

The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and accompanying prospectus are not offers to sell these securities, and we are not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER 15, 2021

PRELIMINARY PROSPECTUS SUPPLEMENT
(to Prospectus dated March 24, 2021)

\$75,000,000



Shares of Common Stock
Pre-Funded Warrants to Purchase Shares of Common Stock

We are offering \$75 million of shares of our common stock and, to certain investors in lieu thereof, pre-funded warrants to purchase shares of our common stock, or the Pre-Funded Warrants.

The purchase price of each Pre-Funded Warrant equals the price per share at which shares of common stock are being sold in this offering, minus \$0.0001, and the exercise price of each Pre-Funded Warrant equals \$0.0001 per share. The Pre-Funded Warrants are exercisable at any time, provided that each Pre-Funded Warrant holder will be prohibited from exercising such Pre-Funded Warrants into shares of our common stock if, as a result of such exercise, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of our common stock then issued and outstanding, which percentage may change at the holders' election to any other number less than or equal to 19.99% upon 61 days' notice to us in respect of any increase. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the Pre-Funded Warrants.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "SNDX." On December 15, 2021, the last reported sale price of our common stock was \$18.97 per share. There is no established public market for the Pre-Funded Warrants, and we do not intend to list the Pre-Funded Warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Our business and an investment in our securities involve significant risks. These risks are described under the caption "[Risk Factors](#)" beginning on page S-8 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

We are an "emerging growth company" and a "smaller reporting company" under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements for this prospectus and future filings.

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

	PER SHARE	PER PRE-FUNDED WARRANT	TOTAL
Public offering price	\$	\$	\$
Underwriting discounts and commissions (1)	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$

(1) See "Underwriting" for a description of compensation payable to the underwriters.

The underwriters may also purchase up to an aggregate of 15% of the total number of shares of common stock we are offering plus the shares underlying the Pre-Funded Warrants from us at the public offering price of the common stock, less the underwriting discounts and commissions, within 30 days from the date of this prospectus supplement.

Delivery of the shares of common stock and the Pre-Funded Warrants in this offering is expected to be made on or about _____, 2021.

Goldman Sachs and Co. LLC

The date of this prospectus supplement is December _____, 2021.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process, which automatically became effective upon filing with the SEC on March 24, 2021. The prospectus supplement describes the specific terms of this offering and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The accompanying prospectus gives more general information, some of which may not apply to this offering. If there is a difference between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference, you should rely on the information in this prospectus supplement. Generally, when we refer to the prospectus, we are referring to this prospectus supplement and the accompanying prospectus combined.

We have not, and the underwriters have not, authorized anyone to provide you with information different than or inconsistent with the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents, regardless of the time of delivery of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

Neither we, nor any of the underwriters, has done anything that would permit this offering or possession or distribution of this prospectus supplement or the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. The distribution of this prospectus supplement and the accompanying prospectus and the offering of our securities 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 our securities and the distribution of this prospectus supplement and the accompanying 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 and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context indicates otherwise, references in this prospectus to “Syndax,” “the Company,” “we,” “us,” “our” and similar references refer to Syndax Pharmaceuticals, Inc. and its wholly owned subsidiaries.

“Syndax” is a registered trademark and the “Syndax” and “Syndax Pharmaceuticals” logos are unregistered trademarks of the company. This prospectus also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this prospectus are the property of their respective holders.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. For a more complete understanding of our company and this offering, you should read and consider carefully the more detailed information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, including our historical financial statements and notes to those financial statements. Please read “Risk Factors” in this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2020, in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and in the other documents incorporated by reference, including other documents that we subsequently file with the SEC for more information about important risks that you should consider before investing in our securities.

Company Overview

We are a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Our two lead product candidates are SNDX-5613 and SNDX-6352, or axatilimab. We are developing SNDX-5613, targeting the binding interaction of menin with the mixed lineage leukemia 1, or MLL1, protein for the treatment of MLL-rearranged, or MLLr, acute leukemias and nucleophosmin 1, or NPM1, mutant acute myeloid leukemia, or AML, as well as axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1, or CSF-1 receptor. We have deprioritized the development of entinostat, our once-weekly, oral, small molecule, Class I HDAC inhibitor, to focus resources on advancing the remainder of our pipeline. We plan to continue to leverage the technical and business expertise of our management team and scientific collaborators to license, acquire and develop additional therapeutics to expand our pipeline.

SNDX-5613

Our first clinical-stage product candidate, SNDX-5613, is a potent, orally active inhibitor of the high affinity interaction site on menin with the protein MLL1. This specific interaction is a key driver for two genetically defined acute leukemias: (i) MLLr and (ii) NPM1c AML. Both diseases have a poor prognosis. In preclinical testing, SNDX-5613 has demonstrated complete tumor regression and profound, dose-dependent and long-lasting survival benefit in leukemic models of disease. Initial clinical evidence with SNDX-5613 also supports the hypothesis that disruption of the menin-MLL interaction can lead to responses in acute leukemias.

We are developing SNDX-5613 as a targeted therapy to potentially treat two genetically defined acute leukemias: (i) a genetically defined subset of acute leukemias with chromosomal rearrangements in the mixed lineage leukemia gene, known as MLLr; and (ii) AML, with a somatic mutation in the nucleophosmin 1, or NPM1, gene, also known as NPM1c. Our near-term focus is to rapidly establish proof-of-concept that SNDX-5613 is a targeted therapy that can potentially provide meaningful clinical benefit to adult and pediatric leukemia patients having relapsed or refractory MLLr or NPM1c acute leukemias. Our investigational new drug, or IND, application for SNDX-5613 took effect with the U.S. Food and Drug Administration, or FDA, in the second quarter of 2019 and we commenced AUGMENT-101, a clinical trial consisting initially of a Phase 1 dose escalation portion to determine the maximum tolerated dose, or MTD, and recommended Phase 2 dose of SNDX-5613 in patients with acute leukemia. We are conducting the trial at multiple centers in the United States. We are completing the Phase 1 portion of the trial, and have initiated the Phase 2 portion of the trial with patients to be enrolled in three indication-specific expansion cohorts to determine the efficacy, short- and long-term safety, and tolerability of SNDX-5613 in MLLr ALL, MLLr AML and NPM1c AML.

On September 20, 2021, we participated in a meeting with the FDA to discuss the results of the Phase 1 portion of our AUGMENT-101 trial. At the meeting, the FDA agreed with our recommended Phase 2 dose and

confirmed that we may initiate the Phase 2 registration-directed cohorts of AUGMENT-101. Additionally, the FDA has agreed with our proposed statistical design and endpoints for each of the three Phase 2 expansion cohorts.

Additionally, we announced that we will initiate a frontline trial of SNDX-5613 in combination with venetoclax and azacitidine in newly diagnosed AML patients unable to tolerate induction chemotherapy. The trial will be conducted as part of the Leukemia & Lymphoma Society's Beat AML Master Clinical Trial, and SNDX-5613 is the first menin inhibitor to be included in the Beat AML Master Clinical Trial. We announced that we will also initiate a trial to assess the anti-leukemic efficacy of SNDX-5613 in MLLr or NPM1 patients with measurable residual disease progression following anti-leukemic treatment. This trial will be conducted as part of the Australian Leukemia and Lymphoma Group INTERCEPT Master Clinical Trial, a collaborative clinical trial investigating novel therapies to target early relapse and clonal evolution as pre-emptive therapy in AML. SNDX-5613 is the first menin inhibitor to be included in the INTERCEPT AML Master Clinical Trial. Lastly, we also announced that we plan to initiate a new trial to assess the safety, tolerability, and preliminary anti-leukemic efficacy of SNDX-5613 in combination with chemotherapy in patients with relapsed or refractory MLLr or mNPM1 acute leukemias. We expect that the Phase 1b trial, which we refer to as AUGMENT-102, will enroll up to 27 patients.

In January 2020, the FDA granted SNDX-5613 Orphan Drug Designation for the treatment of adult and pediatric acute myeloid leukemia and in June 2021, the FDA granted Fast Track Designation to SNDX-5613 for the treatment of adult and pediatric patients with relapsed or refractory acute leukemias harboring a MLLr or NPM1 mutation.

Axatilimab

We are also developing axatilimab a monoclonal antibody targeting the colony stimulating factor-1 receptor, or CSF-1R, a cell surface protein thought to control the survival and function of monocytes and macrophages. Axatilimab binds with high affinity to CSF-1R and blocks the binding of the two known CSF-1R ligands CSF-1 and IL-34. CSF-1R is expressed on the surface of specific immune cells known as macrophages and their precursor cells known as monocytes. CSF-1R signaling on these cells has been demonstrated in preclinical studies conducted in animal models of skin and lung chronic graft versus host disease, or cGVHD, to be the key regulatory pathway involved in the expansion and infiltration of the macrophages that mediate fibrosis and the cGVHD disease process. Blocking CSF-1R activity with an experimental CSF-1R antibody in these studies was shown to prevent and treat the symptoms of cGVHD. We believe that by inhibiting CSF-1R activation on monocytes and macrophages, that axatilimab has the potential to be used to treat cGVHD as well as other fibrotic diseases where monocyte-derived macrophages have been shown to play a significant role.

Our near-term focus is to rapidly establish that axatilimab can provide meaningful clinical benefit in patients with advanced cGVHD where prior therapies are no longer effective and to establish proof-of-concept of using axatilimab to treat other fibrotic diseases where monocyte-derived macrophages have been shown to play a role.

We announced that following our end of Phase 1 meeting with the FDA, we have aligned on a regulatory path for axatilimab for the treatment of cGVHD. We commenced a pivotal Phase 2 trial, AGAVE-201, to assess the safety and efficacy of different doses and schedules of axatilimab for the treatment of patients with cGVHD. The primary endpoint is the objective response rate based on the 2014 NIH consensus criteria for GVHD with key secondary endpoints including duration of response and improvement in modified Lee Symptom Scale score. We anticipate releasing topline data in 2023. We completed enrollment of the Phase 1/2 trial evaluating axatilimab for the treatment of patients with cGVHD in the second quarter of 2021. In March and April of 2021, we announced that the FDA granted Orphan Drug Designation to axatilimab for the treatment of patients with cGVHD and idiopathic pulmonary fibrosis, or IPF.

Recent Clinical Developments

Axatilimab

On December 11, 2021, we presented positive data from the Phase 1/2 trial of axatilimab in patients with recurrent or refractory chronic cGVHD despite two or more prior lines of therapy in an oral presentation during the American Society of Hematology (ASH) Virtual Annual Meeting.

During the presentation, and in a press release that we issued on the presentation date, we shared that as of October 22, 2021 (data cutoff) a total of 40 patients were treated in the SNDX-6352-503 trial, who received a median of four prior systemic therapies. There were 31 evaluable patients treated at 1mg/kg every 2 weeks or 3mg/kg every 4 weeks, the doses that we are testing in the ongoing AGAVE-201 global pivotal study. Of the evaluable patients, responses were observed in 68% (n=21/31) of patients, with a best ORR (complete response (CR) plus partial response) of 72% (n=18/25) at 1mg/kg every two weeks and 50% (n=3/6) at 3mg/kg every four weeks. Responses observed across a range of organ systems with difficult to treat manifestations such as lung (n=5/15), skin (n=3/28), and joints and fascia (n=16/24). Fifty-three percent of patients (n=16/30) reported clinically meaningful improvement as measured by at least a 7-point decrease in Lee Symptom Scale score. As of data cutoff 43% (n=17/40) of patients remained on treatment.

In the data that we presented at ASH, axatilimab was well-tolerated with a favorable safety profile. The most common observed adverse events were consistent with on-target effects on liver enzyme pharmacology. There was no incidence of cytomegalovirus or other viral reactivation and no apparent increases in risk for infection. Enrollment remains ongoing in the global pivotal Phase 2 AGAVE-201 trial of axatilimab in patients with cGVHD, with topline data expected in 2023.

SNDX-5613

On December 13, 2021, we presented positive data from the Phase 1 portion of our AUGMENT-101 trial in heavily pretreated patients with MLLr or NPM1c mutations in an oral presentation during the ASH Virtual Annual Meeting.

During the presentation, and in a press release that we issued on the presentation date, we shared that as of October 18, 2021 (data cutoff), a total of 59 patients with a median of four prior therapies, including 42% (n=25/59) who received a prior stem cell transplant and 59% (n=35/59) who received prior venetoclax, were dosed in the Phase 1 portion of the trial. Across evaluable patients with mNPM1 (n=13) or MLLr (n=38) acute leukemia who received at least one dose of SNDX-5613, the ORR (CR plus CR with partial hematologic recovery (CRh) plus CR with incomplete platelet recovery (CRp) plus CR with incomplete recovery (CRi) plus morphologic leukemia-free state) was 55% (n=28/51), with a CR/CRh rate of 24% (n=12/51) and nine patients proceeding to stem cell transplant (two patients achieving a CRp with no evidence of minimal residual disease (MRD-), and seven patients who achieved MRD- CR or CRh). The overall MRD negative rate was 31% (n=16/51). The ORR in evaluable patients harboring an NPM1 mutation was 38% (n=5/13), with a CR/CRh rate of 23% (n=3/13). The ORR in evaluable patients harboring an MLL-rearrangement was 61% (n=23/38), with a CR/CRh rate of 24% (n=9/38).

Among those patients who achieved CR/CRh, 92% (n=11/12) were MRD negative, including 100% (n=3/3) of NPM1 patients and 89% (n=8/9) of MLLr patients. Median time to response for patients achieving a CR/CRh was two months. Median duration of response was not reached, inclusive of patients who received stem cell transplant, and 50% (n=6/12) of patients who achieved CR/CRh have a duration of response greater than six months.

In the data that we presented at ASH, SNDX-5613 was well tolerated, with no discontinuations due to treatment-related adverse events observed. The only dose limiting toxicity observed was Grade 3 QT

prolongation, which occurred in 7% (n=3/43) of patients treated at the four doses that met the study's pre-defined recommended Phase 2 dose criteria.

Collaboration with Incyte

In September 2021, we entered into a collaboration and license agreement, or the Incyte Agreement, with Incyte Corporation, or Incyte, for the development and commercialization of axatilimab. Under the terms of the Incyte Agreement, Incyte received exclusive commercialization rights outside of the United States, and we and Incyte will, subject to the exercise of our co-promotion option, have co-commercialization rights in the United States, with respect to axatilimab. Incyte is responsible for leading commercialization strategy and booking all revenue from worldwide sales of axatilimab, subject to its royalty payment obligations set forth below. The parties will share equally the profits and losses from the co-commercialization efforts. We and Incyte are co-developing axatilimab and sharing development costs associated with global and U.S.-specific clinical trials, with Incyte responsible for 55% of such costs and we are responsible for 45% of such costs. Each company is responsible for funding any independent development activities. All development costs related to the collaboration are subject to a joint development plan. A joint development committee between us and Incyte will govern future development of axatilimab. In addition to the ongoing AGAVE-201 trial, we and Incyte expect to initiate additional trials of axatilimab in patients with cGVHD in 2022, including a Phase 2 trial in combination with a JAK inhibitor in patients with steroid-refractory cGVHD. Beyond cGVHD, we plan to commence a Phase 2 proof-of-concept trial of axatilimab in the first half of 2022 in patients with idiopathic pulmonary fibrosis.

Pursuant to the Incyte Agreement, in December 2021, we received an upfront license fee of \$117 million. Incyte has also purchased 1,421,523 shares of common stock for an aggregate purchase price of \$35 million, or \$24.62 per share. We are eligible to receive up to \$220 million in future contingent development and regulatory milestones and up to \$230 million in commercialization milestones as well as tiered royalties ranging in the mid-teens on sales outside of the United States.

In December 2021, we and Incyte entered into a letter agreement memorializing how the parties would work together in the event that the government intervened in the proposed collaboration and the parties are forced to terminate and unwind the collaboration. Pursuant to the letter agreement, the parties agreed, in part, (i) to permit Incyte to terminate the Incyte Agreement through September 2022 if, prior to March 23, 2022, either party for the first time receives a formal request from either the Federal Trade Commission or the Department of Justice, Antitrust Division, regarding the Incyte Agreement, which we refer to as the Termination Right, and (ii) to provide the parties with a mechanism to settle any gain or loss related to Incyte's equity investment in the Company solely in the event that Incyte exercises its Termination Right. If Incyte exercises its Termination Right, (x) we will refund to Incyte the \$117 million upfront license fee and any payments made by Incyte for royalties, milestones and development costs and any other amounts paid by Incyte to us under the Incyte Agreement, and (y) we will waive any remaining lock-up restrictions and Incyte will sell the shares of our common stock that it purchased in connection with its equity investment pursuant to the Incyte Agreement. Following the sale of its shares, Incyte will remit to us any gain that it received, or, alternatively, we will repay Incyte for any loss that it incurred in each case in connection with the sale of the shares. The Termination Right expires if the parties do not receive a formal request before March 23, 2022. To date, the parties have not received any formal request from either the Federal Trade Commission or the Department of Justice, Antitrust Division.

Our Pipeline

SNDX-5613						
Menin Inhibitor	PreClin	Phase 1	Phase 2	Pivotal	Indication(s)	
AUGMENT-101-2A (monotherapy)				●	MLLr ALL/MPAL	
AUGMENT-101-2B (monotherapy)				●	MLLr AML	
AUGMENT-101-2C (monotherapy)				●	mNPM1 AML	
Axatilimab (SNDX-6352)						
CSF-1R mAB	PreClin	Phase 1	Phase 2	Pivotal	Indication(s)	
AGAVE-201 (monotherapy)				●	Chronic GVHD	
SNDX-6352-0503 (monotherapy)			●		Chronic GVHD	
Entinostat (SNDX-275)						
Class 1 HDAC inhibitor	PreClin	Phase 1	Phase 2	Pivotal	Indication(s)	
Entinostat					Under review	

Corporate Information

We were incorporated in Delaware in 2005. In 2011, we established a wholly owned subsidiary in the United Kingdom, in 2014 we established a wholly owned U.S. subsidiary, and in 2021 we established a wholly owned subsidiary in the Netherlands. Our principal executive offices are located at 35 Gatehouse Drive, Building D, Floor 3, Waltham, Massachusetts 02451 and our telephone number is (781) 419-1400. Our common stock is listed on The Nasdaq Global Select Market under the symbol “SNDX.” Our corporate website address is www.syndax.com. Information contained on or accessible through our website is not incorporated by reference into this prospectus supplement.

Emerging Growth Company and Smaller Reporting Company Status

We are an “emerging growth company,” or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies. We will cease to be an “emerging growth company” on December 31, 2021.

As of June 30, 2021, we no longer qualify as a smaller reporting company as defined in the Securities Exchange Act of 1934, as amended. We have historically taken, and may continue through the filing of our Annual Report on Form 10-K for the year ending December 31, 2021 to take, advantage of certain scaled disclosures available to smaller reporting companies.

THE OFFERING

Common stock to be offered by us:

shares

Pre-Funded Warrants offered by us:

In lieu of shares of common stock, we are offering to certain purchasers Pre-Funded Warrants to purchase _____ shares of common stock. The purchase price of each Pre-Funded Warrant will equal the price per share at which the shares of common stock are being sold in this offering, minus \$0.0001, and the exercise price of each Pre-Funded Warrant will be \$0.0001 per share. Each Pre-Funded Warrant will be exercisable upon issuance. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such Pre-Funded Warrants.

There is currently no market for the Pre-Funded Warrants and none is expected to develop after this offering. We do not intend to list the Pre-Funded Warrants on The Nasdaq Stock Market, any other national securities exchange or other nationally recognized trading system. See “Description of Pre-Funded Warrants—Pre-Funded Warrants” for additional information.

The shares of common stock and the Pre-Funded Warrants will be issued separately.

Option to purchase additional shares from us:

We have granted the underwriters an option for a period of 30 days to purchase up to _____ additional shares of our common stock from us at the public offering price, less the underwriting discounts and commissions. The number of shares subject to the underwriters’ option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the Pre-Funded Warrants.

Common stock to be outstanding immediately following this offering:

_____ shares, or _____ shares if the underwriters’ option to purchase additional shares from us is exercised in full (in each case, excluding any shares of common stock issuable upon the exercise of the Pre-Funded Warrants).

Use of proceeds:

We intend to use the net proceeds from the offering for general corporate purposes, including (i) ongoing and expanded clinical development of axatilimab and SNDX-5613, (ii) expenses related to the potential U.S. commercial launch of axatilimab in patients with cGVHD and SNDX-5613 in defined subsets of acute leukemias patients, (iii) continued manufacturing scale-up of axatilimab and SNDX-5613, (iv) development of other preclinical programs, (v) opportunistically acquire or invest in businesses, products or technologies that are complementary to our own, although we have no current plans, commitments or agreements with respect to any

acquisitions as of the date of this prospectus supplement; and (vi) for working capital. See “Use of Proceeds.”

Risk factors:

Investing in our securities involves a high degree of risk. See “Risk Factors” on page S-8 of this prospectus supplement and under similar headings in other documents incorporated by reference herein.

Nasdaq Global Select Market Symbol:

SNDX

The above discussion is based on 48,850,539 shares of our common stock outstanding as of September 30, 2021, and excludes:

- 3,307,952 shares of our common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2021;
- 7,340,654 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2021 under our 2015 Omnibus Incentive Plan, or 2015 Plan, and our 2007 Stock Plan, as amended, collectively, our Stock Plans, at a weighted average exercise price of \$11.70 per share;
- 132,333 shares of our common stock issuable upon the vesting of restricted stock units, or RSUs, outstanding as of September 30, 2021;
- 1,001,470 shares of common stock reserved for future issuance under our 2015 Plan, plus any additional shares of our common stock that may become available under our 2015 Plan;
- 1,296,410 shares of our common stock reserved for issuance under our 2015 Employee Stock Purchase Plan, or ESPP, as of September 30, 2021, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP;
- 1,421,523 shares of our common stock issued to Incyte on December 9, 2021, pursuant to a stock purchase agreement, dated September 24, 2021; and
- shares of common stock underlying the Pre-Funded Warrants being offered hereby.

Except as otherwise indicated, the information in this prospectus supplement assumes:

- no exercise of the outstanding stock options or outstanding pre-funded warrants;
- no exercise of the Pre-Funded Warrants being offered hereby; and
- no exercise by the underwriters of their option to purchase additional shares of our common stock from us.

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the following risk factors and the risk factors discussed under the section entitled “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2020, as updated by our subsequent filings, which are incorporated by reference into this prospectus supplement and accompanying prospectus in their entirety, together with all of the other information contained in this prospectus supplement and the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus. The risks and uncertainties described in these documents are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below or incorporated by reference actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment.

Risks Related to this Offering

If you purchase our securities in this offering, you will experience immediate and substantial dilution in investment. You will experience further dilution if we issue additional equity securities in future financing transactions.

Since the offering price per share of our common stock is higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. As a result, investors purchasing shares of common stock or Pre-Funded Warrants in this offering will incur immediate dilution of approximately \$ per share, based upon the offering price of \$ per share of common stock, \$ per Pre-Funded Warrant, which equals the offering price per share of the common stock less the \$0.0001 per share exercise price of each such Pre-Funded Warrant (and excluding shares of common stock issued or any resulting accounting associated with the Pre-Funded Warrants), and our pro forma as adjusted net tangible book value as of September 30, 2021, after giving effect to this offering and the Incyte Agreement, including the issuance of 1,421,523 shares of common stock for an aggregate purchase price of \$35 million and the receipt of an upfront cash payment of \$117 million. See the section titled “Dilution” below for a more detailed discussion of the dilution you will incur if you purchase common stock or Pre-Funded Warrants in this offering.

In addition, we have a significant number of stock options and pre-funded warrants outstanding. To the extent that these have been or may be exercised, investors purchasing in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders or result in downward pressure on the price of our common stock.

Our management might apply the net proceeds from this offering in ways with which you do not agree and in ways that may impair the value of your investment.

We currently intend to use the net proceeds from this offering primarily to fund our current clinical development efforts, acquire or invest in businesses, products or technologies that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus, and for working capital and general corporate purposes. Pending the use of net proceeds, we intend to invest the net proceeds in short-term, investment-grade, interest bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States. Our management has broad discretion as to the use of these proceeds and you will be relying on the judgment of our management regarding the application of these proceeds. We might apply these proceeds in ways with which you do not agree, or in ways that do not yield

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a favorable return. If our management applies these proceeds in a manner that does not yield a significant return, if any, on our investment of these net proceeds, it could compromise our ability to pursue our growth strategy and adversely affect the market price of our common stock.

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

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

Holders of Pre-Funded Warrants purchased in this offering will have no rights as common stockholders until such holders exercise their warrants and acquire our common stock.

Until holders of the Pre-Funded Warrants acquire shares of our common stock upon exercise of such warrants, the holders will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of the Pre-Funded Warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Risks Related to our Business

We are dependent upon our collaboration with Incyte to further develop and commercialize axatilimab. If we or Incyte fail to perform as expected or if the collaboration is terminated as a result of actions by the Federal Trade Commission or the Department of Justice, the potential for us to generate future revenues under the collaboration could be significantly reduced, the development and/or commercialization of axatilimab may be terminated or substantially delayed, and our business could be adversely affected.

In September 2021, we entered into a collaboration and license agreement with Incyte, or the Incyte Agreement, to collaborate on the development and commercialization of axatilimab. Pursuant to the Incyte Agreement, Incyte paid an upfront initial license fee of \$117 million, in addition to purchasing \$35 million of our common stock. We are eligible to receive up to \$450 million in aggregate regulatory, development and commercial milestone payments plus the tiered royalties. The parties have agreed to co-develop axatilimab and to share development costs associated with global and U.S.-specific clinical trials, with Incyte responsible for 55% of such costs and we are responsible for 45% of such costs. Incyte is responsible for 100% of future development costs for trials that are specific to ex-U.S. countries.

In December 2021, we entered into a letter agreement with Incyte which provides, in part, that in the event either party receives for the first time a formal request from the Federal Trade Commission or the Department of Justice regarding the Incyte Agreement prior to March 23, 2022, then Incyte may terminate the Incyte Agreement through September 2022 and receive a refund of the upfront initial license fee and any payments made by Incyte for royalties, milestones and development costs and any other amounts paid by Incyte to us under the Incyte Agreement. In addition, upon termination of the Incyte Agreement, we will waive any remaining lock-up restrictions and Incyte will sell the shares it purchased in connection with its equity investment in the Company. Following the sale of its shares, Incyte will remit to us any gain that it received, or, alternatively, we will repay Incyte for any loss that it incurred in each case in connection with the sale of the shares. The termination right expires if the parties do not receive a formal request before March 23, 2022.

There is no assurance that the parties will achieve any of the regulatory development or sales milestones, that we will receive any future milestone or royalty payments under the collaboration agreement or that the collaboration will not be unwound as a result of actions by the Federal Trade Commission or the Department of Justice. Incyte's activities may be influenced by, among other things, the efforts and allocation of resources by Incyte, which we cannot control. If Incyte does not perform in the manner we expect or fulfill its responsibilities

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in a timely manner, or at all, the clinical development, manufacturing, regulatory approval, and commercialization efforts related to axatilimab could be delayed or terminated. In addition, our license with Incyte may be unsuccessful due to other factors, including, without limitation, the following:

- Incyte may terminate the agreement for convenience upon 90 or 180 days' notice depending on whether or not the parties have commercialized axatilimab in an indication in the respective territory;
- Incyte may change the focus of its development and commercialization efforts or prioritize other programs more highly and, accordingly, reduce the efforts and resources allocated to axatilimab;
- Incyte may, within its commercially reasonable discretion, choose not to develop and commercialize axatilimab in all relevant markets or for one or more indications, if at all; and
- if Incyte is acquired during the term of our collaboration, the acquirer may have competing programs or different strategic priorities that could cause it to reduce its commitment to our collaboration or to terminate the collaboration.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, or the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC.

Any statements in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein, and any free writing prospectus, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, these forward-looking statements include statements regarding:

- the impact of the COVID-19 pandemic and its effects on our operations, research and development and clinical trials and potential disruption in the operations and business of third-party manufacturers, contract research organizations, or CROs, other service providers, and collaborators with whom we conduct business;
- our estimates regarding our expenses, future revenues, anticipated capital requirements and our needs for additional financing;
- the timing of the progress and receipt of data from the Phase 1/2 clinical trial of SNDX-5613 in patients with relapsed/refractory acute leukemia and the potential use of SNDX-5613 to treat acute leukemias;
- the timing of the progress and receipt of data from the expansion cohort from the Phase 1/2 clinical trial of axatilimab in chronic Graft Versus Host Disease (cGVHD);
- the timing of the progress and receipt of data from the Phase 2 trial, AGAVE-201, of axatilimab in cGVHD;
- our ability to replicate results in future clinical trials;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates as well as the potential use of our product candidates to treat various cancer indications and fibrotic diseases;
- our ability to obtain and maintain regulatory approval for our product candidates and the timing or likelihood of regulatory filings and approvals for such candidates;
- our ability to maintain our licenses with Bayer Pharma AG, Eddingpharm Investment Company Limited, UCB Biopharma Sprl, and Vitae Pharmaceuticals, Inc., a subsidiary of Allergan plc, which was acquired by AbbVie Inc.;
- the success of the Collaboration and License Agreement with Incyte Corporation;
- the potential milestone and royalty payments under certain of our license agreements;
- the implementation of our strategic plans for our business and development of our product candidates;
- the scope of protection we establish and maintain for intellectual property rights covering our product candidates and our technology;

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- the market adoption of our product candidates by physicians and patients;
- developments relating to our competitors and our industry;
- political, social and economic instability, natural disasters or public health crisis, including but not limited to the COVID-19 pandemic, in countries where we or our collaborators do business; and
- the use of proceeds from this offering.

In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expects,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative or plural of those terms, and similar expressions intended to identify statements about the future, although not all forward-looking statements contain these words. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should refer to the risks and uncertainties described in the “Risk Factors” section contained in this prospectus supplement, the accompanying prospectus and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus supplement and the accompanying prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus supplement, even if new information becomes available in the future.

USE OF PROCEEDS

We expect to receive approximately \$ million in net proceeds from the sale of shares of common stock and Pre-Funded Warrants to purchase shares of common stock offered by us in this offering (or approximately \$ million if the underwriters exercise their option to purchase additional shares in full), after deducting underwriting discounts and commissions and estimated offering expenses payable by us and excluding any proceeds we may receive upon exercise of the Pre-Funded Warrants.

We intend to use the net proceeds from the offering for general corporate purposes, including ongoing and expanded clinical development of each of axatilimab and SNDX-5613, expenses related to the potential U.S. commercial launch of each of axatilimab in patients with cGVHD and SNDX-5613 in defined subsets of acute leukemias patients, continued manufacturing scale-up of each of axatilimab and SNDX-5613, the development of other preclinical programs, the opportunistic acquisition or investment in businesses, products or technologies that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement, and for working capital.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering efforts, and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from the shares of common stock we are selling this offering. We will retain broad discretion in determining how we will allocate the net proceeds from this offering. Pending the use of net proceeds, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States.

DILUTION

Our historical net tangible book value as of September 30, 2021 was approximately \$199.0 million, or \$4.07 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2021 (excluding the shares of common stock underlying the outstanding pre-funded warrants).

Our pro forma net tangible book value as of September 30, 2021 was \$351.0 million, or \$6.98 per share, based on the total number of shares of our common stock outstanding as of September 30, 2021. Pro forma net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2021, after giving effect to the issuance of 1,421,523 shares of our common stock for an aggregate purchase price of \$35 million and receipt of an upfront cash payment of \$117 million in connection with the Incyte Agreement subsequent to September 30, 2021.

After giving effect to the sale of _____ shares of our common stock and Pre-Funded Warrants to purchase shares of our common stock at the offering price of \$ _____ per share of common stock and \$ _____ per Pre-Funded Warrant, which equals the offering price per share of the common stock less the \$0.0001 per share exercise price of each such Pre-Funded Warrant (and excluding shares of common stock issued or any resulting accounting associated with the Pre-Funded Warrants), and after deducting estimated offering commissions and offering expenses payable by us and excluding the proceeds, if any, from the exercise of the Pre-Funded Warrants issued pursuant to this offering, our pro forma as adjusted net tangible book value as of September 30, 2021 would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in pro forma net tangible book value of \$ _____ per share to existing stockholders and immediate dilution of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share		\$
Historical net tangible book value per share as of September 30, 2021	\$4.07	
Pro forma increase in net tangible book value per share as of September 30, 2021 attributable to the pro forma transactions described above	<u>2.91</u>	
Pro forma net tangible book value per share as of September 30, 2021	6.98	
Increase in pro forma net tangible book value per share attributable to new investors purchasing shares of common stock and Pre-Funded Warrants in this offering	<u> </u>	
Pro forma as adjusted net tangible book value per share as of September 30, 2021, after giving effect to this offering		<u> </u>
Dilution per share to investors purchasing our common stock and Pre-Funded Warrants in this offering		<u><u>\$</u></u>

The above discussion is based on 48,850,539 shares of our common stock outstanding as of September 30, 2021, and excludes:

- 3,307,952 shares of our common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2021;
- 7,340,654 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2021 under our Stock Plans, at a weighted average exercise price of \$11.70 per share;
- 132,333 shares of common stock issuable upon the vesting of RSUs outstanding as of September 30, 2021;

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- 1,001,470 shares of our common stock available for future issuance under our 2015 Plan as of September 30, 2021, plus any additional shares of our common stock that may become available under our 2015 Plan;
- 1,296,410 shares of our common stock reserved for issuance under our ESPP, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP;
- 1,421,523 shares of our common stock issued to Incyte on December 9, 2021, pursuant to a stock purchase agreement, dated September 24, 2021; and
- shares of common stock underlying the Pre-Funded Warrants being offered hereby.

If the underwriters exercise in full their option to purchase up to additional shares of common stock at the public offering price of \$ _____ per share, the pro forma as adjusted net tangible book value after this offering would be \$ _____ per share, representing an increase in pro forma as adjusted net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering.

Assuming all of the Pre-Funded Warrants issued pursuant to this offering and the outstanding pre-funded warrants were immediately cash exercised, this would result in a pro forma as adjusted net tangible book value per share of \$ _____, after giving effect to the proceeds from such cash exercise, which represents a dilution per share to new investors of \$ _____, and an increase in pro forma as adjusted net tangible book value per share to existing shareholders of \$ _____.

To the extent that options outstanding as of September 30, 2021 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DESCRIPTION OF PRE-FUNDED WARRANTS

Pre-Funded Warrants

General

The term “pre-funded” refers to the fact that the purchase price of the Pre-Funded Warrants in this offering includes almost the entire exercise price that will be paid under the Pre-Funded Warrants, except for a nominal remaining exercise price of \$0.0001. The purpose of the Pre-Funded Warrants is to enable investors that may have restrictions on their ability to beneficially own more than 9.99% of our outstanding common stock following the consummation of this offering the opportunity to invest capital into the Company without triggering their ownership restrictions, by receiving Pre-Funded Warrants in lieu of shares of our common stock which would result in such ownership of more than 9.99%, and receiving the ability to exercise their option to purchase the shares underlying the Pre-Funded Warrants at a nominal price at a later date.

The following is a brief summary of certain terms and conditions of the Pre-Funded Warrants being offered by this prospectus supplement. The following description is subject in all respects to the provisions contained in the Pre-Funded Warrants. The terms and conditions of the Pre-Funded Warrants being offered by this prospectus supplement are substantially similar to the terms and conditions of the Outstanding Pre-Funded Warrants.

Form

The Pre-Funded Warrants will be issued as individual warrant agreements to the investors. The form of Pre-Funded Warrant will be filed as an exhibit to our Current Report on Form 8-K that we expect to file with the SEC in connection with this offering.

Exercise price

Pre-Funded Warrants will have an exercise price of \$0.0001 per share. The exercise price is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Exercisability

The Pre-Funded Warrants are exercisable at any time after their original issuance. The Pre-Funded Warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full of the exercise price in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may elect to exercise the Pre-Funded Warrant through a cashless exercise, in which the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the Pre-Funded Warrant. No fractional shares of common stock will be issued in connection with the exercise of a Pre-Funded Warrant.

Exercise limitations

The Pre-Funded Warrants may not be exercised by the holder to the extent that the holder, together with its affiliates, would beneficially own, after such exercise more than 9.99% of the shares of our common stock then outstanding (including for such purpose the shares of our common stock issuable upon such exercise). However, any holder may increase or decrease such beneficial ownership limitation upon notice to us, provided that such limitation cannot exceed 19.99%, and provided that any increase in the beneficial ownership limitation shall not be effective until 61 days after such notice is delivered.

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Term

The Pre-Funded Warrants expire 20 years from the date of issuance.

Transferability

Subject to applicable laws, the Pre-Funded Warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange listing

There is no established trading market for the Pre-Funded Warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the Pre-Funded Warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the Pre-Funded Warrants will be limited.

Fundamental transactions

In the event of a fundamental transaction, as described in the Pre-Funded Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, upon consummation of such a fundamental transaction, the holders of the Pre-Funded Warrants will be entitled to receive upon exercise of the Pre-Funded Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-funded Warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the Pre-Funded Warrants.

No rights as a stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a Pre-Funded Warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the Pre-Funded Warrant.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares and Pre-Funded Warrants being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares of our common stock and Pre-Funded Warrants indicated in the following table. Goldman Sachs & Co. LLC is acting as the representative of the underwriters:

<u>Name</u>	<u>Number of Shares</u>	<u>Pre-Funded Warrants</u>
Goldman Sachs & Co. LLC		
Total		

The underwriters are committed to purchase all the common shares and Pre-Funded Warrants offered by us if they purchase any securities. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated. The offering of the securities by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters propose to offer the shares of common stock and Pre-Funded Warrants directly to the public at the public offering price set forth on the cover page of this prospectus supplement. After the public offering of the shares and Pre-Funded Warrants, the offering price and other selling terms may be changed by the underwriters.

The underwriters have a 30 day option to buy up to _____ additional shares of common stock from us. The number of shares subject to the underwriters' option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the Pre-Funded Warrants. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to _____ additional shares from us.

	<u>No Exercise</u>	<u>Full Exercise</u>
Per share	\$	\$
Total to be paid by us	\$	\$

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus, and the Pre-Funded Warrants to certain investors at the public offering price per share, minus \$0.0001. Any shares of common stock and Pre-Funded Warrants sold by the underwriters to securities dealers may be sold at a discount of up to \$ _____ per share of common stock or Pre-Funded Warrant from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. Sales of securities made outside of the United States may be made by affiliates of the underwriters.

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$ _____ million. We have agreed to reimburse the underwriters up to an aggregate of \$15,000 for fees incurred by them in connection with any required filings with the Financial Industry Regulatory Authority.

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We and our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which we and each of these persons for a period of 60 days, after the date of this prospectus supplement, may not, subject to limited exceptions, without the prior written consent of Goldman Sachs & Co. LLC (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any other securities convertible into or exercisable or exchangeable for shares of our common stock or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise.

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

Our common stock is listed on the Nasdaq Global Select Market under the symbol "SNDX." There is no established public market for the Pre-Funded Warrants, and we do not intend to list the Pre-Funded Warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The Nasdaq Global Select Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The Nasdaq Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

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

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the Company and to persons and entities with relationships with the Company, for which they received or will receive customary fees and expenses. For example, Goldman Sachs & Co. LLC acted as our exclusive financial advisor in connection with the Collaboration and License Agreement with Incyte Corporation.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the Company (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the Company. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling Restrictions

European Economic Area and United Kingdom

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

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation); or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Securities shall require us or any representative to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the representatives and us that it is a “qualified investor” as defined in the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5 of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and

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agreed that the shares acquired by it in the offer have not been acquired on a nondiscretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

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

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (“FSMA”) received by it in connection with the issue or sale of the shares of our common stock and Pre-Funded Warrants in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock and Pre-Funded Warrants in, from or otherwise involving the United Kingdom.

Canada

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

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

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The shares and Pre-Funded Warrants may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (the “Companies (Winding Up and Miscellaneous Provisions) Ordinance”) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the

“Securities and Futures Ordinance”), or (ii) to “professional investors” as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares and Pre-Funded Warrants may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares or Pre-Funded Warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) where such transfer arises from an offer in that corporation’s securities pursuant to Section 275(1A) of the SFA, (iii) where no consideration is or will be given for the transfer, (iv) where the transfer is by operation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (“Regulation 32”).

Where the shares or Pre-Funded Warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (iii) where no consideration is or will be given for the transfer, (iv) where the transfer is by operation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended) (the “FIEA”). The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any

corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Israel

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

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

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Cooley LLP, Palo Alto, California. The underwriters are being represented in connection with this offering by Goodwin Procter, LLP, New York, New York.

EXPERTS

The consolidated financial statements, incorporated in this prospectus supplement by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2020, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such consolidated financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all of the information set forth or incorporated by reference in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including Syndax. The address of the SEC website is www.sec.gov.

We maintain a website at www.syndax.com. Information contained in or accessible through our website does not constitute a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement. We incorporate by reference into this prospectus supplement the information or documents listed below that we have filed with the SEC (File No. 001-37708):

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on [March 12, 2021](#) and as amended on [April 30, 2021](#);
- our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 1, 2021 (other than the portions thereof which are furnished and not filed);
- our Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2021](#), [June 30, 2021](#) and [September 30, 2021](#), filed with the SEC on May 11, 2021, August 9, 2021 and November 15, 2021, respectively;
- our Current Reports on Form 8-K filed with the SEC on [February 5, 2021](#), [May 13, 2021](#), [September 15, 2021](#), [September 27, 2021](#), [October 4, 2021](#), [December 9, 2021](#) and [December 13, 2021](#), to the extent the information in such reports is filed and not furnished, to the extent the information in such reports is filed and not furnished; and
- the description of our common stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC on March 2, 2016, including, but not limited to, [Exhibit 4.5](#) to our Annual Report on [Form 10-K](#) for the year ended December 31, 2019, filed with the SEC on March 5, 2020, and any other amendments or reports filed for the purposes of updating this description.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus supplement.

We also incorporate by reference into this prospectus supplement all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

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We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus supplement but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Syndax Pharmaceuticals, Inc., Attn:

Luke J. Albrecht, General Counsel, 35 Gatehouse Drive, Building D, Floor 3, Waltham, Massachusetts 02451; telephone: (781) 419-1400.

PROSPECTUS



**Common Stock
Preferred Stock
Debt Securities
Warrants**

From time to time, we may offer any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market, or Nasdaq, under the symbol "SNDX." On March 18, 2021, the last reported sale price of our common stock was \$23.02 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on Nasdaq or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section titled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus as described on page 6 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 24, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement on Form S-3 that we filed with the Securities and Exchange Commission (“SEC”) using a “shelf” registration process as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended (the “Securities Act”). Under this shelf Registration Statement, we may sell from time to time, in one or more offerings, common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities described in this prospectus. There is no limit on the aggregate amount of the securities that we may offer pursuant to the Registration Statement of which this prospectus is a part. This prospectus provides you with a general description of the securities we may offer.

Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. We may also add, update or change in a prospectus supplement or free writing prospectus any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. You should carefully read both this prospectus and the applicable prospectus supplement and any related free writing prospectus, together with the additional information described under “Where You Can Find More Information,” before buying any of the securities being offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus 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, any applicable supplement to this prospectus or any related free writing prospectus 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, any applicable prospectus supplement or any related free writing prospectus 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, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

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

SUMMARY

The following summary highlights information contained elsewhere in this prospectus. This summary is not complete and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless the context indicates otherwise, references in this prospectus to “Syndax,” “the Company,” “we,” “us,” “our” and similar references refer to Syndax Pharmaceuticals, Inc. and its wholly owned subsidiaries.

Company Overview

We are a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Our two lead product candidates are, SNDX-5613 and SNDX-6352, or axatilimab. We are developing SNDX-5613, targeting the binding interaction of menin with the mixed lineage leukemia 1 (MLL1) protein for the treatment of MLL-rearranged, or MLLr, acute leukemias and nucleophosmin 1, or NPM1, mutant acute myeloid leukemia (AML), as well as axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1, or CSF-1 receptor. We have deprioritized the development of entinostat, our once-weekly, oral, small molecule, Class I HDAC inhibitor, to focus resources on advancing the remainder of our pipeline. We plan to continue to leverage the technical and business expertise of our management team and scientific collaborators to license, acquire and develop additional therapeutics to expand our pipeline.

Corporate Information

We were incorporated in Delaware in 2005. In 2011, we established a wholly owned subsidiary in the United Kingdom and in 2014 we established a wholly owned U.S. subsidiary. Our principal executive offices are located at 35 Gatehouse Drive, Building D, Floor 3, Waltham, Massachusetts 02451 and our telephone number is (781) 419-1400. Our corporate website address is www.syndax.com. Information contained on or accessible through our website is not incorporated by reference into this prospectus, and you should not consider such information as part of this prospectus or in deciding whether to purchase our securities.

“Syndax” is a registered trademark and the “Syndax” and “Syndax Pharmaceuticals” logos are unregistered trademarks of the company. This prospectus also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this prospectus are the property of their respective holders.

Summary of Selected Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled “Risk Factors” immediately following this prospectus summary and those described under similar headings in the documents incorporated by reference into this prospectus. These risks include:

- COVID-19 could adversely impact our business, including our clinical trials.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any of our product candidates.
- We are currently developing several product candidates. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize our product candidates, our business prospects will be significantly harmed.

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- Our strategy for developing SNDX-5613 has undergone limited clinical testing and we may fail to show that the drug is well tolerated and provides sufficient clinical benefit for patients.
- Our strategy for developing axatilimab has undergone limited clinical testing and we may fail to show that this drug is well tolerated and provides a clinical benefit for patients.
- Interim top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- If we are or our collaborators are unable to enroll patients in clinical trials, these clinical trials may not be completed on a timely basis or at all.
- The regulatory approval processes of the FDA and foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates could harm our business.
- We rely on third-party suppliers to manufacture and distribute our clinical drug supplies for our product candidates, we intend to rely on third parties for commercial manufacturing and distribution of our product candidates and we expect to rely on third parties for manufacturing and distribution of preclinical, clinical and commercial supplies of any future product candidates.
- Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial scope of their approved use, or result in significant negative consequences following any marketing approval.
- We have incurred net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- We currently have no source of product revenue and may never achieve or maintain profitability.
- We will require additional capital to finance our planned operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of, or obtain regulatory approval for our existing product candidates or develop new product candidates.
- If we are unable to obtain or protect intellectual property rights, we may not be able to compete effectively in our market.
- We may not be able to protect our intellectual property rights throughout the world.
- The market price of our stock may be volatile and you could lose all or part of your investment.
- We may sell additional equity or debt securities or enter into other arrangements to fund our operations, which may result in dilution to our stockholders and impose restrictions or limitations on our business.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

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- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of: (i) December 31, 2021; (ii) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion; (iii) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock held by non-affiliates exceeds \$700 million as of June 30 of such fiscal year; or (iv) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period. We may choose to take advantage of some or all of these available exemptions. We have taken advantage of some reduced reporting requirements in our public filings. Accordingly, the information that we provide stockholders may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

We are also a smaller reporting company as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) our voting and non-voting common stock held by nonaffiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter or (ii) our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount;
- rates and times of payment of interest or dividends;

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- redemption, conversion, exchange or sinking fund terms;
- ranking;
- restrictive covenants;
- voting or other rights;
- conversion or exchange prices or rates and any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange; and
- important U.S. federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the estimated net proceeds to us.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Common Stock. We may issue shares of our common stock from time to time. Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders and does not have cumulative voting rights. Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock. Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future. In this prospectus, we have summarized certain general features of our common stock under the heading “Description of Capital Stock—Common Stock.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority, without further action by our stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption,

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liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. Any convertible preferred stock we may issue will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under the heading "Description of Capital Stock—Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under the heading "Description of Debt Securities." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures and any supplemental indentures that contain the terms of the debt securities. We have filed a form of indenture as an exhibit to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, supplemental indentures and forms of debt securities containing the terms of the debt securities being offered.

Warrants. We may issue warrants for the purchase of common stock, preferred stock or debt securities, from time to time, in one or more series. We may issue warrants independently or in combination with common stock, preferred stock or debt securities. In this prospectus, we have summarized certain general features of the warrants under the heading "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that we may offer as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2020 and in our most recent Quarterly Report on Form 10-Q, as updated by our subsequent filings, which are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, results of operations, financial condition and cash flows, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus contain forward-looking statements. These statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto, filed with the SEC.

Any statements in this prospectus, or incorporated herein by reference, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act these forward-looking statements include statements regarding:

- the impact of the COVID-19 pandemic and its effects on our operations, research and development and clinical trials and potential disruption in the operations and business of third-party manufacturers, contract research organizations, or CROs, other service providers, and collaborators with whom we conduct business;
- our estimates regarding our expenses, future revenues, anticipated capital requirements and our needs for additional financing;
- the timing of the progress and receipt of data from the Phase 1/2 clinical trial of SNDX-5613 in patients with relapsed/refractory (R/R) acute leukemia and the potential use of SNDX-5613 to treat acute leukemias;
- the timing of the progress and receipt of data from the expansion cohort from the Phase 1/2 clinical trial of axatilimab in chronic Graft Versus Host Disease (cGVHD);
- the timing of the progress and receipt of data from the Phase 2 trial, AGAVE-201, of axatilimab in cGVHD
- our ability to replicate results in future clinical trials;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- our ability to obtain and maintain regulatory approval for our product candidates and the timing or likelihood of regulatory filings and approvals for such candidates;
- our ability to maintain our licenses with Bayer Pharma AG, Eddingpharm Investment Company Limited, Kyowa Kirin Co., Ltd., UCB Biopharma Sprl, and Vitae Pharmaceuticals, Inc., a subsidiary of AbbVie plc.;
- the potential milestone and royalty payments under certain of our license agreements;
- the implementation of our strategic plans for our business and development of our product candidates;
- the scope of protection we establish and maintain for intellectual property rights covering our product candidates and our technology;
- the market adoption of our product candidates by physicians and patients;
- developments relating to our competitors and our industry; and
- political, social and economic instability, natural disasters or public health crisis, including but not limited to the COVID-19 pandemic, in countries where we or our collaborators do business.

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In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “could,” “estimate,” “expects,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative or plural of those terms, and similar expressions intended to identify statements about the future, although not all forward-looking statements contain these words. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should refer to the “Risk Factors” section contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any applicable prospectus supplement or in any free writing prospectuses that we may authorize to be provided to you in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered hereby, if any, to fund research and development of our product candidates, acquire or invest in businesses, products or technologies that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus, and for working capital and general corporate purposes. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending the use of net proceeds, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States government.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries. You should also refer to the amended and restated certificate of incorporation and the amended and restated bylaws, which are filed as exhibits to the registration statement of which this prospectus is part.

General

Under our amended and restated certificate of incorporation we are authorized to issue up to 100,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share, all of which shares of preferred stock are undesignated. Our board of directors may establish the rights and preferences of the preferred stock from time to time. As of December 31, 2020, we had outstanding 47,881,223 shares of common stock.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least 66 $\frac{2}{3}$ % of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose on a non-cumulative basis.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

Rights and Preferences

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

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such

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series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action, or make the removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock.

Our board of directors will fix the designations, voting powers, preferences and rights of each series, as well as the qualifications, limitations or restrictions thereof, of the preferred stock of each series that we offer under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special 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 if we liquidate, dissolve or wind up our affairs;

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- any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock.

The Delaware General Corporation Law, or DGCL, which is the law of the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value, the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be, or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Warrants

In March 2019, we issued pre-funded warrants to purchase 2,500,000 shares of common stock and, in January 2020, we issued additional pre-funded warrants to purchase 1,338,287 shares of common stock, or, together, the Pre-Funded Warrants, to certain investors. The Pre-Funded Warrants are exercisable immediately upon issuance at an exercise price of \$0.0001 per share. The Pre-Funded Warrants may not be exercised by the holder to the extent that the holder, together with its affiliates, would beneficially own, after such exercise more than 9.99% of the shares of our common stock then outstanding (subject to the right of the holder to increase or decrease such beneficial ownership limitation upon notice to us, provided that such limitation cannot exceed 19.99%) and provided that any increase in the beneficial ownership limitation shall not be effective until 61 days after such notice is delivered. The Pre-Funded Warrants have a term of 20 years. As of December 31, 2020, there were 3,557,952 Pre-Funded Warrants outstanding.

Anti-Takeover Provisions

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- ***Issuance of Undesignated Preferred Stock.*** Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.
- ***Classified Board.*** Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our board.
- ***Board of Directors Vacancies.*** Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominee.

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- **Stockholder Action; Special Meetings of Stockholders.** Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our amended and restated certificate of incorporation further provides that only the chairman of our board of directors or a majority of our board of directors may call special meetings of our stockholders.
- **Advance Notice Requirements for Stockholder Proposals and Director Nominations.** Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.

We designed these provisions to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us, and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that 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 began, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least $66\frac{2}{3}\%$ of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a "business combination" to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or

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- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the entity or person’s affiliates and associates, beneficially owns, or is an affiliate or associate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may “opt out” of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change of control attempts of us.

Choice of Forum

Our amended and restated certificate of incorporation will provide that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware), the Court of Chancery of the State of Delaware will be the exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action or proceeding commenced by any of our stockholders (including any class action) asserting a breach of fiduciary duty owed, or other wrongdoing, by any director, officer, employee or agent to us or our stockholders, (3) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against us arising pursuant to the DGCL or our amended and restated certificate of incorporation or our amended and restated bylaws, (4) any action or proceeding commenced by any of our stockholders (including any class action) to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, or (5) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against us that is governed by the internal affairs doctrine.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent’s address is P.O. Box 505000, Louisville, KY 40233-5000. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Listing on Nasdaq

Our common stock is listed on Nasdaq under the symbol “SNDX.”

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

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

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

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- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

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- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any, and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

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If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

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- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale”;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities—General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;

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- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or the DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange of any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or

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use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that contains the terms of the particular series of warrants we are offering, as well as any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectus, and the complete form of warrant or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

In the applicable prospectus supplement, we will describe the terms of the series of warrants being offered, including, to the extent applicable:

- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;
- the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- the date on and after which the warrants and the related securities will be separately transferable;
- the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable on exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased on such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable on the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased on such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- the terms of any rights to force the exercise of the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable on exercise of the warrants;

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- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable on exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable on such exercise, including:

- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any; or
- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as described in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the expiration date that we list in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

On receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable on such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

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

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depository maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depository or its participants. Consequently, for global securities, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

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For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, the DTC, New York, New York, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under “—Special Situations When a Global Security Will Be Terminated.” As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depository in any way;
- the depository may, and we understand that the DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or

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- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

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

We may also sell equity securities covered by this registration statement in an “at the market offering” as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of Nasdaq or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- other than on Nasdaq or such other securities exchanges or quotation or trading services.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

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We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallocation, stabilizing transactions, short covering transactions and penalty bids. Overallocation 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 stabilizing or 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. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters who are qualified market makers on Nasdaq may engage in passive market making transactions in the securities on Nasdaq in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements, incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including Syndax. The address of the SEC website is www.sec.gov.

We maintain a website at www.syndax.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be a part of this prospectus, and the information that we file later with the SEC will automatically update and, where applicable, supersede the information already incorporated by reference. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement. The SEC file number for the documents incorporated by reference in this prospectus is 001-37708.

The following documents are incorporated by reference into this document:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 12, 2021;
- our Current Report on [Form 8-K](#) filed with the SEC on February 5, 2021; and
- the description of our common stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC on March 2, 2016, including, but not limited to, [Exhibit 4.5](#) to our Annual Report on [Form 10-K](#) for the year ended December 31, 2019, and any other amendments or reports filed for the purposes of updating this description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

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Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Syndax Pharmaceuticals, Inc., Attn: Luke Albrecht, General Counsel, 35 Gatehouse Drive, Building D, Floor 3, Waltham, Massachusetts 02451; telephone: (781) 419-1400.

\$75,000,000



Shares of Common Stock
Pre-Funded Warrants to Purchase **Shares of Common Stock**

PRELIMINARY PROSPECTUS SUPPLEMENT

Goldman Sachs & Co. LLC

December , 2021
