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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 11, 2021

SYNDAX PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37708**	**32-0162505**
(state or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

Building D, Floor 3 **35 Gatehouse Drive** **Waltham, Massachusetts**	**02451**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (781) 419-1400

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	SNDX	The Nasdaq Stock Market, LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☑

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☑

Item 8.01. Other Events.

On December 11, 2021, Syndax Pharmaceuticals, Inc. ("***our***," "***we***," or the "***Company***") issued a press release announcing updated data from our Phase 1/2 trial of axatilimab in patients with recurrent or refractory chronic graft-versus-host disease (cGVHD) despite two or more prior lines of therapy. Additionally, on December 13, 2021, we issued a press release announcing updated data from the Phase 1 portion of our AUGMENT-101 trial in heavily pretreated patients with mixed lineage leukemia rearranged (MLLr) or nucleophosmin (NPM1c) mutations. The data from each press release were featured during oral sessions at the 63rd Annual Society of Hematology (ASH) Annual Meeting. A copy of each press release is filed herewith as Exhibit 99.1 and Exhibit 99.2, respectively. The information contained in each press release is incorporated by reference into this Current Report on Form 8-K.

Forward Looking Statements

This Current Report on Form 8-K contains "forward-looking statements," including, but not limited to, statements regarding the Company's development plans for axatilimab for patients with cGVHD and SNDX-5613 for patients with MLLr and NPM1c. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause the Company's actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "could," "expects," "plans," "anticipates," "believes," and similar expressions intended to identify forward-looking statements. These statements reflect the Company's current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Any forward-looking statements set forth in this Current Report speak only as of the date of this Current Report. The Company does not intend to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof other than as required by law. You are cautioned not to place undue reliance on any forward-looking statements.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release dated December 11, 2021
99.2	Press release dated December 13, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SYNDAX PHARMACEUTICALS, INC.

By: /s/ Briggs W. Morrison, M.D.
Briggs W. Morrison, M.D.
Chief Executive Officer

Dated: December 13, 2021

Syndax Pharmaceuticals Announces Updated Positive Data Demonstrating Broad Activity and Tolerability of Axatilimab in Patients with Chronic Graft-Versus-Host Disease

– 68% overall response rate and broad multiorgan clinical benefit observed in highly refractory patients treated at doses being assessed in ongoing AGAVE-201 pivotal study –

– Axatilimab well-tolerated at all doses and schedules –

WALTHAM, Mass., December 11, 2021 (PRNEWSWIRE) – Syndax Pharmaceuticals, Inc. (“Syndax,” the “Company” or “we”) (Nasdaq: SNDX), a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced updated positive data from its Phase 1/2 trial of axatilimab in patients with recurrent or refractory chronic graft-versus-host disease (cGVHD) despite two or more prior lines of therapy. Axatilimab is the Company’s anti-CSF-1R monoclonal antibody. The data are being featured during an oral session at the 63rd American Society of Hematology (ASH) Annual Meeting on Saturday, December 11, 2021 at 3:05 p.m. ET.

“There exists an urgent need for novel and effective therapies in patients with cGVHD,” said Michael Meyers, M.D, M.P.H., Chief Medical Officer of Syndax. “The broad activity and tolerability observed underscores axatilimab’s potential to play a meaningful role in the cGVHD treatment landscape, and further supports the importance of the ongoing AGAVE-201 trial.”

“Durable responses and multiorgan clinical benefit reported today from the ongoing pivotal Phase 2 AGAVE-201 trial continue to support axatilimab’s potential to serve as an intervention for patients with cGVHD,” said Briggs W. Morrison, M.D., Chief Executive Officer of Syndax. “We are committed to maximizing the clinical impact of axatilimab across multiple lines of treatment in cGVHD as well as additional fibrotic diseases where the monocyte-macrophage lineage plays a vital role, such as idiopathic pulmonary fibrosis. We look forward to providing updates on our progress in the coming months.”

A total of 40 patients with refractory disease who received a median of four prior systemic therapies, including ibrutinib, ruxolitinib, and belumosudil, were treated in the Company's Phase 1/2 trial of axatilimab. As of an October 22, 2021 data cutoff date, 31 patients treated at two of the doses being tested in the Company's ongoing AGAVE-201 global pivotal study were evaluable for response. A best ORR (complete response + partial response) of 72% (18/25) at 1mg/kg every two weeks and 50% (3/6) at 3mg/kg every four weeks was observed, for an ORR of 68% (21/31). Of note, responses were observed across a range of organ systems with difficult to treat manifestations such as lung (5/15), skin (3/28), and joints and fascia (16/24). Fifty-three percent of patients reported clinically meaningful improvement in their symptoms via the Lee Symptom Scale. As of the data cutoff date, 43% (17/40) of patients remained on treatment.

Axatilimab was well-tolerated with a favorable safety profile. The most common adverse events were consistent with on-target effects on liver enzyme pharmacology. There was no incidence of cytomegalovirus (CMV) or other viral reactivation, and no apparent increases in risk for infection.

Enrollment is ongoing in the Company's global pivotal Phase 2 AGAVE-201 trial of axatilimab in patients with cGVHD, with topline data expected in 2023. The trial will evaluate the safety and efficacy of three doses and schedules of axatilimab. The primary endpoint will assess objective response rate based on the 2014 NIH consensus criteria for cGVHD, with key secondary endpoints including duration of response and improvement in modified Lee Symptom Scale score.

A copy of today’s presentation will be available in the Publications and Meeting Presentations section of Syndax’s website.

About Chronic Graft-Versus-Host Disease

Chronic graft-versus-host disease (cGVHD), an immune response of the donor-derived hematopoietic cells against recipient tissues, is a serious, potentially life-threatening complication of allogeneic hematopoietic stem cell transplantation (HSCT) which can last for years. Chronic GVHD is estimated to develop in approximately 40% of transplant recipients, and affects approximately 14,000 patients in the U.S.[1,2] Chronic GVHD typically manifests across multiple organ systems, with skin and mucosa being commonly involved, and is characterized by the development of fibrotic tissue.[3]

About Axatilimab

Axatilimab is an investigational monoclonal antibody that targets colony stimulating factor-1 receptor, or CSF-1R, a cell surface protein thought to control the survival and function of monocytes and macrophages. In pre-clinical models, inhibition of signaling through the CSF-1 receptor has been shown to reduce the number of disease-mediating macrophages along with their monocyte precursors, which has been shown to play a key role in the fibrotic disease process underlying diseases, such as chronic graft-versus-host disease (cGVHD) and idiopathic pulmonary fibrosis (IPF). Axatilimab data has demonstrated deep, durable responses and multiorgan clinical benefit in patients with cGVHD refractory to multiple therapeutic agents, and is currently being evaluated in the global pivotal Phase 2 AGAVE-201 trial in patients with cGVHD. Axatilimab was granted Orphan Drug Designation by the U.S. Food and Drug Administration for the treatment of patients with cGVHD and IPF. In September 2021, Syndax and Incyte entered into an exclusive worldwide collaboration and license agreement to develop and commercialize axatilimab. Axatilimab is being developed under an exclusive worldwide license from UCB entered into between Syndax and UCB in 2016.

About Syndax Pharmaceuticals, Inc.

Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. The Company's pipeline includes SNDX-5613, a highly selective inhibitor of the Menin–MLL binding interaction, axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, and entinostat, a class I HDAC inhibitor. For more information, please visit www.syndax.com or follow the Company on Twitter and LinkedIn.

Syndax's Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "plan," "anticipate," "estimate," "intend," "believe" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Syndax's expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this press release include, but are not limited to, statements about the progress, timing, clinical development and scope of clinical trials and the reporting of clinical data for Syndax's product candidates, and the potential use of our product candidates to treat various cancer indications and fibrotic diseases. Many factors may cause differences between current expectations and actual results including unexpected safety or efficacy data observed during preclinical or clinical trials, clinical trial site activation or enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity, failure of Syndax's collaborators to support or advance collaborations or product candidates and unexpected litigation or other disputes. Other factors that may cause Syndax's actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in Syndax's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on September 15, 2021, as well as in other filings we may make with the SEC in the future. Except as required by law, Syndax assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Reference

1. SmartAnalyst 2020 SmartImmunology Insights chronic GVHD report.
2. Bachier, CR. et al. ASH annual meeting 2019; abstract #2109 Epidemiology and Real-World Treatment of Chronic Graft-Versus-Host Disease Post Allogeneic Hematopoietic Cell Transplantation: A U.S. Claims Analysis.
3. Kantar 2020 GVHD Expert Interviews N=32 interviews.

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SNDX-G

Syndax Pharmaceuticals Announces Additional Positive Data Demonstrating Continued Robust Clinical Activity with Durable Responses in Phase 1 Portion of AUGMENT-101 Trial of SNDX-5613

– 55% overall response rate and 24% CR/CRh rate in relapsed/refractory acute leukemia patients with NPM1 or MLLr mutations; no discontinuations due to treatment-related adverse events –

– CR/CRh rates of 23% and 24% in mNPM1 and MLLr patients, respectively –

– CR/CRh responses were durable; median duration of response was not reached; 50% persisted longer than 6 months –

WALTHAM, Mass., December 13, 2021 (PRNEWSWIRE) – Syndax Pharmaceuticals, Inc. (“Syndax,” the “Company” or “we”) (Nasdaq: SNDX), a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced updated positive data from the Phase 1 dose escalation portion of the AUGMENT-101 trial of SNDX-5613 in patients with mutant nucleophosmin (mNPM1) or mixed lineage leukemia rearranged (MLLr) relapsed/refractory (R/R) acute leukemias. SNDX-5613 is the Company's highly selective oral menin inhibitor. The data are being featured during an oral session at the 63rd American Society of Hematology (ASH) Annual Meeting on Monday, December 13, 2021 at 3:15 p.m. ET.

“Patients with relapsed or refractory leukemia harboring NPM1 mutations or MLL-rearrangements face a particularly poor prognosis,” said Eytan M. Stein, M.D., Assistant Attending Physician and Director, Program for Drug Development in Leukemia, Department of Medicine at Memorial Sloan Kettering Cancer Center, and the trial's principal investigator. “Data being reported today show highly encouraging clinical activity and favorable tolerability across a heavily pretreated population. In addition to very high MRD negative rates in those patients achieving complete response (CR) or CR with partial hematologic recovery (CRh), we are also seeing response durations greater than six months.”

“The updated data presented today at ASH from our ongoing AUGMENT-101 trial strongly support the potential of SNDX-5613 to serve as a best-in-class treatment option for patients with NPM1 or MLLr leukemia, which together represents approximately 40% of all acute leukemias,” said Briggs W. Morrison, M.D., Chief Executive Officer of Syndax. “We are also very pleased that discussions with the U.S. Food and Drug Administration (FDA) have confirmed that the ongoing Phase 2 AUGMENT-101 trial may potentially serve as the basis for regulatory filings in each of its three indication-specific cohorts of NPM1 mutant acute myeloid leukemia (AML), MLLr AML, and MLLr acute lymphoblastic leukemia (ALL), and that patients will be able to restart treatment with SNDX-5613 following a stem cell transplant.”

Dr. Morrison continued, “We also remain focused on executing on our strategy to expand into earlier lines of therapy and pediatric populations, and we look forward to initiating the BEAT AML

trial in frontline MLLr and mNPM1 AML in combination with venetoclax and azacitidine, the INTERCEPT trial in AML patients with MRD positive disease, and the AUGMENT-102 trial in combination with chemotherapy in adult and pediatric relapsed/refractory MLLr and mNPM1 acute leukemia patients."

As of an October 18, 2021 data cutoff date, a total of 59 patients with a median of four prior therapies, including 42% who received a prior stem cell transplant and 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 overall response rate[1] (ORR) was 55%, with a CR/CRh rate of 24% and nine patients proceeding to stem cell transplant (two patients achieving a CR with incomplete platelet recovery [CRp] with no evidence of minimal residual disease [MRD], and seven patients who achieved MRD- CR or CRh). The ORR in evaluable patients harboring an NPM1 mutation was 38% (5/13), with a CR/CRh rate of 23% (3/13). The ORR in evaluable patients harboring an MLL-rearrangement was 61% (23/38), with a CR/CRh rate of 24% (9/38).

The overall MRD negative rate was 31% (16/51). Among those patients who achieved CR/CRh, 92% (11/12) were MRD negative, including 100% (3/3) of NPM1 patients and 89% (8/9) of MLLr patients. Median time to response for patients achieving a CR/CRh was two months. Median duration of response (DOR) was not reached, inclusive of patients who received stem cell transplant, and 6/12 patients who achieved CR/CRh had a duration of response greater than six months.

SNDX-5613 was well-tolerated, with no discontinuations due to treatment-related adverse events observed in heavily pretreated patients. The only dose limiting toxicity observed was Grade 3 QT prolongation, which occurred in 7% (3/43) of patients treated at the four doses that met the study's pre-defined recommended Phase 2 dose criteria. Differentiation syndrome was reported in 14% of patients (8/59) with all cases being Grade 1 or 2 and readily managed with standard therapies.

As data from the Phase 1 portion of the trial have continued to mature, the results have demonstrated consistent and compelling anti-leukemic activity with favorable tolerability in patients with both R/R MLLr and NPM1 acute leukemias. The following table summarizes select efficacy and safety data that has been presented by the Company throughout 2021.

Best Response in Response Evaluable Patients	**April '21 n = 31 (%)**	**May '21 n = 31 (%)**	**Dec '21 n = 51 (%)**
Overall Response Rate* (ORR)	**15/31 (48%)**	**15/31 (48%)**	**28/51 (55%)**
CR/CRh	5 (16%)	7 (23%)	12 (24%)
CRp	5 (16%)	4 (13%)	7 (14%)
CRi/MLFS	5 (16%)	4 (13%)	9 (18%)
Received HSCT	4	4	9
MLLr ORR	13/24 (54%)	13/24 (54%)	23/38 (61%)
mNPM1 ORR	2/7 (29%)	2/7 (29%)	5/13 (38%)
≥Gr3 QTc prolonged (all doses)	14%	14%	12%
≥Gr3 QTc prolonged (RP2D doses)	9%	9%	7%

* Overall Response Rate = CR + CRh + CRp + CRi + MLFS

The Phase 2 portion of AUGMENT-101, which will assess 163 mg every 12 hours of SNDX-5613 in patients receiving concomitant strong CYP3A4 inhibitor treatment, is currently underway. A total of 64 adult and up to ten pediatric patients will be enrolled across each of the following three distinct trial populations: patients with NPM1 mutant AML, patients with MLLr AML, and patients with MLLr ALL. Discussions with the FDA have confirmed that AUGMENT-101 may potentially serve as the basis for regulatory filings in each of the three distinct trials. The primary endpoint for each of the three trials will be efficacy as measured by complete remission rate (CR + CRh), with key secondary endpoints including DOR and overall survival.

A copy of today’s presentation will be available in the Publications and Meeting Presentations section of Syndax’s website.

About SNDX-5613

SNDX-5613 is a potent, selective, small molecule inhibitor of the menin-MLL binding interaction that is being developed for the treatment of mixed lineage leukemia rearranged (MLLr) acute leukemias including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), and NPM1 mutant AML. In preclinical models of MLLr acute leukemias, SNDX-5613 demonstrated robust, dose-dependent inhibition of tumor growth, resulting in a marked survival benefit. Menin-MLL interaction inhibitors have also demonstrated robust treatment benefit in multiple preclinical models of NPM1 mutant AML, which represents the most frequent genetic abnormality in adult AML. SNDX-5613 is currently being evaluated in the Company's AUGMENT-101 Phase 1/2 open-label clinical trial for the treatment of relapsed/refractory (R/R) acute leukemias. SNDX-5613 was granted Orphan Drug Designation by the U.S. Food and Drug Administration for the treatment of patients with AML, and Fast Track designation for the treatment of adult and pediatric patients with relapsed or refractory acute leukemias harboring a mixed lineage leukemia rearranged MLLr or NPM1 mutation.

About Mixed Lineage Leukemia Rearranged Acute Leukemias

Rearrangements of the MLL gene give rise to mixed lineage leukemia rearranged (MLLr) acute leukemias known to have a poor prognosis, with less than 25% of adult patients surviving past five years. MLL rearrangements produce fusion proteins that require interaction with the protein called menin to drive leukemic cancer growth. Disruption of the menin-MLLr interaction has been shown to halt the growth of MLLr leukemic cells. MLLr leukemias, which are routinely diagnosed through currently available cytogenetic or molecular diagnostic techniques, occur in approximately 80% of infant acute leukemias and up to 10% of all acute leukemias. There are currently no approved therapies indicated for MLLr leukemias.

About NPM1 Mutant Acute Myeloid Leukemia

NPM1 mutant acute myeloid leukemia (AML), which is distinguished by point mutations in the NPM1 gene that drive the leukemic phenotype, is the most common type of cytogenetically normal adult AML and represents approximately 30% of all adult AML cases. This subtype of AML has a

five-year overall survival rate of approximately 50%. Similar to mixed lineage leukemia rearranged (MLLr) leukemias, NPM1 mutant AML is highly dependent on the expression of specific developmental genes shown to be negatively impacted by inhibitors of the menin-MLL interaction. NPM1 mutant AML is routinely diagnosed through currently available screening techniques. There are currently no approved therapies indicated for NPM1 mutant AML.

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Reference

1. ORR = CR + CRh + CRp + MLFS

Disclosure: Dr. Stein has provided consulting services for Syndax

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