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As filed with the Securities and Exchange Commission on September 14, 2018

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

AMENDMENT NO. 2

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

MERSANA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

04-3562403
(I.R.S Employer
Identification No.)

**840 Memorial Drive
Cambridge, Massachusetts 02139
(617) 498-0020**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive office)

**Anna Protopapas
President and Chief Executive Officer
Mersana Therapeutics, Inc.
840 Memorial Drive
Cambridge, Massachusetts 02139
(617) 498-0020**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:

**Marc A. Rubenstein, Esq.
Ropes & Gray LLP
Prudential Tower
800 Boylston St.
Boston, Massachusetts 02199
(617) 951-7000**

**From time to time after the effectiveness of the registration statement
(Approximate date of commencement of proposed sale to the public)**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)(2)	Amount of registration fee(2)(3)(4)
Common Stock, \$0.0001 par value per share(4)	—	—
Preferred Stock(5)	—	—
Warrants(6)	—	—
Units(7)	—	—
Total	\$250,000,000	\$31,125

- (1) Pursuant to Rule 457(i) under the Securities Act of 1933, as amended, or the Securities Act, the securities registered hereunder include such indeterminate number of securities as may be issued upon conversion or exchange of any preferred stock, warrants or units registered hereunder that provide for conversion or exchange, upon exercise of warrants or pursuant to the anti-dilution provisions of any such securities.
- (2) The proposed maximum per unit and aggregate offering prices per class of securities will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered under this registration statement and is not specified as to each class of security pursuant to General Instruction II.D of Form S-3 under the Securities Act.
- (3) Calculated pursuant to Rule 457(o) under the Securities Act.
- (4) This amount was previously paid in connection with the initial filing of this Registration Statement on July 2, 2018.
- (5) Includes an indeterminate number of shares of common stock or preferred stock as may be sold from time to time, at indeterminate prices.
- (6) Any securities registered hereunder with respect to the primary offering may be sold separately or as units with other securities registered hereunder. The proposed maximum offering price per unit will be determined by the registrant in connection with the issuance of the securities. In no event will the aggregate offering price of all securities issued from time to time pursuant to this registration statement exceed \$250,000,000.
- (7) Each unit will be issued under a unit agreement and will represent an interest in two or more securities, which may or may not be separable from one another.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains a prospectus and a prospectus supplement:

- a base prospectus covering the offering, issuance and sale of up to \$250,000,000 of common stock, preferred stock, warrants or units of Mersana Therapeutics, Inc. by us; and
- a sales agreement prospectus supplement covering the offering, issuance and sale of up to \$75,000,000 of our common stock that may be issued and sold under a sales agreement with Cowen and Company, LLC.

The base prospectus immediately follows this explanatory note. The sales agreement prospectus supplement immediately follows the base prospectus. Upon termination of the sales agreement with Cowen, any portion of the \$75,000,000 included in the sales agreement prospectus supplement that is not sold pursuant to the sales agreement will be available for sale in other offerings pursuant to the base prospectus, and if no shares are sold under the sales agreement, the full \$250,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated September 14, 2018

PROSPECTUS

\$250,000,000



Common Stock

Preferred Stock

Warrants

Units

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, up to an aggregate amount of \$250,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities and their compensation will be described in the applicable prospectus supplement.

Our common stock is traded on The Nasdaq Global Select Market under the symbol "MRSN." On September 12, 2018, the closing price of our common stock was \$14.23.

Investing in our securities involves risks. See "Risk Factors" on page 3, and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

Prospectus dated _____, 2018

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You should rely only on the information contained in, or incorporated by reference into, this prospectus. We have not authorized anyone to give you information different from that contained in this prospectus. We are not making an offer to sell these securities in any jurisdiction where the offer is not permitted. The information contained in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of when this prospectus is delivered or when any sale of our securities occurs. Our business, financial condition, results of operations and prospects may have changed since that date.

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this shelf registration process, we may offer to sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$250,000,000. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the applicable prospectus supplement, including all documents incorporated herein by reference, together with additional information described under "Where You Can Find More Information" below.

This prospectus does not include all of the information that is in the registration statement. We omitted certain parts of the registration statement from this prospectus as permitted by the SEC. We refer you to the registration statement and its exhibits for additional information about us and the securities that may be sold under this prospectus.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement, if any, is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

"Mersana Therapeutics," "Mersana," the "Company," "we," "us," "our" and similar names refer to Mersana Therapeutics, Inc. and its consolidated subsidiary, unless we state otherwise or the context otherwise requires.

SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. The summary may not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, including "Risk Factors" contained in this prospectus and the documents incorporated by reference herein, before making an investment decision.

Overview

We are a clinical stage biopharmaceutical company focused on developing antibody drug conjugates, or ADCs, that offer a clinically meaningful benefit for cancer patients with significant unmet need. We have leveraged 20 years of industry learning in the ADC field to develop proprietary technologies that enable us to design ADCs to have improved efficacy, safety and tolerability relative to existing ADC therapies. Our most advanced platform, Dolaflexin, has been used to generate a pipeline of proprietary ADC product candidates to address patient populations that are not currently amenable to treatment with traditional ADC-based therapies. Our first product candidate, XMT-1522, is a HER2-targeted ADC currently in a Phase 1 dose escalation study primarily in breast cancer patients as well as non-small cell lung cancer, or NSCLC, and gastric cancer. Upon the completion of dose escalation, we plan to expand clinical development of XMT-1522 into additional breast cancer, NSCLC, and gastric cancer patient populations, all of which are not adequately addressed by existing HER2 therapies. Our second product candidate, XMT-1536, is an ADC targeting NaPi2b, an antigen broadly expressed in ovarian cancer and NSCLC. XMT-1536 entered clinical development in late 2017 and is currently in a Phase 1 dose escalation study. Beyond our two lead product candidates, we continue to invest in our earlier stage product candidates and in our ADC technologies. In addition, we have established a strategic partnership with Takeda Pharmaceutical Company Limited, or Takeda, under which it obtained rights to XMT-1522 outside of the United States and Canada. We have also established strategic research and development partnerships with Takeda and Merck KGaA for the development and commercialization of additional ADC product candidates against a limited number of targets selected by our partners based on our Dolaflexin platform. We believe the potential of our ADC technologies, supported by our world-class management team and protected by our robust intellectual property portfolio, will allow us to develop targeted and highly tailored therapies to help cancer patients triumph over cancer.

We were incorporated in the state of Delaware in February 2002 as Nanopharma Corp., and we changed our name to Mersana Therapeutics, Inc. in November 2005. Our principal executive offices are located at 840 Memorial Drive, Cambridge, Massachusetts 02139, and our telephone number is (617) 498-0020. Our Internet website is www.mersana.com.

RISK FACTORS

Investing in our securities involves a high degree of risk. See "Part I, Item 1A—Risk Factors" in our most recent Annual Report on Form 10-K and "Part II, Item 1A—Risk Factors" in any subsequent Quarterly Report on Form 10-Q incorporated by reference in this prospectus, in any other documents we file with the SEC that are deemed incorporated by reference into this prospectus and the "Risk Factors" section in the applicable prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our securities. Before you invest in our securities, you should carefully consider these risks as well as other information we include or incorporate by reference into this prospectus and the applicable prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus.

FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the other documents we have filed with the SEC that are incorporated herein by reference, contain forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. The words "anticipate," "believe," "estimate," "expect," "goal," "intend," "may," "seek," "plan," "predict," "project," "target," "potential," "will," "would," "possible," "could," "should," "continue," "contemplate" or the negative of these terms or other 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:

- the initiation, cost, timing, progress and results of our current and future research and development activities, preclinical studies and clinical trials;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- the timing of, and our ability to obtain and maintain, regulatory approvals for our product candidates;
- our ability to quickly and efficiently identify and develop additional product candidates;
- our ability to advance any product candidate into, and successfully complete, clinical trials;
- our intellectual property position, including with respect to our trade secrets; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2017 and any subsequent Quarterly Reports on Form 10-Q, each incorporated by reference in this prospectus, and in the "Risk Factors" section in the applicable prospectus supplement. See "Where You Can Find More Information." Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we make.

We cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds we receive from our sale of the securities covered by this prospectus primarily for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include, without limitation, research and development expenditures, clinical development of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds. Additional information on the use of net proceeds we receive from the sale of securities covered by this prospectus may be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

We may sell securities in any of the ways described below or in any combination:

- to or through underwriters or dealers;
- through one or more agents;
- directly to purchasers or to a single purchaser; or
- in "at the market offerings," within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, or an exchange or otherwise.

The distribution of the securities by us may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement will describe the terms of the offering of the securities, including the following:

- name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Any offering price and any discounts or concessions allowed or reallocated or paid to dealers will be specified in the applicable prospectus supplement and may be changed from time to time.

Only the agents or underwriters named in each prospectus supplement are agents or underwriters in connection with the securities being offered thereby.

We may authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in each applicable prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will be subject only to those conditions set forth in each applicable prospectus supplement, and each prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, underwriters and other third parties described above may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution from us with respect to payments which the agents, underwriters or other third parties may be required to

make in respect thereof. Agents, underwriters and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business. We may also use underwriters or such other third parties with whom we have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority.

Our common stock is listed on The Nasdaq Global Select Market. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the development, maintenance or liquidity of any trading market for the securities.

Certain persons participating in an offering may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock does not purport to be complete and is qualified in its entirety by reference to our fifth amended and restated certificate of incorporation and amended and restated by-laws, both of which are on file with the SEC as exhibits to previous filings, and the applicable provisions of the Delaware General Corporation Law, or the DGCL. We refer in this section to our fifth amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated by-laws as our by-laws.

General

Our authorized capital stock consists of 175,000,000 shares of our common stock, par value \$0.0001 per share. As of August 13, 2018, we had 23,153,418 shares of common stock outstanding.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. A contested election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election; otherwise, a nominee is elected if the votes properly cast for such nominee exceed the votes properly cast against such nominee. Holders of common stock are entitled to receive any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation, dissolution or winding up, whether voluntary or involuntary, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the

corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Anti-Takeover Effects of Our Certificate of Incorporation and Our By-Laws

Our certificate of incorporation and by-laws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors.

These provisions include:

Classified Board. Our certificate of incorporation provides that our board of directors is divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Our board of directors currently consists of six members.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and by-laws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called pursuant to a resolution adopted by a majority of our board of directors. Except as described above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the by-laws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the by-laws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The DGCL generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless either a corporation's certificate of incorporation or by-laws requires a greater percentage. Our certificate of incorporation and by-laws provide that the affirmative vote of holders of at least 75% of the total votes eligible to be cast in the election of directors is required to amend, alter, change or repeal specified provisions. This requirement of a supermajority vote to approve amendments to our certificate of incorporation and by-laws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in the name of the Company, actions against directors, officers and employees for breach of a fiduciary duty and other similar actions may be brought only in specified courts in the State of Delaware. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021.

Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol "MRSN."

DESCRIPTION OF PREFERRED STOCK

Under the terms of our certificate of incorporation, our board of directors is authorized to issue up to 25,000,000 shares of our preferred stock, par value \$0.0001 per share, in one or more series without stockholder approval. As of June 30, 2018, we had no shares of preferred stock outstanding. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

If we offer a specific class or series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company; and
- any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Transfer Agent and Registrar

The transfer agent and registrar for any series or class of preferred stock will be set forth in each applicable prospectus supplement.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

As of June 30, 2018, we had warrants outstanding that represent the right to acquire 110,365 shares of common stock.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the 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;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that class or series of our preferred stock;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent 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 or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock and/or preferred stock will be separately transferable;
- 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 anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC for the securities offered by this prospectus. This prospectus does not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information.

We are required to file annual and quarterly reports, current reports, proxy statements, and other information with the SEC. We make these documents publicly available, free of charge, on our website at www.mersana.com as soon as reasonably practicable after filing such documents with the SEC. The information contained on our website is not part of this prospectus. You can read our SEC filings, including the registration statement, on the SEC's website at <http://www.sec.gov>. You also may read and copy any document we file with the SEC at its public reference facility at:

Public Reference Room
100 F Street N.E.
Washington, DC 20549

Please call the SEC at 1-800-732-0330 for further information on the operation of the public reference facilities.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings, including all filings made after the date of the filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement, made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

- Our Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the SEC on March 28, 2018;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement on Schedule 14A, as filed with the SEC on April 30, 2018;
- Our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2018 and June 30, 2018, as filed with the SEC on May 15, 2018 and August 14, 2018, respectively;
- Our Current Reports on Form 8-K filed with the SEC on March 2, 2018, March 12, 2018, March 19, 2018, April 10, 2018, June 29, 2018 and July 23, 2018; and
- Description of our common stock contained in our Registration Statement on Form 8-A, as filed with the SEC on June 23, 2017, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
Mersana Therapeutics, Inc.
840 Memorial Drive
Cambridge, Massachusetts 02139
(617) 498-0020

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.mersana.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. The validity of any securities will be passed upon for any underwriters or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Mersana Therapeutics, Inc. appearing in Mersana Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2017, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

\$250,000,000



Common Stock

Preferred Stock

Warrants

Units

PROSPECTUS

, 2018

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any shares in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

The information in this prospectus supplement and the accompanying prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated September 14, 2018

PROSPECTUS SUPPLEMENT
(To Prospectus Dated September 14, 2018)

\$75,000,000



Common Stock

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$75,000,000 from time to time through Cowen acting as our agent.

Our common stock is traded on The Nasdaq Global Select Market under the symbol "MRSN." On September 12, 2018, the last reported sale price of our common stock was \$14.23 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3.0% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page S-4 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

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 or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Cowen

, 2018

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering and certain other matters relating to us and our business. The second part, the accompanying prospectus, contains and incorporates by reference important business and financial information about us, a description of our common stock and certain other information about us and this offering. This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to \$250,000,000. Under this prospectus supplement, we may offer shares of our common stock having an aggregate offering price of up to \$75,000,000 from time to time at prices and on terms to be determined by the market conditions at the time of the offering. You should read both this prospectus supplement and the accompanying prospectus, including all documents incorporated herein and therein by reference, together with additional information described under "Where You Can Find More Information" below.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

"Mersana Therapeutics," "Mersana," the "Company," "we," "us," "our" and similar names refer to Mersana Therapeutics, Inc. and its consolidated subsidiary, unless we state otherwise or the context otherwise requires.

SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. The summary may not contain all the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including "Risk Factors" contained in this prospectus supplement and the documents incorporated by reference herein, before making an investment decision.

Overview

We are a clinical stage biopharmaceutical company focused on developing antibody drug conjugates, or ADCs, that offer a clinically meaningful benefit for cancer patients with significant unmet need. We have leveraged 20 years of industry learning in the ADC field to develop proprietary technologies that enable us to design ADCs to have improved efficacy, safety and tolerability relative to existing ADC therapies. Our most advanced platform, Dolaflexin, has been used to generate a pipeline of proprietary ADC product candidates to address patient populations that are not currently amenable to treatment with traditional ADC-based therapies. Our first product candidate, XMT-1522, is a HER2-targeted ADC currently in a Phase 1 dose escalation study primarily in breast cancer patients as well as non-small cell lung cancer, or NSCLC, and gastric cancer. Upon the completion of dose escalation, we plan to expand clinical development of XMT-1522 into additional breast cancer, NSCLC, and gastric cancer patient populations, all of which are not adequately addressed by existing HER2 therapies. Our second product candidate, XMT-1536, is an ADC targeting NaPi2b, an antigen broadly expressed in ovarian cancer and NSCLC. XMT-1536 entered clinical development in late 2017 and is currently in a Phase 1 dose escalation study. Beyond our two lead product candidates, we continue to invest in our earlier stage product candidates and in our ADC technologies. In addition, we have established a strategic partnership with Takeda Pharmaceutical Company Limited, or Takeda, under which it obtained rights to XMT-1522 outside of the United States and Canada. We have also established strategic research and development partnerships with Takeda and Merck KGaA for the development and commercialization of additional ADC product candidates against a limited number of targets selected by our partners based on our Dolaflexin platform. We believe the potential of our ADC technologies, supported by our world-class management team and protected by our robust intellectual property portfolio, will allow us to develop targeted and highly tailored therapies to help cancer patients triumph over cancer.

We were incorporated in the state of Delaware in February 2002 as Nanopharma Corp., and we changed our name to Mersana Therapeutics, Inc. in November 2005. Our principal executive offices are located at 840 Memorial Drive, Cambridge, Massachusetts 02139, and our telephone number is (617) 498-0020. Our Internet website is www.mersana.com.

THE OFFERING

Common stock offered by us	Shares of common stock having an aggregate offering price of up to \$75,000,000.
Common stock to be outstanding after this offering	Up to 28,388,293 shares, assuming sales at a price of \$14.23 per share, which was the closing price on The Nasdaq Global Select Market on September 12, 2018. Actual number of shares issued will vary depending on the price at which shares may be sold from time to time under this offering.
Manner of offering	"At the market offering" that may be made from time to time through our agent, Cowen. See "Plan of Distribution" on page S-10.
Use of proceeds	If we receive all \$75,000,000 of gross proceeds of the sale of shares of our common stock under this prospectus supplement, we anticipate our net proceeds, after deducting estimated commissions and expenses payable by us, will be approximately \$72.5 million. We intend to use the net proceeds from this offering primarily for general corporate purposes, which may include, without limitation, research and development expenditures, clinical development of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures. See "Use of Proceeds" on page S-6.
Nasdaq Global Select Market symbol	MRSN
Risk factors	See "Risk Factors" beginning on page S-4 of this prospectus supplement for a discussion of factors that you should read and consider before investing in our securities.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 23,117,738 shares outstanding as of June 30, 2018. The number of shares outstanding as of June 30, 2018 as used throughout this prospectus supplement, unless otherwise indicated, excludes, each as of June 30, 2018:

- 110,365 shares of common stock issuable upon the exercise of warrants at a weighted-average exercise price of \$0.05 per share;
- 3,635,541 shares of common stock issuable upon the exercise of outstanding stock options at a weighted-average exercise price of \$6.42 per share;
- 1,366,503 shares of common stock reserved for future issuance under our 2017 Stock Incentive Plan; and
- 225,000 shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan.

RISK FACTORS

Investing in our securities involves a high degree of risk. See "Part I, Item 1A—Risk Factors" in our most recent Annual Report on Form 10-K incorporated by reference in this prospectus supplement and the accompanying prospectus and "Part II, Item 1A—Risk Factors" in any subsequent Quarterly Report on Form 10-Q and the "Risk Factors" section in this prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our securities. Before you invest in our securities, you should carefully consider these risks as well as other information we include or incorporate by reference into this prospectus supplement and the accompanying prospectus. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus supplement and the accompanying prospectus.

Risks Relating to this Offering

We may allocate the net proceeds from this offering in ways that you or other stockholders may not approve.

We currently intend to use the net proceeds of this offering, if any, for general corporate purposes that may include, without limitation, research and development expenditures, clinical development of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital, and capital expenditures. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. Because the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock. See "Use of Proceeds."

You may experience immediate and substantial dilution in the book value per share of the common stock you purchase.

Because the prices per share at which shares of our common stock are sold in this offering may be substantially higher than the book value per share of our common stock, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. The shares sold in this offering, if any, will be sold from time to time at various prices. After giving effect to the sale of our common stock in the maximum aggregate offering amount of \$75,000,000 at an assumed offering price of \$14.23 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on September 12, 2018, and after deducting estimated offering commissions and estimated fees payable by us, our net tangible book value as of June 30, 2018 would have been \$118,143,000, or \$4.16 per share of common stock. This represents an immediate increase in the net tangible book value of \$2.18 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$10.07 per share to new investors who purchase our common stock in the offering. See "Dilution" for a more detailed discussion of the dilution you may incur in connection with this offering.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other documents we have filed with the SEC that are incorporated herein by reference, contain forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. The words "anticipate," "believe," "estimate," "expect," "goal," "intend," "may," "seek," "plan," "predict," "project," "target," "potential," "will," "would," "possible," "could," "should," "continue," "contemplate" or the negative of these terms or other 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:

- the initiation, cost, timing, progress and results of our current and future research and development activities, preclinical studies and clinical trials;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- the timing of, and our ability to obtain and maintain, regulatory approvals for our product candidates;
- our ability to quickly and efficiently identify and develop additional product candidates;
- our ability to advance any product candidate into, and successfully complete, clinical trials;
- our intellectual property position, including with respect to our trade secrets; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2017 and any subsequent Quarterly Reports on Form 10-Q, each incorporated by reference in this prospectus supplement and the accompanying prospectus, and in the "Risk Factors" section in this prospectus supplement. See "Where You Can Find More Information." Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we make.

We cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

USE OF PROCEEDS

If we receive all \$75,000,000 of gross proceeds from the sale of the shares of our common stock under this prospectus supplement, we anticipate that the net proceeds we will receive from this offering will be approximately \$72,450,000, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The amount of the proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Cowen as a source of financing.

We currently estimate that we will use the net proceeds from this offering as follows:

- research and development expenditures, clinical development of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, or collaborations; and
- the balance to fund working capital, capital expenditures and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering described above, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our common stock. We do not intend to pay any dividends on our common stock for the foreseeable future.

PRICE RANGE OF OUR COMMON STOCK

Our common stock has been listed on The Nasdaq Global Select Market under the symbol "MRSN" since our initial public offering on June 27, 2017. The following table summarizes the high and low sale prices per share for our common stock for the fiscal periods indicated as reported on The Nasdaq Global Select Market.

	<u>High</u>	<u>Low</u>
Year ending December 31, 2018		
First Quarter	\$ 19.44	\$ 12.45
Second Quarter	\$ 23.96	\$ 13.72
Third Quarter (through September 12, 2018)	\$ 19.60	\$ 8.76
Year ended December 31, 2017		
Second Quarter (beginning June 28, 2017)	\$ 14.70	\$ 12.71
Third Quarter	\$ 18.48	\$ 13.03
Fourth Quarter	\$ 21.01	\$ 14.50

On September 12, 2018, the last reported sale price for our common stock on The Nasdaq Global Select Market was \$14.23 per share. As of September 12, 2018, we had 34 holders of record of our common stock.

DILUTION

Our net tangible book value as of June 30, 2018 was approximately \$45,693,000, or \$1.98 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding.

After giving effect to the sale by us of the full \$75,000,000 of common stock that may be offered in this offering at an assumed offering price of \$14.23 per share, which was the closing price of our common stock on The Nasdaq Global Select Market on September 12, 2018, and after deducting estimated offering commissions and expenses payable by us, our as-adjusted net tangible book value as of June 30, 2018 would have been approximately \$118,143,000, or \$4.16 per share of common stock. This represents an immediate increase in the net tangible book value of \$2.18 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$10.07 per share to new investors. The following table illustrates this hypothetical per share dilution:

Assumed offering price per share	\$ 14.23
Net tangible book value per share as of June 30, 2018	\$ 1.98
Increase per share attributable to new investors	\$ 2.18
As-adjusted net tangible book value per share after this offering	\$ 4.16
Net dilution per share to new investors	\$ 10.07

The foregoing table is based on 23,117,738 shares of our common stock outstanding and excludes the following, each as of June 30, 2018:

- 110,365 shares of common stock issuable upon the exercise of warrants at a weighted-average exercise price of \$0.05 per share;
- 3,635,541 shares of common stock issuable upon the exercise of outstanding stock options at a weighted-average exercise price of \$6.42 per share;
- 1,366,503 shares of common stock reserved for future issuance under our 2017 Stock Incentive Plan; and
- 225,000 shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan.

The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$14.23 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$75,000,000 is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$4.21 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$11.02 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease in the price at which the shares are sold to \$1.00 per share, assuming all of our common stock in the aggregate amount of \$75,000,000 is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$4.10 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$9.13 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only and will adjust based on the actual public offering price and the actual number of shares that we sell in the offering.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to \$75,000,000 of our common stock through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an "at the market" offering as defined in Rule 415 under the Securities Act, including sales made directly on The Nasdaq Global Select Market or any other trading market for our common stock. If authorized by us in writing, Cowen may purchase shares of our common stock as principal.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen's actual outside legal expenses incurred by Cowen in connection with this offering. We have also agreed to reimburse Cowen for its FINRA counsel fees in an amount up to \$10,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$300,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted-average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Select Market and trades under the symbol "MRSN." The transfer agent of our common stock is Computershare Trust Company, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC for the securities offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus do not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information.

We are required to file annual and quarterly reports, current reports, proxy statements, and other information with the SEC. We make these documents publicly available, free of charge, on our website at www.mersana.com as soon as reasonably practicable after filing such documents with the SEC. The information contained on our website is not part of this prospectus supplement or the accompanying prospectus. You can read our SEC filings, including the registration statement, on the SEC's website at <http://www.sec.gov>. You also may read and copy any document we file with the SEC at its public reference facility at:

Public Reference Room
100 F Street N.E.
Washington, DC 20549

Please call the SEC at 1-800-732-0330 for further information on the operation of the public reference facilities.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus supplement and the accompanying prospectus the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement and the accompanying prospectus. We incorporate by reference into this prospectus supplement and the accompanying prospectus the documents listed below and any future filings, including all filings made after the date of the filing of the registration statement of which this prospectus supplement and the accompanying prospectus are part and prior to the effectiveness of such registration statement, made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus supplement or the accompanying prospectus, until the termination of the offering of securities described in this prospectus supplement. We hereby incorporate by reference the following documents:

- Our Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the SEC on March 28, 2018;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement on Schedule 14A, as filed with the SEC on April 30, 2018;
- Our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2018 and June 30, 2018, as filed with the SEC on May 15, 2018 and August 14, 2018, respectively;
- Our Current Reports on Form 8-K filed with the SEC on March 2, 2018, March 12, 2018, March 19, 2018, April 10, 2018, June 29, 2018 and July 23, 2018; and
- Description of our common stock contained in our Registration Statement on Form 8-A, as filed with the SEC on June 23, 2017, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus supplement or the accompanying prospectus will be deemed modified, superseded or replaced for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus modifies, supersedes or replaces such statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
Mersana Therapeutics, Inc.
840 Memorial Drive
Cambridge, Massachusetts 02139
(617) 498-0020

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.mersana.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus supplement or the accompanying prospectus.

LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus supplement will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Cowen and Company, LLC is being represented in connection with this offering by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Mersana Therapeutics, Inc. appearing in Mersana Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2017, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report by Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

\$75,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Cowen

, 2018

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

The following table sets forth the various expenses in connection with the sale and distribution of the securities being registered.

Securities and Exchange Commission Registration Fee	\$ 31,125
FINRA Fee	38,000
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer Agent and Registrar fees	*
Miscellaneous	*
Total	\$ *

* These fees are calculated based on the number of issuances and the amount of securities offered and accordingly cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers.

As permitted by Section 102(b)(7) of the DGCL, our amended and restated certificate of incorporation includes a provision to eliminate the personal liability of our directors for monetary damages for breach of their fiduciary duties as directors, subject to certain exceptions. In addition, our amended and restated certificate of incorporation and by-laws provide that we are required to indemnify our officers and directors under certain circumstances, including those circumstances in which indemnification would otherwise be discretionary, and we are required to advance expenses to our officers and directors as incurred in connection with proceedings against them for which they may be indemnified, in each case except to the extent that the DGCL prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145(a) of the DGCL provides that a corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interest of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his conduct was unlawful.

Section 145(b) of the DGCL provides that a corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or

is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by him in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

We have entered into indemnification agreements with our directors and each of our officers. These indemnification agreements provide broader indemnity rights than those provided under the DGCL and our amended and restated certificate of incorporation. These indemnification agreements are not intended to deny or otherwise limit third-party or derivative suits against us or our directors or officers, but to the extent a director or officer were entitled to indemnity or contribution under the indemnification agreement, the financial burden of a third-party suit would be borne by us, and we would not benefit from derivative recoveries against the director or officer. Such recoveries would accrue to our benefit but would be offset by our obligations to the director or officer under the indemnification agreement.

We maintain directors' and officers' liability insurance for the benefit of our directors and officers.

Also, see "Undertakings."

Item 16. Exhibits.

The following is a list of exhibits filed as part of this registration statement.

<u>Exhibit Number</u>	<u>Exhibit</u>
1.1*	Form of Underwriting Agreement
1.2**	Sales Agreement dated July 2, 2018 by and between the Company and Cowen and Company, LLC
3.1	Fifth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No. 001-38129, filed on July 10, 2017)
3.2	Amended and Restated By-laws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, File No. 001-38129, filed on July 10, 2017)
4.1	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Company's Form S-1, File No. 333-218412, filed on June 1, 2017)
4.2	Third Amended and Restated Investor Rights Agreement, dated as of June 15, 2016, by and among Mersana Therapeutics Inc. and the Stockholders listed therein (incorporated by reference to Exhibit 4.2 to the Company's Form S-1, File No. 333-218412, filed on June 1, 2017)
4.3*	Form of Common Stock Warrant Agreement and Warrant Certificate
4.4*	Form of Preferred Stock Warrant Agreement and Warrant Certificate
5.1**	Opinion of Ropes & Gray LLP
5.2**	Opinion of Ropes & Gray LLP

Exhibit Number	Exhibit
23.1	Consent of Ernst & Young LLP (filed herewith)
23.2**	Consent of Ropes & Gray LLP (included in Exhibit 5.1)
24.1**	Powers of Attorney (included on signature page to the Company's Registration Statement on Form S-3, filed on July 2, 2018.)

* To be filed, if necessary, subsequent to the effectiveness of this registration statement by an amendment to this registration statement or incorporated by reference pursuant to a Current Report on Form 8-K in connection with the offering of securities.

** Previously filed.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that:

(A) Paragraphs (a)(1)(i) and (a)(1)(ii) of this section do not apply if the registration statement is on Form S-8, and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement; and

(B) Paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the registration statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(C) *Provided further, however*, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the registration statement is for an offering of asset-backed securities on Form S-1 or Form S-3, and the information required to be included in a post-effective amendment is provided pursuant to Item 1100(c) of Regulation AB.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant

undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser: (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424; (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant; (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(7) That, for purposes of determining any liability under the Securities Act of 1933:

(i) the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of the registration statement as of the time it was declared effective; and

(ii) each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(8) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Trust Indenture Act.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is therefore unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933, and will be governed by the final adjudication of such issue.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
* _____ Andrew A. F. Hack, M.D., Ph.D.	Director	September 14, 2018
* _____ Kristen Hege, M.D.	Director	September 14, 2018
*By: _____ /s/ EVA M. JACK _____ Eva M. Jack <i>Attorney-in-Fact</i>		

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption "Experts" in Amendment No. 2 to the Registration Statement (Form S-3) and related Prospectus and Prospectus Supplement of Mersana Therapeutics, Inc. for the registration of common stock, preferred stock, warrants or units and to the incorporation by reference therein of our report dated March 28, 2018, with respect to the consolidated financial statements of Mersana Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2017, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
September 11, 2018

QuickLinks

[Exhibit 23.1](#)