1b clinical trial of camsirubicin for the treatment of advanced soft tissue sarcoma ("ASTS"). We also continue to move forward with our three preclinical programs, which include MNPR-101, a urokinase plasminogen activator receptor ("uPAR")-targeted antibody for the potential treatment of various cancers; MNPR-101 RIT, a radioimmunotherapeutic ("RIT") based on MNPR-101 which continues development for the potential treatment of cancer and severe COVID-19 in collaboration with our partner, NorthStar Medical Radioisotopes, LLC; and 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.

Summary Risks Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors" immediately following this prospectus summary and in the documents incorporated herein by reference. 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.

- Funds raised to date are not sufficient to 1) 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 potential MNPR-101-derived radioimmunotherapeutics and companion diagnostics to treat cancer and severe COVID-19 (patients with SARS-CoV-2 infection); or 4) support continued development of MNPR-101, 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 enter into a clinical or commercial partnership, we will likely have to terminate one or more programs. There can be no assurance that we will find a suitable 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 approval 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 subjects 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.

- We rely on 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 conflict and resulting sanctions against Russia and Russian entities have increased fuel costs and may cause shipping delays and the broader economic, trade and financial market consequences are uncertain at this time, which may increase the cost of supplies for our clinical materials and may delay the manufacture of our clinical materials 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.

- We face significant competition from other biotechnology and pharmaceutical companies, 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 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 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 ongoing COVID-19 pandemic could have a substantial negative impact on our business, financial condition, operating results, stock price and ability to raise additional funds.

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 may 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 $1.07 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 our most recent 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.

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 prospectus supplement or the accompanying prospectus.

Trademark Notice

We have a registered trademark with the USPTO for "Validive." All other trademarks, service marks and trade names in this prospectus supplement, the accompanying prospectus or the documents incorporated reference herein are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks used herein.

THE OFFERING	
Common Stock Offered By Us	Shares of our Common Stock having an aggregate offering price up to $4,870,000
Manner of Offering	At the market offering" that may be made from time to time on Nasdaq through or to the Agent, as sales agent or principal. See the section entitled "Plan of Distribution" below.
Common Stock to be Outstanding After This Offering[(1)]	Up to 14,669,824 shares, assuming sales price at a price of $2.3765 per share, which was the Closing price of our Common Stock on Nasdaq on April 18, 2022. The actual number of shares issued will vary depending on the sales price under this offering.
Use of Proceeds	We intend to use the net proceeds of this offering for our operations, including, but not limited to, general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of product and working capital. See the section entitled "Use of Proceeds" below.
Nasdaq Capital Market Symbol	MNPR
Risk Factors	See "Risk Factors" beginning on page S-6 and the other information included in, or incorporated by reference into, this prospectus for a discussion of certain factors you should carefully consider before deciding to invest in our Common Stock.

(1) The Common Stock outstanding after the offering is based on approximately 12,620,592 shares of our Common Stock outstanding as of April 18, 2022 and the sale of 2,049,232 shares of our Common Stock at an assumed offering price of $2.3765 per share, the last reported sale price of our Common Stock on Nasdaq on April 18, 2020, and excludes the following:

- 1,930,439 shares of our Common Stock issuable upon the exercise of outstanding stock options (weighted-average exercise price of $4.12; 1,257,211 shares vested) and 394,260 shares of our Common Stock issuable upon the vesting of restricted stock units; and
- 670,945 shares of our Common Stock reserved for issuance under our 2016 Stock Incentive Plan.

RISK FACTORS

Investing in our Common Stock involves a high degree of risk. Before deciding to invest in our Common Stock, you should consider carefully the risk factors described below, together with the risk factors, and all of the other information, in our Annual Report on Form 10-K for the year ended December 31, 2021, as well as the risks, uncertainties and other information in subsequent filings with the SEC under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), after the date of this prospectus supplement, all of which are incorporated by reference herein. This risk factor disclosure should be viewed together with all other information contained or incorporated by reference in this prospectus, any prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our Common Stock. If any of the following risks, or the risk factors incorporated by reference herein, were to materialize, our business, financial condition, results of operations, and future growth prospects could be materially and adversely affected. In that event, the market price of our Common Stock could decline, and you could lose part of or all of your investment in our Common Stock.

Risks Related to this Offering

We have broad discretion in the use of the net proceeds from this offering, and our use of those proceeds may not yield a favorable return on your investment.

We intend to use the net proceeds of this offering for our operations, including, but not limited to, general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of product and working capital, We have not specifically allocated the amount of net proceeds that will be used for these purposes, and our management will have broad discretion over how these proceeds are used and could spend the proceeds in ways with which you may not agree. In addition, we may not use the proceeds of this offering effectively or in a manner that increases our market value or enhances our profitability. We have not established a timetable for the effective deployment of the proceeds, and we cannot predict how long it will take to deploy the proceeds.

Future sales of substantial amounts of shares of our Common Stock, or the possibility that such sales could occur, could adversely affect the market price of our Common Stock.

We may issue shares of our Common Stock from time to time in this offering in an aggregate price to the public of up to $4.87 million. The issuance from time to time of shares in this offering, as well as our ability to issue such shares in this offering, could have the effect of depressing the market price or increasing the market price volatility of our Common Stock.

It is not possible to predict the actual number of shares of our Common Stock we will sell in this offering agreement or the gross proceeds resulting from those sales.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver placement notices to the sales agent from time to time throughout the term of the sales agreement. Our decisions as to whether and when to deliver placement notices will depend on a variety of factors, including our financing needs and available alternatives at the time and the market price of our Common Stock. If and when we do deliver placement notices, the number of shares of our Common Stock that are sold through the sales agent after delivering a placement notice will fluctuate based on a number of factors, including the market price of our Common Stock during the sales period, the limits we set with the sales agent in any applicable placement notice, and the demand for our Common Stock during the sales period. Therefore, it is not currently possible to predict the number of shares of our Common Stock that will be sold or the proceeds to be raised in connection with those sales, if any.

We are likely to require substantial additional funding regardless of the number of shares of our Common Stock we sell in this offering or the gross proceeds resulting from those sales.

The amount of proceeds from this offering will depend upon the number of shares of our Common Stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement as a source of financing. Even if we are able to sell the full $4.87 million of shares offered hereby, we will likely require substantial additional funding and there can be no assurance such funding will be available.

The shares of our Common Stock offered hereby will be sold in*"*at the market offerings,*" *and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares of our Common Stock in this offering at different times will likely pay different prices and therefore may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and number of shares of our Common Stock sold from time to time in this offering. In addition, there is no minimum or maximum sales price for shares of our Common Stock to be sold in this offering. Investors may experience a decline in the value of the shares of our Common Stock they purchase in this offering as a result of sales made at prices lower than the prices they paid.

You may experience immediate and substantial dilution.

Because the price per share of our Common Stock being offered may be higher than the book value per share of our Common Stock, you may suffer immediate substantial dilution in the net tangible book value of the Common Stock you purchase in this offering. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase Common Stock in this offering.

Because the sales of the shares offered hereby will be made directly into the market, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell will experience significant dilution if we sell additional shares at prices significantly below the price at which they invested.

FORWARD-LOOKING STATEMENTS

This prospectus 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 34 Act. All statements other than statements of historical facts included in this Prospectus 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:

- our ability to raise sufficient funds within the next 12 months in order for us to 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, to continue the clinical development of camsirubicin through and beyond our ongoing Phase 1b dose escalation clinical trial, to support further development of potential MNPR-101-derived radioimmunotherapeutics (RITs) and companion diagnostics to treat cancer and severe COVID-19 (patients with SARS-CoV-2 infection), and to support further development of MNPR-101, 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, including direct price controls driving lower prices and other governmental regulations affecting cost requirements and structures required to deliver therapeutic products;
- the uncertain impact of the COVID-19 pandemic on our ability to advance our clinical programs and raise additional financing;
- the uncertain impact of the Russia-Ukraine conflict on our clinical material manufacturing expenses and timeline, as well as on general economic, trade and financial market conditions; and
- uncertainty of our financial and operational projections and the development of new competitive products and technologies.

Although we believe that the expectations reflected in such forward-looking statements are appropriate, we can give no assurance that such expectations will be realized. 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 above and made elsewhere in this prospectus supplement and future supplemental prospectuses. We undertake no obligation to update any statements made in this prospectus supplement or elsewhere, including without limitation any forward-looking statements, except as required by law.

You should read this prospectus supplement and the documents that we reference in this prospectus supplement with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

USE OF PROCEEDS

The amount of proceeds from this offering will depend upon the number of shares of our Common Stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with the Agent as a source of financing. Even if we are able to sell the full $4,870,000 of shares offered pursuant to this prospectus supplement, we will likely require substantial additional funding.

We intend to use the net proceeds of this offering for our operations, including, but not limited to, general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of product and working capital. The precise amount, use, and timing of the application of such proceeds will depend upon our funding requirements and the availability and cost of other capital. Pending application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities and/or savings accounts.

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.

DILUTION

Our historical net tangible book value as of December 31, 2021, was $18.9 million, or $1.50 per share of our Common Stock.

After giving effect to the sale of our Common Stock in the aggregate amount of $4.87 million at an assumed price of $2.3765 per share, the last reported sale price of our Common Stock on Nasdaq on April 18, 2022, and after deducting estimated offering commissions and expenses payable by us, our as adjusted net tangible book value as of December 31, 2021, would have been $23.6 million, or $1.61 per share. This represents an immediate increase in net tangible book value per share of $0.11 to existing stockholders and immediate dilution of $0.7665 in net tangible book value per share to new investors purchasing our Common Stock in this offering.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the assumed price per share paid by new investors. The following table illustrates this dilution on a per share basis.

Assumed Price Per Share		$ 2.3765
Historical Net Tangible Book Value Per Share as of December 31, 2021	$ 1.50	
Increase in Net Tangible Book Value Per Share Attributable to New Investors	0.11	
As Adjusted Net Tangible Book Value Per Share After this Offering		1.61
Dilution Per Share to New Investors		$ 0.7665

The foregoing table is based on an aggregate 12,598,125 shares of our Common Stock outstanding as of December 31, 2021, and excludes:

- 1,543,989 shares of our Common Stock issuable upon the exercise of outstanding stock options (weighted-average exercise price of $4.78; 1,198,703 shares vested) and 111,462 shares of our Common Stock issuable upon the vesting of restricted stock units; and
- 1,368,289 shares of our Common Stock reserved for issuance under our 2016 Stock Incentive Plan.

All of the foregoing is illustrative only. There can be no assurance we will sell all, or any, of the shares offered by this prospectus, when any such sales will occur or what the sales prices will be.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, for use in the operation of our business and do not anticipate paying any cash dividends on our Common Stock in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our Board and will depend on various factors, including applicable laws, our results of operations, our financial condition, our capital requirements, general business conditions, our future prospects and other factors that our Board may deem relevant. Additionally, our ability to pay dividends on our capital stock could be limited by terms and covenants of any future indebtedness. Investors should not purchase our Common Stock with the expectation of receiving cash dividends.

PLAN OF DISTRIBUTION

On April 20, 2022, we entered into a Sales Agreement (the "Sales Agreement") with JonesTrading Institutional Services LLC (the "Agent"). Pursuant to this prospectus supplement and the Sales Agreement, we may offer and sell our Common Stock having an aggregate gross sales price of up to $4,870,000 from time to time through or to the Agent, acting as agent or principal. A copy of the Sales Agreement is incorporated by reference as an exhibit herein.

Each time that we wish to issue and sell shares of our Common Stock under the Sales Agreement, if any, we will provide the Agent with a placement notice describing the amount of shares to be sold or the gross proceeds to be raised in a given time period, the time period during which sales are requested to be made, any limitation on the amount of shares of Common Stock that may be sold in any single day, any minimum price below which sales may not be made or any minimum price requested for sales in a given time period and any other instructions relevant to such requested sales. Upon delivery of a placement notice and subject to the terms and conditions of the Sales Agreement, the Agent may sell our Common Stock by any method permitted by law deemed to be "at the market offerings" as defined in Rule 415 under the Securities Act. We may instruct the Agent not to sell our Common Stock if the sales cannot be effected at or above the price designated by us from time to time. We or the Agent may suspend the offering of our Common Stock upon notice and subject to other conditions.

We will pay the Agent commissions, in cash, for its services in acting as an agent in the sale of our Common Stock. The Agent will be entitled to compensation of up to 3.0% of the gross proceeds from each sale of our Common Stock. Because there is no minimum offering amount required as a condition to this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse the Agent for certain specified expenses, including the fees and disbursements of their legal counsel in an amount not to exceed $40,000. Additionally, pursuant to the terms of the sales agreement, we agreed to reimburse the Agent for the documented fees and costs of its legal counsel reasonably incurred in connection with the Agent's ongoing diligence in an amount not to exceed $5,000 per year. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to the Agent under the terms of the Sales Agreement, will be approximately $40,000.

Settlement for sales of our Common Stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and the Agent in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our Common Stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and the Agent may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

The Agent will use their commercially reasonable best efforts, consistent with its sales and trading practices, to solicit offers to purchase our Common Stock under the terms and subject to the conditions set forth in the Sales Agreement. In connection with the sale of our Common Stock on our behalf, the Agent will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the Agent will be deemed to be an underwriting commission or discount. We have agreed to provide indemnification and contribution to the Agent against certain civil liabilities, including liabilities under the Securities Act.

The offering of our Common Stock pursuant to the Sales Agreement will terminate upon the termination of the Sales Agreement as permitted therein. We and the Agent may terminate the Sales Agreement at any time upon five days' prior notice or by the Agent at any time in certain circumstances, including the occurrence of a material and adverse change in our business or financial condition that makes it impractical or inadvisable to market our Common Stock or to enforce contracts for the sale of our Common Stock.

The Agent and its respective affiliates have in the past and may in the future provide various investment banking, commercial banking and other financial services for us, for which services they may in the future receive customary fees.

This prospectus in electronic format may be made available on a website maintained by the Agent who may distribute this prospectus electronically.

LEGAL MATTERS

Certain legal matters will be passed upon for us by Baker & Hostetler, LLP, Columbus, Ohio. Certain legal matters in connection with this offering will be passed upon for the Agent by Duane Morris LLP, New York, New York.

EXPERTS

The financial statements of Monopar Therapeutics Inc. as of December 31, 2021 and 2020, and for each of the two years in the period ended December 31, 2021, incorporated in this Prospectus by reference have been so incorporated in reliance on the report of BPM LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a shelf registration statement on Form S-3 under the Securities Act with respect to the Common Stock we are offering by this prospectus supplement. This prospectus supplement does not contain all of the information included in the registration statement. For further information pertaining to us and our Common Stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus supplement to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

We file annual, quarterly and current reports, information statements and proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. We also maintain a website at http://www.monopartx.com. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10- Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not a part of, and should not be construed as being incorporated by reference into, this prospectus supplement or the accompanying prospectus.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information and documents listed below that we have filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 24, 2022;
- our Current Report on Form 8-K, filed with the SEC on April 1, 2022; and
- the description of our Common Stock contained in our Registration Statement on Form 8-A, registering our Common Stock under Section 12(b) under the Exchange Act, filed with the SEC on September 30, 2019, as supplemented by the "Description of Capital Stock" included as an exhibit to our most recent Annual Report on Form 10-K and incorporated by reference herein.

We also incorporate by reference any future filings (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until we file a post-effective amendment that indicates the termination of the offering of the common stock made by this prospectus supplement and will become a part of this prospectus supplement from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Monopar Therapeutics Inc., Attention: Corporate Secretary, 1000 Skokie Blvd., Suite 350, Wilmette, IL 60091. Our phone number is (847) 388-0349. You may also view the documents that we file with the SEC and incorporate by reference in this prospectus supplement on our corporate website at www.monopartx.com. The information on our website is not incorporated by reference and is not a part of this prospectus supplement.

PROSPECTUS

$75,000,000

Common Stock

We may offer and sell an indeterminate number of shares of our Common Stock from time to time under this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest.

We may offer our Common Stock in one or more offerings in amounts, at prices, and on terms determined at the time of the offering. We may sell our Common Stock through agents we select or through underwriters and dealers we select. If we use agents, underwriters or dealers, we will name them and describe their compensation in a prospectus supplement.

This prospectus provides a general description of our Common Stock that we may offer. Each time we sell our Common Stock, we will provide specific terms of the Securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in our Common Stock. This prospectus may not be used to consummate a sale of our Common Stock unless accompanied by the applicable prospectus supplement.

Our Common Stock is listed for trading on the Nasdaq Capital Market under the symbol "MNPR." On January 2, 2020 the last reported sale price of our Common Stock was $17.27 per share. As of that date, and based on that price, the aggregate market value of our voting and non-voting common equity held by non-affiliates was approximately $37.9 million.

We have not offered and sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus.

Investing in our Common Stock involves significant risks. See "Risk Factors" included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase our Common Stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this Prospectus is January 13, 2020

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SUMMARY

We are a clinical stage biopharmaceutical company focused on developing proprietary therapeutics designed to improve clinical outcomes for cancer patients. We are building a drug development pipeline through the licensing and acquisition of oncology 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. We currently have three compounds in development: Validive® (clonidine mucobuccal tablet; clonidine MBT), a Phase 3-ready, first-in-class mucoadhesive buccal tablet for the prevention and treatment of radiation-induced severe oral mucositis in oropharyngeal cancer patients; camsirubicin (generic name for 5-imino-13-deoxydoxorubicin; previously known as MNPR-201, GPX-150), a proprietary Phase 2 clinical stage topoisomerase II-alpha selective analog of doxorubicin engineered specifically to retain anticancer activity while minimizing toxic effects on the heart; and MNPR-101 (formerly huATN-658), a pre-IND stage humanized monoclonal antibody, which targets the urokinase plasminogen activator receptor ("uPAR"), for the treatment of advanced solid cancers.

Our principal executive offices are located at 1000 Skokie Blvd, Suite 350, Wilmette, IL 60091. Our telephone number is (847) 388-0349.

RISK FACTORS

You should consider carefully the risks discussed under the section captioned "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2018 and in our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), each of which is incorporated by reference in this prospectus in its entirety, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus, any prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our securities. If any of these events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment.

IMPORTANT INFORMATION ABOUT THIS PROSPECTUS

In this prospectus, unless the context suggests otherwise, references to "Monopar Therapeutics," "Monopar," the "Company," "we," "us" and "our" refer to Monopar Therapeutics Inc.

This prospectus is part of a "shelf" registration statement. By using a shelf registration statement, we may sell our Common Stock, as described in this prospectus, from time to time in one or more offerings. Each time we sell our Common Stock, we will provide a prospectus supplement to this prospectus that contains specific information about the terms of such offering. The prospectus supplement may also add, update or change information contained in this prospectus. Before purchasing our Common Stock, you should carefully read both this prospectus and any prospectus supplement, together with the additional information incorporated into this prospectus or described under the heading "*Where You Can Find More Information*."

You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell our Common Stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, and have incorporated by reference, is accurate only as of the date on the front cover of this prospectus, or when such document was filed with the Securities and Exchange Commission ("SEC"). Our business, financial condition, results of operations and prospects may have changed since the relevant date.

Neither we, nor any of our officers, directors, agents, representatives or underwriters, make any representation to you about the legality of an investment. You should not interpret the contents of this prospectus, any prospectus supplement, or any free writing prospectus to be legal, business, investment or tax advice. You should consult with your own advisors for that type of advice and consult with them about the legal, tax, business, financial and other issues that you should consider before investing in our Common Stock.

We will not use this prospectus to offer and sell our Common Stock unless it is accompanied by a prospectus supplement that more fully describes the terms of the offering.

FORWARD-LOOKING STATEMENTS

This Prospectus 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 34 Act. All statements other than statements of historical facts included in this Prospectus 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:

- our ability to raise sufficient funds in the coming months in order for us to start our Validive Phase 3 clinical trial;
- our ability to find a suitable pharmaceutical partner to further our development of Validive, if we are unable to raise sufficient additional financing;
- risks and uncertainties associated with our research and development activities, including our clinical trials;
- estimated timeframes for our clinical trials and regulatory reviews for approval to market products;
- plans to research, develop and commercialize our current and future product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- commercialization, marketing and manufacturing capabilities and strategy;
- intellectual property position and strategy;
- future financial performance;
- estimates regarding expenses, capital requirements and need for additional financing;
- the impact of government laws and regulations;
- ability to attract and retain key personnel; and
- financial and operational projections.

Although we believe that the expectations reflected in such forward-looking statements are appropriate, we can give no assurance that such expectations will be realized. 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 above and made elsewhere in this prospectus and future supplemental prospectuses. We undertake no obligation to update any statements made in this Prospectus or elsewhere, including without limitation any forward-looking statements, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

DESCRIPTION OF CAPITAL STOCK

We have the authority to issue 40,000,000 shares of Common Stock, $0.001 par value. As of January 3, 2020, there were 10,587,632 shares of our Common Stock issued and outstanding.

We have reserved 1,600,000 shares of our Common Stock for issuance under our 2016 Stock Incentive Plan, as subsequently amended (the "Plan"), and as of January 3, 2020, we have outstanding stock options to purchase up to 1,087,463 shares of our Common Stock and 494,104 shares of our Common Stock available for future stock awards under the Plan.

Common Stock

Voting Rights

The holders of shares of our Common Stock are entitled to one vote per share for the election of directors and on all other matters submitted to a vote of stockholders. Shares of our Common Stock do not have cumulative voting rights. The election of our Board of Directors ("Board") is decided by a plurality of the votes cast at a meeting of our stockholders by the holders of stock entitled to vote in the election.

Dividends

Holders of our Common Stock are entitled to receive such dividends as may be declared by our Board out of funds legally available therefor.

Liquidation

Upon our dissolution and liquidation, holders of our Common Stock are entitled to a ratable share of our net assets remaining after payments to our creditors.

Rights and Preferences

Our stockholders have no preemptive rights to acquire additional shares of our Common Stock or other securities. The shares of our Common Stock are not subject to redemption.

Preferred Stock

We have no preferred stock authorized or outstanding.

Anti-Takeover Provisions

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our Board or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Authorized but Unissued Shares

The authorized but unissued shares of our Common Stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of any exchange on which our shares are listed. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved Common Stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Election of Director by Plurality of Shares; Vacancies

Our Amended and Restated By-laws provide that directors will be elected by a plurality of votes cast by the shares present in person or by proxy at a meeting of the stockholders and entitled to vote thereon, a quorum being present at such meeting. There is no cumulative voting, meaning that Directors may be elected with a vote of holders of less than a majority of the outstanding common stock.

Our Amended and Restated By-laws also provide that vacancies occurring on our Board may be filled by the affirmative votes of a majority of the remaining members of our Board or by the sole remaining director, and not by our stockholders. Such provisions in our corporate organizational documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us. The inability to make changes to our Board could prevent or discourage an attempt to take control of the Company by means of a proxy contest, tender offer, merger or otherwise.

Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations; Stockholder Action

Our Amended and Restated By-laws provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our Board. Stockholders at a special meeting may only consider matters set forth in the notice of the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that may be favored by the holders of a majority of our outstanding voting securities.

Super Majority Voting

The General Corporation Law of the State of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our Amended and Restated By-laws may be amended or repealed by a majority vote of our Board or the affirmative vote of the holders of at least a majority of the votes that all our stockholders would be entitled to cast in any election of Directors.

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 at any time after we have been subject to the reporting requirements of the 1934 Act for at least twelve months (the “Initial Holding Period”). 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. 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. TacticGem has agreed to enter into a lock-up agreement and to not exercise any rights of resale for 180 days after the date of our initial public offering which was December 18, 2019.

Listing

Our Common Stock is listed on the Nasdaq Capital Market under the symbol “MNPR.”

Transfer Agent and Registrar

The transfer agent and registrar for our Common Stock is VStock Transfer, LLC (“VStock”). VStock’s address is 18 Lafayette Place, Woodmere, NY 11598

PLAN OF DISTRIBUTION

We may sell our Common Stock covered in this prospectus in any of three ways (or in any combination):

- through underwriters or dealers;
- directly to a limited number of purchasers or to a single purchaser; or
- through agents.

The distribution of our Common Stock may be effected from time to time in one or more transactions:

- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each time that we use this prospectus to sell our Common Stock, we will also provide a prospectus supplement that contains the specific terms of the offering. The prospectus supplement will set forth the terms of the offering of our Common Stock, including:

- the name or names of any underwriters, dealers or agents and the amounts of any of our Common Stock underwritten or purchased by each of them; and
- the public offering price of our Common Stock and the proceeds to us and any discounts, commissions or concessions allowed or reallowed or paid to dealers.

Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

If underwriters are used in the sale of our Common Stock, our Common Stock will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Our Common Stock may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase our Common Stock will be subject to certain conditions precedent. The underwriters may be obligated to purchase all of our Common Stock if they purchase any of our Common Stock.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of our Common Stock and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase our Common Stock from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

We may enter into derivative transactions with third parties, or sell our Common Stock not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell our Common Stock covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use our Common Stock pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of our Common Stock, and may use our Common Stock received from us in settlement of those derivatives to close out any related open borrowings of our Common Stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment).

LEGAL MATTERS

Certain legal matters will be passed upon for us by Baker & Hostetler, LLP, Columbus, Ohio.

EXPERTS

The financial statements as of December 31, 2018 and 2017, and for the years then ended, included in this Prospectus have been so included in reliance on the report of BPM LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC this shelf registration statement on Form S-3 under the Securities Act with respect to our Common Stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our Common Stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

We file annual, quarterly and current reports, information statements and proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. We also maintain a website at http://www.monopartx.com. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10- Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not a part of, and should not be construed as being incorporated by reference into, this prospectus or the accompanying prospectus supplement.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information and documents listed below that we have filed with the SEC (Commission File No. 000-55866):

- our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed with the SEC on November 12, 2019;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, filed with the SEC on August 8, 2019;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the SEC on May 10, 2019;
- our Information Statement regarding our Annual Meeting of Stockholders on June 27, 2019, on DEF14C, filed with the SEC on May 22, 2019;
- our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 26, 2019;
- our Current Reports on Form 8-K, filed with the SEC on June 27, 2019, June 5, 2018, and July 2, 2018, to the extent the information in such reports is filed and not furnished; and
- the description of our Common Stock contained in our Registration Statement on Form 8-A, registering our Common Stock under Section 12(b) under the Exchange Act, filed with the SEC on September 30, 2019, as supplemented by the "Description of Capital Stock" beginning on page 5 of this prospectus and including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the common stock made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Monopar Therapeutics, Inc., Attention: Corporate Secretary, 1000 Skokie Blvd., Suite 350, Wilmette, IL 60091. Our phone number is (847) 388-0349. You may also view the documents that we file with the SEC and incorporate by reference in this Prospectus on our corporate website at www.monopartx.com. The information on our website is not incorporated by reference and is not a part of this prospectus.

$4,870,000

Monopar Therapeutics

Common Stock

PROSPECTUS SUPPLEMENT

JonesTrading

April 20, 2022