

Prospectus Supplement
(To prospectus dated September 9, 2025)**1,034,433 Shares of Common Stock**
Pre-Funded Warrants to Purchase 960,542 Shares of Common Stock

We are offering 1,034,433 shares of our common stock, \$0.001 par value per share (“Common Stock”), and in lieu of offering shares of our Common Stock to certain investors that so choose, pre-funded warrants (“Pre-Funded Warrants”) to purchase 960,542 shares of our Common Stock (and the shares of Common Stock issuable from time to time upon exercise of each of the Pre-Funded Warrants) pursuant to this prospectus supplement and the accompanying prospectus. The Pre-Funded Warrants will be exercisable immediately and expire when exercised in full are each exercisable for one share of our Common Stock. The purchase price of each Pre-Funded Warrant is equal to the public offering price at which a share of Common Stock is sold to the public in this offering, minus \$0.001, and the exercise price of each Pre-Funded Warrant is \$0.001 per share of Common Stock.

We intend to use up to \$35 million of the net proceeds from this offering to repurchase 520,229 shares of our Common Stock at \$63.6098 per share, which is the same price per share as the price at which the shares are being sold to the public in this offering, less underwriting discounts and commissions, from Tactic Pharma, LLC, an existing stockholder. We intend to use the remaining net proceeds from this offering to fund 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 “Use of Proceeds.”

Our Common Stock is listed for trading on the Nasdaq Capital Market under the symbol “MNPR.” On September 23, 2025, the last reported sale price of our Common Stock was \$67.67 per share.

We are a “smaller reporting company” under applicable federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements. See “*Prospectus Supplement Summary – Implications of Being a Smaller Reporting Company.*”

Investing in our securities involves significant risks. These risks are described under the caption “Risk Factors” beginning on page S-8 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

	Per share	Per Pre-Funded Warrant	Total
Public offering price	\$ 67.6700	\$ 67.6690	\$ 134,998,998
Underwriting discounts and commissions (1)	\$ 4.0602	\$ 4.0602	\$ 8,099,997
Proceeds to Monopar, before expenses	\$ 63.6098	\$ 63.6088	\$ 126,899,000

(1) See “Underwriting” beginning on page S-19 of this prospectus supplement for additional disclosure regarding the underwriting compensation.

The underwriters expect to deliver the Common Stock and Pre-Funded Warrants to purchasers against payment therefor on or about September 25, 2025.

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.

Morgan Stanley Leerink Partners Barclays

The date of this prospectus supplement is September 23, 2025

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement on Form S-3 (File No. 333-289947) that we filed with the Securities and Exchange Commission (the “SEC”), utilizing a “shelf” registration process. Under this prospectus supplement and the accompanying prospectus, we may offer and sell our securities from time to time as described herein.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of our securities and also supplements information contained in the accompanying prospectus. The second part, the accompanying prospectus dated September 9, 2025, gives more general information, some of which may not apply to this offering.

This prospectus supplement may add, update or change information contained in the accompanying prospectus. If there is any inconsistency between the information in this prospectus supplement and the information contained in the accompanying prospectus, the information in this prospectus supplement will apply and will supersede the information in the accompanying prospectus.

In addition, to the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any earlier dated document incorporated by reference herein, on the other hand, you should rely on the information in this prospectus supplement. Additional prospectus supplements or free writing prospectuses 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 additional prospectus supplements or related free writing prospectuses, together with the information incorporated herein and therein by reference as described under the heading “Incorporation of Documents by Reference,” before buying any of our securities 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 additional prospectus supplements or related free writing prospectuses that we may authorize to be provided to you. We have not, and the underwriters have 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 or the accompanying prospectus or any additional prospectus supplements or related free writing prospectuses 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 securities 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 and any additional prospectus supplements or related free writing prospectuses 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 additional prospectus supplements or related free writing prospectuses, or any sale of our securities.

This prospectus supplement and the accompanying prospectus contain 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 and the accompanying prospectus are 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 and the accompanying prospectus, the terms “we”, “us”, “our”, “Company”, “Monopar Therapeutics” and “Monopar” refer to Monopar Therapeutics Inc., a Delaware corporation.

SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. For a more complete understanding of our Company and this offering, we encourage you to read and consider carefully the more detailed information incorporated by reference into this prospectus supplement, and the information referred to under the heading “Risk Factors” in this prospectus supplement beginning on page S-8.

Overview

Monopar Therapeutics Inc. is a clinical-stage biopharmaceutical company developing an innovative treatment for Wilson disease and novel radiopharmaceuticals for oncology. Our Wilson disease product candidate is ALXN1840, a late-stage, investigational once-daily, oral medicine. Our radiopharmaceutical programs consist of Phase 1-stage MNPR-101-Zr for imaging advanced cancers, and Phase 1a-stage MNPR-101-Lu and late preclinical-stage MNPR-101-Ac for the treatment of advanced cancers, that express urokinase plasminogen activator receptor (“uPAR”). We build our drug development pipeline through both in-house efforts and licensing of late preclinical- and clinical-stage therapeutics, leveraging our scientific and clinical expertise to mitigate risk and to accelerate development.

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

Recent Developments

On September 14, 2025, Monopar presented an analysis of the pooled efficacy outcomes from three independent clinical trials and safety data from a fourth independent clinical trial for ALXN1840. Key findings presented included:

- Statistically significant neurologic improvement from baseline on the Unified Wilson Disease Rating Scale Part II (patient-reported symptoms) and Part III (clinician-reported symptoms) was sustained over six years;
- Patients who crossed over from standard of care (“SoC”) to ALXN1840 showed additional neurological improvement, including a majority of patients who had worsened on SoC demonstrating a reversal on ALXN1840;
- Statistically significant psychiatric improvement from baseline was sustained over multiple years, as measured by the Brief Psychiatric Rating Scale;
- Neurological benefit was observed consistently across multiple independent studies; and
- Across more than 645 patient-years on ALXN1840, less than 1% of patients experienced a drug-related neurological serious adverse event.

In addition, on September 19, 2025, the Journal of Hepatology published a peer-reviewed Letter to the Editor, authored by leading Wilson disease physicians, entitled “Oral Bis-choline Tetrathiomolybdate Rapidly Improves Copper Balance in Patients with Wilson Disease.” In the Letter to the Editor, the authors explain that the earlier conclusion from the Phase 2 ALXN1840-WD-204 study (NCT04573309) – that ALXN1840 did not promote copper excretion – was based on a methodological limitation in the copper balance equation, which only accounted for certain routes of copper loss. By controlling for the other routes of copper loss by comparing pre- and post-ALXN1840 treatment, the analysis demonstrates that ALXN1840 statistically significantly improved copper balance (increases copper excretion) over the duration of the study.

Key findings on the effect of ALXN1840 on copper balance reported in the Letter include:

- **15 mg/day treatment period:** mean daily difference -0.367 mg (p=0.005)
- **Overall treatment period** (includes patients with dose changes to 15 mg every other day and to 30 mg/day): mean daily difference -0.289 mg (p=0.023)

- **Cumulative mean change from baseline:** -6.08 mg (95% CI: -10.18 mg to -1.98 mg).

Resources and Financial Condition

Our cash, cash equivalents and investments as of June 30, 2025, were \$53.3 million. After giving effect to our receipt of net proceeds of approximately \$91.9 million in this offering, after deducting underwriting discounts and commissions and before estimated offering expenses payable by us and after giving effect to the Stock Repurchase (as defined below), we estimate we will have sufficient funds to meet our obligations and anticipated spending needs based on our current business plan at least through December 31, 2027.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company” as defined in the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Smaller reporting companies may take advantage of certain scaled disclosures, including, among other things, providing only two years of audited financial statements in their Annual Report on Form 10-K and having reduced disclosure obligations regarding executive compensation. In addition, as a non-accelerated filer, we are not required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. We will continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. For so long as we remain a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosures.

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.

Trademark Notice

All trademarks, service marks and trade names in this prospectus supplement 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

Securities Offered by Us	1,034,433 shares of Common Stock 960,542 Pre-Funded Warrants
Pre-Funded Warrants Offered by Us	In lieu of shares of Common Stock to certain investors that so choose, we are offering Pre-Funded Warrants to purchase shares of Common Stock. Each Pre-Funded Warrant will have an initial exercise price per share of \$0.001, subject to certain adjustments. The purchase price of each Pre-Funded Warrant is equal to the price at which the share of Common Stock is being sold to the public in this offering, minus \$0.001. The Pre-Funded Warrants are exercisable immediately and do not expire. For more information, see the section titled “Description of Pre-Funded Warrants.” This prospectus supplement also relates to the offering of the shares of Common Stock issuable upon the exercise of such Pre-Funded Warrants.
Common Stock and Pre-Funded Warrants to be Outstanding After This Offering and the Stock Repurchase (1)	6,611,661 shares of Common Stock 1,843,303 Pre-Funded Warrants (includes previously issued and outstanding pre-funded warrants)
Use of Proceeds and Stock Repurchase	We intend to use up to \$35 million of the net proceeds from this offering to repurchase 550,229 shares of our Common Stock held by Tactic Pharma, LLC at \$63.6098 per share, which is the same price per share as the price at which the shares are being sold to the public in this offering, less underwriting discounts and commissions (the “Stock Repurchase”). The Stock Repurchase is expected to occur in a privately negotiated transaction between us and the Selling Stockholder. However, as of the date of this prospectus supplement, we have not yet entered into any agreement with respect to the Stock Repurchase, so no assurance can be provided that it will be completed. Tactic Pharma, LLC is an existing significant stockholder of the Company, holding approximately 13.3% of our outstanding shares of Common Stock prior to this offering and the Stock Repurchase. Chandler D. Robinson, our Chief Executive Officer and a member of our board of directors, is a managing member of Tactic Pharma, LLC. This offering is not contingent on the Stock Repurchase. After giving effect to the Stock Repurchase, 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. There is no established public trading market for the Pre-Funded Warrants, and we do not expect a market to develop. In addition, we do not intend to list the Pre-Funded Warrants on The Nasdaq Capital Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the Pre-Funded Warrants will be limited.
Risk Factors	See “Risk Factors” beginning on page S-8 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 6,127,457 shares of our Common Stock outstanding as of June 30, 2025, plus the 1,034,433 shares of Common Stock issued in this offering, less the 550,229 shares of Common Stock intended to be repurchased in the Stock Repurchase. Such amount excludes, as of such date:
- 960,542 shares of Common Stock underlying the Pre-Funded Warrants issued in this offering, each with an exercise price of \$0.001 per share, and 882,761 shares of Common Stock underlying pre-funded warrants previously issued and outstanding, each with an exercise price of \$0.001 per share;
 - 128,408 shares of Common Stock issuable upon the vesting of restricted stock units;
 - 606,525 shares of Common Stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$26.6663 per share; and
 - 430,761 shares of Common Stock reserved for future issuance under our 2016 Stock Incentive Plan.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding to invest in our securities, 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, 2024 and subsequent Quarterly Reports on Form 10-Q, 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”), 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 supplement and the accompanying prospectus and any additional prospectus supplements or free writing prospectuses that we have authorized for use in connection with this offering before you make a decision to invest in our securities. 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 securities.

Risks Related to this Offering

The price of our Common Stock may decline and/or remain volatile.

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 experienced a significant price increase and volatility recently. The price per share of our Common Stock could significantly decrease and return to prior levels, and we may experience continued volatility and volume fluctuations. Our small public float and relatively low and inconsistent trading volumes exacerbate volatility.

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 to give effect to the Stock Repurchase and to fund 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 numbers 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 cannot predict the effect, if any, that market sales of shares of our Common Stock or the availability of shares of our Common Stock for sale will have on the market price of our Common Stock prevailing from time to time. Sales of substantial numbers of shares of our Common Stock in the public market, or the perception that those sales will occur, could cause the market price of our Common Stock to decline or be depressed. The shares of Common Stock issued in connection with this offering (and upon exercise of the Pre-Funded Warrants) will be freely tradable without restriction or further registration under the Securities Act. In connection with this offering, we and our directors and executive officers have agreed with the underwriters to a “lock-up,” pursuant to which neither we nor they will sell, hedge or otherwise dispose of any shares, for 60 days after the closing of this offering pursuant to this prospectus supplement, subject to certain exceptions. See “Underwriting.” Following the expiration of the applicable lock-up period, all these shares of our Common Stock will also be eligible for future sale. In the future, we may also issue our securities if we need to raise capital. As a clinical and preclinical stage biotechnology company, we require substantial capital to further the development of our programs through potential approval and commercialization. We could also issue shares for acquisitions or strategic partnerships. The number of shares of our Common Stock issued in the future could constitute a material portion of our then-outstanding shares of Common Stock. Any perceived excess in the supply of our shares in the market could negatively impact our share price and any issuance of additional securities may result in additional dilution to you.

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.

We do not anticipate paying cash dividends and, accordingly, stockholders must rely on share appreciation for any return on their investment.

We currently intend to retain our future earnings, if any, to fund the development and growth of our businesses and do not anticipate that we will declare or pay any cash dividends on our capital stock in the foreseeable future. See the section titled “Dividend Policy” in this prospectus supplement. In addition, our ability to pay may be limited by covenants of any future indebtedness we incur. As a result, capital appreciation, if any, of our Common Stock will be your sole source of gain on your investment for the foreseeable future. Investors seeking cash dividends should not invest in our Common Stock.

There is no public market for the Pre-Funded Warrants being offered by us in this offering.

There is no established public trading market for the Pre-Funded Warrants being sold in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the Pre-Funded Warrants on any securities exchange or recognized trading system. Without an active market, the liquidity of the Pre-Funded Warrants will be limited.

Holders of the Pre-Funded Warrants will have no rights as common stockholders until they acquire our Common Stock.

Until you acquire shares of our Common Stock upon exercise of the Pre-Funded Warrants, you will have no rights with respect to our Common Stock issuable upon exercise of the Pre-Funded Warrants, including the right to receive dividend payments, vote or respond to tender offers. Upon exercise of your Pre-Funded Warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Significant holders or beneficial holders of shares of our Common Stock may not be permitted to exercise the Pre-Funded Warrants that they hold.

A holder (together with its affiliates and other attribution parties) may not exercise any portion of a Pre-Funded Warrant to the extent that after giving effect to such exercise, the holder would own more than 9.99% of our outstanding Common Stock immediately after exercise, which percentage may be changed at the holder’s election to a higher or lower percentage not in excess of 19.99% upon 61 days’ notice to us, subject to the terms of the Pre-Funded Warrants. As a result, you may not be able to exercise your Pre-Funded Warrants for shares of our Common Stock at a time when it would be financially beneficial for you to do so. In such a circumstance, you could seek to sell your Pre-Funded Warrants to realize value, but you may be unable to do so in the absence of an established trading market and due to applicable transfer restrictions.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompany prospectus, and any documents we incorporate by reference herein and in the accompanying prospectus, contain certain forward-looking statements that involve substantial risks and uncertainties. All statements contained in this prospectus supplement and accompanying prospectus and any documents we incorporate by reference, other than statements of historical facts, are forward-looking statements including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

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

- our ability to raise sufficient funds in order for us to support continued clinical, regulatory and commercial development of our programs and to make contractual future milestone payments, as well as our ability to further raise additional funds in the future to support any existing or future product candidate programs through completion of clinical trials, the approval processes and, if applicable, commercialization;
- our ability to raise funds on acceptable terms;
- 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 or any development partners’ research and development activities, including preclinical studies, clinical trials, regulatory submissions, and manufacturing and quality expenses;
- known and unknown risks associated with developing copper-chelating therapies and radiopharmaceutical therapeutics and imaging agents;
- the uncertainty of timeframes for our clinical trials and regulatory reviews for approval to market products;
- uncertainties related to the regulatory discussions we may initiate related to ALXN1840 and the outcome(s) thereof;
- potential delays and/or additional significant expenses related to developing and filing a New Drug Application (“NDA”) for ALXN1840;
- our ability to address the fulfillment and logistical challenges posed by the potential time-limited shelf-life of our current radiopharmaceutical programs or future drug candidates;
- our ability to obtain an adequate supply at reasonable costs of radioisotopes that we are currently using or that we may incorporate in the future into our drug candidates;
- market uptake and competitiveness in terms of pricing, efficacy and safety, of any products for which we receive marketing approval, and our ability to competitively market and position any such products as compared to larger pharmaceutical companies;

- 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 or at all;
- U.S. political leadership developments may affect the economy and future laws, tariffs, and regulations or executive orders, and may in turn lead to increased or decreased governmental control of healthcare and pharmaceuticals, governmental regulations impacting cost requirements and structures for importing ingredients or products or selling therapeutic or imaging products, and governmental legislation, executive orders and/or tariffs affecting other industries which may indirectly increase our costs of obtaining goods and services and our cost of capital;
- the uncertain impact of any COVID-19 resurgence or of another pandemic may have 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 potential for an economic recession, resulting in higher costs for obtaining goods and services and/or making financing more difficult to obtain on acceptable terms or at all;
- the uncertain impact of the Russia-Ukraine war, the Israel-Hamas war, and/or any potential future conflicts on our clinical material manufacturing expenses and timelines, as well as on general political, economic, trade and financial market conditions; and
- the 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. Any forward-looking statements in this prospectus supplement and the accompanying prospectus 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.

You should read this prospectus supplement and the accompanying prospectus and the documents that we incorporate by reference 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

We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and before estimated offering expenses payable by us, will be approximately \$126.9 million.

We intend to use up to \$35 million of the net proceeds from this offering to repurchase 550,229 shares of our Common Stock held by Tactic Pharma, LLC at \$63.6098 per share, which is the same price per share as the price at which the shares are being sold to the public in this offering, less underwriting discounts and commissions (the “Stock Repurchase”). The Stock Repurchase is expected to occur in a privately negotiated transaction between us and Tactic Pharma, LLC. However, as of the date of this prospectus supplement, we have not yet entered into any agreement with respect to the Stock Repurchase, so no assurance can be provided that it will be completed. Tactic Pharma, LLC is an existing significant stockholder of the Company, holding approximately 13.3% of our outstanding shares of Common Stock prior to this offering and the Stock Repurchase. Chandler D. Robinson, our Chief Executive Officer and a member of our board of directors, is a managing member of Tactic Pharma, LLC.

After giving effect to the Stock Repurchase, we intend to use the remainder of 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.

DILUTION

If you invest in our Common Stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our Common Stock immediately after this offering.

The net tangible book value of our Common Stock as of June 30, 2025 was \$52.2 million, or \$8.52 per share, based upon 6,127,457 shares of Common Stock outstanding. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares of Common Stock outstanding as of June 30, 2025.

After giving effect to (i) our issuance and sale of 1,034,433 shares of our Common Stock at the public offering price of \$67.67 per share, (ii) our issuance and sale of Pre-Funded Warrants to purchase 960,542 shares of our Common Stock, (iii) the assumed exercise of all of the Pre-Funded Warrants, as well as 882,761 previously issued and outstanding pre-funded warrants, (iv) the Stock Repurchase in the maximum amount of \$35 million and (v) deduction of underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted pro forma net tangible book value as of June 30, 2025 would have been \$143.7 million, or \$17.00 per share. This represents an immediate increase in net tangible book value of \$8.48 per share to our existing stockholders and immediate dilution in as adjusted pro forma net tangible book value of \$50.67 per share to new investors participating in this offering. Dilution per share to new investors participating in this offering is determined by subtracting as adjusted pro forma net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this calculation on a per share basis.

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.

Public Offering Price Per Share		\$	67.67
Historical Net Tangible Book Value Per Share as of June 30, 2025	\$	8.52	
Increase in Net Tangible Book Value Per Share Attributable to New Investors		8.48	
As Adjusted Pro Forma Net Tangible Book Value Per Share After this Offering	\$	17.00	
Dilution Per Share to New Investors	\$	50.67	

The As Adjusted Pro Forma Net Tangible Book Value Per Share After this Offering is based on 6,127,457 shares of our Common Stock outstanding as of June 30, 2025, plus the 1,034,433 shares of Common Stock issued in this offering and the 960,542 shares of Common Stock issuable pursuant to the Pre-Funded Warrants and 882,761 previously issued and outstanding pre-funded warrants, less the 550,229 shares of Common Stock intended to be repurchased in the Stock Repurchase. Such amount excludes, as of such date:

- 128,408 shares of Common Stock issuable upon the vesting of restricted stock units;
- 606,525 shares of Common Stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$26.6663 per share; and
- 430,761 shares of Common Stock reserved for future issuance under our 2016 Stock Incentive Plan.

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.

DESCRIPTION OF CAPITAL STOCK

We have the authority to issue 40,000,000 shares of Common Stock, \$0.001 par value. As of September 19, 2025, there were 6,169,961 shares of our Common Stock issued and outstanding.

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 by the holders of stock entitled to vote at a meeting of stockholders.

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 (the “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

Our 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 meeting of stockholders actions that may otherwise be favored by the holders of a majority of our outstanding voting securities.

By-law Amendments by the Board

Without limiting the power of our stockholders to amend or repeal our By-laws, our By-laws may be amended or repealed by a majority vote of our Board without any stockholder action.

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.

DESCRIPTION OF PRE-FUNDED WARRANTS

The material terms and provisions of the Pre-Funded Warrants being issued in this offering are summarized below. The following description is subject to, and qualified in its entirety by, the form of Pre-Funded Warrant which will be filed as an exhibit to a Current Report on Form 8-K to be filed by us with the SEC in connection with this offering. You should review the form of Pre-Funded Warrant for a complete description of the terms and conditions applicable to the Pre-Funded Warrants.

Form

The Pre-Funded Warrants will be issued as individual warrant agreements to each individual purchaser of a Pre-Funded Warrant. The form of Pre-Funded Warrant will be filed as an exhibit to a Current Report on Form 8-K that we will file with the SEC.

Term

The Pre-Funded Warrants do not expire.

Exercisability

The Pre-Funded Warrants are exercisable at any time after their original issuance. The Pre-Funded Warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full of the exercise price in immediately available funds for the number of shares of Common Stock purchased upon such exercise. As an alternative to payment of the exercise price in immediately available funds, the holder may, in its sole discretion, elect to exercise the Pre-Funded Warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of our Common Stock determined according to the formula set forth in the Pre-Funded Warrant.

Exercise Limitations

Under the Pre-Funded Warrants, we may not effect the exercise of any Pre-Funded Warrant, and a holder will not be entitled to exercise any portion of any Pre-Funded Warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of our Common Stock beneficially owned by such holder (together with its affiliates and other attribution parties) to exceed 9.99% of the number of issued and outstanding shares of our Common Stock following such exercise, as such percentage ownership is determined in accordance with the terms of the Pre-Funded Warrants. However, any holder of a Pre-Funded Warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior written notice from the holder to us.

Exercise Price

The exercise price of our Common Stock purchasable upon the exercise of the Pre-Funded Warrants is \$0.001 per share. The exercise price of the Pre-Funded Warrants and the number of shares of our Common Stock issuable upon exercise of the Pre-Funded Warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our Common Stock, as well as upon any pro-rata distribution of assets, including cash, stock or other property, to our stockholders.

Transferability

Subject to the restrictions on transfer set forth in the Pre-Funded Warrants and applicable laws, the Pre-Funded Warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

There is no established trading market for the Pre-Funded Warrants, and we do not expect a market to develop. We do not intend to apply for the listing of the Pre-Funded Warrants on the Nasdaq Capital Market or any other national securities exchange or nationally recognized trading system.

Fundamental Transactions

Upon the consummation of a fundamental transaction (as described in the Pre-Funded Warrants, and generally including any reorganization, recapitalization or reclassification of our Common Stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, in which the Company is not the surviving entity, the acquisition of more than 50% of our voting power of our capital stock, or any person or group becoming the beneficial owner of more than 50% of the voting power of our outstanding capital stock), the holders of the Pre-Funded Warrants will be entitled to receive, upon exercise of the Pre-Funded Warrants, the kind and amount of securities, cash or other property that such holders would have received had they exercised the Pre-Funded Warrants immediately prior to such fundamental transaction, without regard to any limitations on exercise contained in the Pre-Funded Warrants.

No Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our Common Stock, the holder of a Pre-Funded Warrant does not have the rights or privileges of a holder of our Common Stock, including any voting rights or the right to receive dividends, until such holder exercises the Pre-Funded Warrant.

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Morgan Stanley & Co. LLC, Leerink Partners LLC and Barclays Capital Inc. are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares of our Common Stock and Pre-Funded Warrants indicated below:

Underwriter	Number of Shares	Number of Pre-Funded Warrants
Morgan Stanley & Co. LLC	486,792	452,020
Leerink Partners LLC	365,094	339,015
Barclays Capital Inc.	182,547	169,507
Total	1,034,433	960,542

The underwriters and the representatives are collectively referred to as the “underwriters” and the “representatives,” respectively. The underwriters are offering the shares of Common Stock and Pre-Funded Warrants subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of Common Stock and Pre-Funded Warrants offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of Common Stock and Pre-Funded Warrants offered by this prospectus supplement if any such shares or Pre-Funded Warrants are taken.

The underwriters initially propose to offer part of the shares of Common Stock and Pre-Funded Warrants directly to the public at the offering prices listed on the cover page of this prospectus supplement and part to certain dealers at a price that represents a concession not in excess of (i) \$0.001 per share of Common Stock under the offering price and (ii) \$0.001 per Pre-Funded Warrant under the offering price. After the initial offering of the shares of Common Stock and Pre-Funded Warrants, the offering price and other selling terms may from time to time be varied by the representatives.

The underwriters have not been engaged to act as warrant agent for the Pre-Funded Warrants or to act as underwriter or agent or otherwise participate in the issuance of the shares of our Common Stock upon the exercise of the Pre-Funded Warrants.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us.

	Per share	Per Pre-Funded Warrant	Total
Public offering price	\$ 67.6700	\$ 67.6690	\$ 134,998,998
Underwriting discounts and commissions	\$ 4.0602	\$ 4.0602	\$ 8,099,997
Proceeds to Monopar, before expenses	\$ 63.6098	\$ 63.6088	\$ 126,899,000

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$0.4 million. We have also agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority up to \$10,000. In addition, the underwriters have agreed to reimburse us for certain expenses in connection with this offering.

Our Common Stock is listed on the Nasdaq Capital Market under the trading symbol “MNPR.” There is no established public trading market for the Pre-Funded Warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Capital Market, any other national securities exchange or any other recognized trading system.

We, our executive officers and directors, and Tactic Pharma, LLC have each agreed not to sell or transfer any Common Stock or securities convertible into or exchangeable or exercisable for Common Stock, for 60 or, in the case of Tactic Pharma, LLC, 90 days after the date of this prospectus supplement without first obtaining the written consent of Morgan Stanley & Co. LLC and Leerink Partners LLC. Specifically, we have agreed, with certain limited exceptions, including the transactions contemplated by the registration of the shares underlying the pre-funded warrants, not to directly or indirectly:

- offer, pledge, sell or contract to sell any Common Stock;
- sell any option or contract to purchase any Common Stock;
- purchase any option or contract to sell any Common Stock;
- grant any option, right or warrant for the sale of any Common Stock;
- otherwise dispose of or transfer any Common Stock;
- request or demand that we file a registration statement related to the Common Stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any Common Stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise;
- publicly disclose an intention to do any of the foregoing

The lock-up provisions apply to Common Stock and to securities convertible into or exchangeable or exercisable for Common Stock. They also apply to common stock owned now or acquired later by the person executing the lock-up agreement or for which the person executing the lock-up agreement later acquires the power of disposition.

In order to facilitate the offering of the Common Stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the Common Stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option to purchase additional shares. The underwriters can close out a covered short sale by exercising the option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option to purchase additional shares. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the Common Stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of Common Stock in the open market to stabilize the price of the Common Stock. These activities may raise or maintain the market price of the Common Stock above independent market levels or prevent or retard a decline in the market price of the Common Stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus supplement in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of Common Stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Selling Restrictions

Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area (each, a Relevant State), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of securities may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- (i) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (ii) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the representatives; or
- (iii) in any other circumstances falling within Article 1(4) of the Prospectus Regulation;

provided that no such offer of the securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to the securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase any securities, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129 (as amended).

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or the FSMA) received by it in connection with the issue or sale of the securities in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

(i) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

(ii) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or

(iii) in any other circumstances falling within Section 86 of the FSMA;

provided that no such offer of the securities shall require us or any of the representatives to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

This prospectus is only for distribution to and directed at: (i) in the United Kingdom, persons having professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and high net worth entities falling within Article 49(2)(a) to (d) of the Order; (ii) persons who are outside the United Kingdom; and (iii) any other person to whom it can otherwise be lawfully distributed, or all such persons together, Relevant Persons. Any investment or investment activity to which this prospectus relates is available only to and will be engaged in only with Relevant Persons, and any person who is not a Relevant Person should not rely on it.

Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, “Japanese Person” means any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, the securities were not offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor;

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law; or

(d) as specified in Section 276(7) of the SFA.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to us, the offering, or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offering of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or the FINMA, and the offering of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities.

Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or the DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The securities to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the securities may only be made to persons, or Exempt Investors, who are “sophisticated investors” (within the meaning of section 708(8) of the Corporations Act), “professional investors” (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the securities without disclosure to investors under Chapter 6D of the Corporations Act.

The securities applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring the securities must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase securities of common stock under the Israeli Securities Law, 5728 - 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 - 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 - 1968, subject to certain conditions, or the Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 - 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our Common Stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 - 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 - 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the securities of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 - 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 - 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

LEGAL MATTERS

Certain legal matters will be passed upon for us by Baker & Hostetler LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Freshfields US LLP.

EXPERTS

The consolidated financial statements of Monopar Therapeutics Inc. as of December 31, 2024 and 2023, and for each of the two years in the period ended December 31, 2024, incorporated in prospectus supplement by reference to its Annual Report on Form 10-K for the year ended December 31, 2024, 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 references 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 of which this prospectus supplement forms a part, at the SEC's website at www.sec.gov. We also maintain a website at <http://www.monopar.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 materials are 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.

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 supplement. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement. We incorporate by reference into this prospectus supplement and the registration statement of which it and the accompanying prospectus are a part the information and documents listed below that we have filed with the SEC:

- our Quarterly Report on [Form 10-Q](#) for the quarter ended June 30, 2025, filed with the SEC on August 12, 2025;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2025, filed with the SEC on May 13, 2025;
- our Annual Report on [Form 10-K](#) for the year ended December 31, 2024, filed with the SEC on March 31, 2025 (“2024 Form 10-K”);
- the information specifically incorporated by reference into the 2024 Form 10-K from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 30, 2025;
- our Current Reports on Form 8-K, filed with the SEC on [February 24, 2025](#), [March 3, 2025](#), and [June 23, 2025](#), 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 S-15 of this prospectus supplement 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 until 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 documents modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus supplement and the accompanying prospectus are 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

\$300,000,000



Monopar Therapeutics

Common Stock
Warrants
Subscription Rights
Units

We may offer and sell an indeterminate number of shares of our common stock, par value \$0.001 per share (the “Common Stock”), warrants to purchase Common Stock (the “Warrants”), subscription rights to purchase securities that may be offered under this prospectus (the “Subscription Rights”) and units comprised of one or more of the other securities that may be offered under this prospectus (the “Units”, and together with our Common Stock, Warrants and Subscription Rights, the “Securities”) from time to time under this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest.

We may offer our Securities in one or more offerings in amounts, at prices, and on terms determined at the time of the offerings. We may sell our Securities through agents, underwriters or 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 Securities that we may offer. Each time we sell our Securities, 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 Securities. This prospectus may not be used to consummate a sale of our Securities unless accompanied by the applicable prospectus supplement.

Investing in our Securities 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 Securities.

Neither the SEC 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 September 9, 2025

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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 Securities. 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 2, and in the documents incorporated by reference into this prospectus.

Overview

Monopar Therapeutics Inc. is a clinical-stage biopharmaceutical company developing an innovative treatment for Wilson disease and novel radiopharmaceuticals for oncology. Our Wilson disease product candidate is ALXN1840, a late-stage, investigational once-daily, oral medicine. Our radiopharmaceutical programs consist of Phase 1-stage MNPR-101-Zr for imaging advanced cancers, and Phase 1a-stage MNPR-101-Lu and late preclinical-stage MNPR-101-Ac for the treatment of advanced cancers, that express urokinase plasminogen activator receptor (“uPAR”). We build our drug development pipeline through both in-house efforts and licensing of late preclinical- and clinical-stage therapeutics, leveraging our scientific and clinical expertise to mitigate risk and to accelerate development.

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

We are a “smaller reporting company” as defined in the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Smaller reporting companies may take advantage of certain scaled disclosures, including, among other things, providing only two years of audited financial statements in their Annual Report on Form 10-K and having reduced disclosure obligations regarding executive compensation. In addition, as a non-accelerated filer, we are not required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. We will continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. For so long as we remain a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosures.

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, 2024 and in our subsequent Quarterly Reports on Form 10-Q, as updated by our subsequent filings under 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 could result in you losing 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 Securities, as described in this prospectus, from time to time in one or more offerings. Each time we sell our Securities, 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 Securities, you should carefully read both this prospectus and any prospectus supplement, together with the additional information incorporated by reference 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 Securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, and 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 SEC, as applicable. 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 Securities.

We will not use this prospectus to offer and sell our Securities 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 “Securities Act”), and Section 21E of the Exchange 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 order for us to support continued clinical, regulatory and commercial development of our programs and to make contractual future milestone payments, as well as our ability to further raise additional funds in the future to support any existing or future product candidate programs through completion of clinical trials, the approval processes and, if applicable, commercialization;
- our ability to raise funds on acceptable terms;
- 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 or any development partners’ research and development activities, including preclinical studies, clinical trials, regulatory submissions, and manufacturing and quality expenses;
- known and unknown risks associated with developing copper-chelating therapies and radiopharmaceutical therapeutics and imaging agents;
- the uncertainty of timeframes for our clinical trials and regulatory reviews for approval to market products;
- uncertainties related to the regulatory discussions we may initiate related to ALXN1840 and the outcome(s) thereof;
- potential delays and/or additional significant expenses related to developing and filing a New Drug Application (“NDA”) for ALXN1840;
- our ability to address the fulfillment and logistical challenges posed by the potential time-limited shelf-life of our current radiopharmaceutical programs or future drug candidates;
- our ability to obtain an adequate supply at reasonable costs of radioisotopes that we are currently using or that we may incorporate in the future into our drug candidates;
- market uptake and competitiveness in terms of pricing, efficacy and safety, of any products for which we receive marketing approval, and our ability to competitively market and position any such products as compared to larger pharmaceutical companies;
- 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 or at all;

- U.S. political leadership developments may affect the economy and future laws, tariffs, and regulations or executive orders, and may in turn lead to increased or decreased governmental control of healthcare and pharmaceuticals, governmental regulations impacting cost requirements and structures for importing ingredients or products or selling therapeutic or imaging products, and governmental legislation, executive orders and/or tariffs affecting other industries which may indirectly increase our costs of obtaining goods and services and our cost of capital;
- the uncertain impact of any COVID-19 resurgence or of another pandemic may have 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 potential for an economic recession, resulting in higher costs for obtaining goods and services and/or making financing more difficult to obtain on acceptable terms or at all;
- the uncertain impact of the Russia-Ukraine war, the Israel-Hamas war, and/or any potential future conflicts on our clinical material manufacturing expenses and timelines, as well as on general political, economic, trade and financial market conditions; and
- the uncertainty of our financial projections and operational timelines 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 to 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.

USE OF PROCEEDS

Unless otherwise specified in a prospectus supplement accompanying this prospectus, the net proceeds from the sale by us of the Securities to which this prospectus relates will be used for general corporate purposes. Net proceeds may be temporarily invested prior to use. When we offer and sell the Securities to which this prospectus relates, the prospectus supplement related to such offering will set forth our intended use of the proceeds, if any, received from the sale of such Securities.

DESCRIPTION OF CAPITAL STOCK

We have the authority to issue 40,000,000 shares of Common Stock, \$0.001 par value. As of August 25, 2025, there were 6,169,961 shares of our Common Stock issued and outstanding.

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 by the holders of stock entitled to vote at a meeting of stockholders.

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 (the “By-laws”) provide that directors will be elected by a plurality of the votes cast by the shares present in person or represented by proxy at a meeting of stockholders at which a quorum is present and entitled to vote at such meeting. There is no cumulative voting, and accordingly, directors may be elected with a vote of holders of fewer than a majority of the outstanding Common Stock.

Our 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

Our 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 meeting of stockholders actions that may otherwise be favored by the holders of a majority of our outstanding voting securities.

By-law Amendments by the Board

Without limiting the power of our stockholders to amend or repeal our By-laws, our By-laws may be amended or repealed by a majority vote of our Board without any stockholder action.

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.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplement and free writing prospectus, summarizes the material terms and provisions of the Warrants that we may offer under this prospectus, which may consist of Warrants to purchase Common Stock. Warrants may be offered independently or in combination with Common Stock offered by any prospectus supplement. While the terms we have summarized below will apply generally to any Warrants that we may offer under this prospectus, we will describe the particular terms of any series of Warrants in more detail in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

General

The applicable prospectus supplement will describe the following terms of any Warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the Warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the Warrants will begin and the date on which that right will expire or, if you may not continuously exercise the Warrants throughout that period, the specific date or dates on which you may exercise the Warrants;
- whether the Warrants will be issued in definitive or global form or in any combination of these forms;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent, if any, for the Warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the Warrants on any securities exchange;
- if applicable, the minimum or maximum amount of the Warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions, and other provisions for changes to or adjustment in the exercise price, of the Warrants, if any;
- any redemption or call provisions; and
- any additional terms of the Warrants, including terms, procedures and limitations relating to the exchange or exercise of the Warrants.

Exercise of Warrants

Each Warrant will entitle the holder to purchase the Common Stock that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, Warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the Warrants offered thereby. After the close of business on the expiration date, unexercised Warrants will become void.

Upon receipt of payment and the properly completed and duly executed Warrant or warrant certificate, as applicable, at the corporate trust office of the warrant agent, if any, or at any other office indicated in the prospectus supplement, including ours, we will, as soon as practicable, issue and deliver the Common Stock purchasable upon such exercise. If fewer than all of the Warrants (or the Warrants represented by such warrant certificate) are exercised, a new Warrant or a new warrant certificate, as applicable, will be issued for the remaining Warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any Warrant. A single bank or trust company may act as a warrant agent for more than one issue of Warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or Warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a Warrant may, without the consent of the related warrant agent or of the holder of any other Warrant, enforce by appropriate legal action its right to exercise, and receive the Common Stock purchasable upon exercise of, its Warrants.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue Subscription Rights to purchase our Common Stock, Warrants, or Units consisting of some or all of these Securities. These Subscription Rights may be offered independently or together with any other Securities offered hereby and may or may not be transferable by the stockholder receiving the Subscription Rights in such offering. In connection with any offering of Subscription Rights, we may enter into a standby arrangement with one or more underwriters or other purchasers, pursuant to which the underwriters or other purchasers may be required to purchase any Securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any Subscription Rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

- the price, if any, for the Subscription Rights;
- the exercise price payable for our Common Stock, Warrants, or Units consisting of some or all of these Securities, upon the exercise of the Subscription Rights;
- the number of Subscription Rights to be issued to each stockholder;
- the number and terms of our Common Stock, Warrants, or Units consisting of some or all of these Securities, which may be purchased per each Subscription Right;
- the extent to which the Subscription Rights are transferable;
- any other terms of the Subscription Rights, including the terms, procedures and limitations relating to the exchange and exercise of the Subscription Rights;
- the date on which the right to exercise the Subscription Rights shall commence, and the date on which the Subscription Rights shall expire;
- the extent to which the Subscription Rights may include an over-subscription privilege with respect to unsubscribed Securities or an over-allotment privilege to the extent the Securities are fully subscribed; and
- if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by us in connection with the offering of Subscription Rights.

DESCRIPTION OF UNITS

We may issue Units comprised of one or more of the other Securities that may be offered under this prospectus, in any combination. The following, together with the additional information we may include in any applicable prospectus supplement, summarizes the material terms and provisions of the Units that we may offer under this prospectus. While the terms summarized below will apply generally to any Units we may offer, we will describe the particular terms of any series of Units in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any Units offered under that prospectus supplement may differ from the terms described below. Specific unit agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus.

Each Unit will be issued so that the holder of the Unit is also the holder of the Securities included in the Unit. Thus, the holder of a Unit will have the rights and obligations of a holder of any included Securities. The unit agreement under which a Unit is issued may provide that the Securities included in the Unit may not be held or transferred separately at any time, or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of Units being offered, including:

- the material terms of the Units and of the Securities comprising the Units, including whether and under what circumstances those Securities may be held or transferred separately;
- any material provisions relating to the issuance, payment, settlement, transfer or exchange of the Units or of the Securities comprising the Units; and
- any material provisions of the governing unit agreement that differ from those described above.

We may issue Units in such amounts and in such numbers of distinct series as we determine.

The provisions described in this section, as well as those described under “*Description of Capital Stock*” and “*Description of Warrants*” will apply to each Unit, as applicable, and to any Common Stock or Warrant included in each Unit, as applicable.

Unit Agent

The name and address of the unit agent, if any, for any Units we offer will be set forth in the applicable prospectus supplement.

Enforceability of Rights by Holders of Units

Each unit agent, if any, will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any Unit. A single bank or trust company may act as a unit agent for more than one series of Units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or Unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a Unit may, without the consent of the related unit agent or of the holder of any other Unit, enforce by appropriate legal action its rights as holder under any security included in the Unit.

PLAN OF DISTRIBUTION

We may sell our Securities covered in this prospectus in one or more of the following ways:

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

The distribution of our Securities 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 Securities, 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, to the extent applicable:

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

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

If underwriters are used in the sale of our Securities, our Securities 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 Securities may be offered to the public either through underwriting syndicates, represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase our Securities will be subject to certain conditions precedent. The underwriters may be obligated to purchase all of our Securities if they purchase any of our Securities.

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 Securities 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 Securities 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, or to contribution with respect to payments which the agents or underwriters may be required to make in connection therewith. Agents and underwriters may, in the ordinary course of business, be customers of, engage in transactions with, or perform services for us.

We may enter into derivative transactions with third parties, or sell our securities 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 Securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, each third party may use our securities pledged by us, or borrowed from us or others, to settle those sales or to close out any related open borrowings of our securities, and may use our Securities received from us in settlement of those derivatives to close out any related open borrowings of our securities. Each 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.

EXPERTS

The consolidated financial statements of Monopar Therapeutics Inc. as of December 31, 2024 and 2023, and for each of the two years in the period ended December 31, 2024, incorporated in this Prospectus by reference to its Annual Report on Form 10-K for the year ended December 31, 2024, 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 this shelf registration statement on Form S-3 under the Securities Act with respect to our Securities 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 Securities, 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, such references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contracts, agreements or other documents.

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 materials are 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.

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 Quarterly Report on Form [10-Q](#) for the quarter ended June 30, 2025, filed with the SEC on August 12, 2025;
- our Quarterly Report on Form [10-Q](#) for the quarter ended March 31, 2025, filed with the SEC on May 13, 2025;
- our Annual Report on Form [10-K](#) for the year ended December 31, 2024, filed with the SEC on March 31, 2025 (“2024 Form 10-K”);
- the information specifically incorporated by reference into our 2024 Form 10-K from our Proxy Statement regarding our Annual Meeting of Stockholders on June 17, 2025, on [DEF14A](#), filed with the SEC on April 30, 2025;
- our Current Reports on Form 8-K, filed with the SEC on [February 24, 2025](#), [March 3, 2025](#), and [June 23, 2025](#), 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 amended and 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.



1,034,433 Shares of Common Stock
Pre-Funded Warrants to Purchase 960,542 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Morgan Stanley Leerink Partners Barclays

The date of this Prospectus Supplement is September 23, 2025

Calculation of Filing Fee Tables

S-3

Monopar Therapeutics

Table 1: Newly Registered and Carry Forward Securities

☒ Not Applicable

		Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid in Connection with Unsold Securities to be Carried Forward
Newly Registered Securities													
Fees to be Paid	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Fees Previously Paid	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Carry Forward Securities													
Carry Forward Securities	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total Offering Amounts:							\$ 0.00		\$ 0.00				
Total Fees Previously Paid:									\$ 0.00				
Total Fee Offsets:									\$ 0.00				
Net Fee Due:									\$ 0.00				

Table 2: Fee Offset Claims and Sources

☒ Not Applicable

		Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
Rules 457(b) and 0-11(a)(2)												
Fee Offset Claims	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Fee Offset Sources	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Rule 457(p)												
Fee Offset Claims	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Fee Offset Sources	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 3: Combined Prospectuses

☒ Not Applicable

	Security Type	Security Class Title	Amount of Securities Previously Registered	Maximum Aggregate Offering Price of Securities Previously Registered	Form Type	File Number	Initial Effective Date
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Narrative Disclosure

The maximum aggregate offering price of the securities to which the prospectus relates is \$134,998,998.00. The prospectus is a final prospectus for the related offering.

The prospectus supplement to which this Exhibit is attached is a final prospectus for the related offering. The maximum aggregate offering price of that offering is \$134,998,998.