Syndax and Incyte Announce Positive Topline Results from the Pivotal AGAVE-201 Trial of Axatilimab in Chronic Graft-Versus-Host Disease

July 24, 2023

– Trial met its primary endpoint across all cohorts with an overall response rate (ORR) of 74% at a dose of 0.3 mg/kg administered every two weeks –

– Data highlight durable response to treatment. At the 0.3 mg/kg dose, 60% of patients who responded to axatilimab were still responding at one year –

– Results continue to support axatilimab's promising safety and efficacy profile, and reinforce its potential as a first-in-class CSF-1R monoclonal antibody in chronic graft-versus-host disease (GVHD) –

– Syndax and Incyte intend to file a Biologics License Application (BLA) by year-end 2023; full dataset to be presented at a future medical meeting –

– Syndax to host conference call today at 8:30 a.m. ET –

WALTHAM, Mass. and WILMINGTON, Del., July 24, 2023 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX) and Incyte (Nasdaq: INCY) today announced positive topline data from the pivotal AGAVE-201 trial of axatilimab, an anti-CSF-1R antibody, in adult and pediatric patients with chronic graft-versus-host disease (GVHD) following two or more prior lines of therapy.

The trial achieved its primary endpoint across all cohorts, with patients treated with axatilimab at doses of 0.3 mg/kg every two weeks, 1.0 mg/kg every two weeks and 3.0 mg/kg every four weeks demonstrating overall response rates (ORR) within the first six months of treatment of 74%, 67% and 50%, respectively (95% Confidence Interval [CI]: [63,83], [55,77] and [39,61], respectively). Responses were achieved across key patient subgroups, including those with prior exposure to ruxolitinib, belumosudil and/or ibrutinib.

Based on these results, and pending agreement from the U.S. Food and Drug Administration (FDA), Syndax and Incyte intend to submit a Biologics License Application (BLA) to the FDA by year-end 2023.

"Today marks an important day not only for Syndax and Incyte, but, more importantly, for patients suffering from chronic GVHD," said Michael A. Metzger, Chief Executive Officer of Syndax. "Axatilimab is the first investigational chronic GVHD treatment to target inflammation and fibrosis through the inhibition of disease associated macrophages, and the AGAVE-201 data demonstrates the potentially pronounced impact this mechanism, alone or in combination with standard of care therapies already available for the management of this disease, may have on patients suffering from chronic GVHD. These results underscore our belief that axatilimab could provide a valuable and highly differentiated therapeutic option for this devastating disease. We look forward to working with our partners at Incyte as we move axatilimab towards regulatory filing. On behalf of the entire Syndax team, I would like to thank the patients, their caregivers and the investigators who made this trial possible."

"The results from the AGAVE-201 study are extremely compelling and underscore the potential benefits axatilimab may offer appropriate patients facing the serious complications associated with chronic GVHD," said Steven Stein, M.D., Chief Medical Officer of Incyte. "At Incyte, we remain committed to advancing our research and understanding of this complex disease and will work closely with Syndax and regulatory authorities to bring this innovative medicine to chronic GVHD patients."

The AGAVE-201 pivotal study enrolled a total of 241 patients across 121 sites in 16 countries. Patients enrolled in the trial had received a median of four prior systemic therapies with 74% having previously received ruxolitinib, 23% having previously received belumosudil and 31% having previously received ibrutinib. 54% of these patients had at least four organs involved at baseline including 45% with lung involvement.

Among responders treated with 0.3 mg/kg of axatilimab, 60% of patients maintained a response at 12 months (measured from first response to new systemic therapy or death, based on the Kaplan Meier estimate). The median duration of response in this population has not been reached. Additionally, in the 0.3 mg/kg group, 55% of patients experienced a clinically meaningful improvement in symptoms, as measured by at least a seven-point decrease in the modified Lee chronic GVHD Symptom Scale score.

The most common adverse events were consistent with the on-target effects of CSF-1R inhibition and with what was previously observed with axatilimab treatment. In the overall population, adverse events in greater than 20% of patients include an increase in aspartate aminotransferase, blood creatine phosphokinase, lipase, blood lactate dehydrogenase, alanine aminotransferase and fatigue (n=239). Serious adverse events in the overall population occurred in 101 (42.3%) patients, with 37 (15.5%) patients experiencing adverse events leading to discontinuation of study treatment. In the 0.3 mg/kg dose group (n=79), fatigue was the only serious adverse event that occurred in greater than 20% of patients. Serious adverse events in the 0.3 mg/kg group occurred in 30 (38%) patients, with five (6.3%) patients experiencing adverse events leading to discontinuation of study treatment.

"Chronic GVHD is a very common complication post allogeneic hematopoietic stem cell transplant that can have profound effects on patient medical burden and quality of life. More effective treatment options for this significant complication are desperately needed," said Carrie Kitko, M.D., Medical Director of the Pediatric Stem Cell Transplant Program at the Vanderbilt-Ingram Cancer Center. "I am highly encouraged by these data which demonstrate robust responses in a heavily pre-treated patient population. These findings further support that axatilimab has the potential to provide a clinically meaningful response for patients suffering from this morbid condition."

Conference Call and Webcast
Syndax will host a conference call and webcast to discuss the results of the Phase 2 AGAVE-201 trial today, July 24, 2023 at 8:30 a.m. ET.

The live webcast may be accessed through the Events & Presentations page in the Investors section of the Company's website. Alternatively, the conference call may be accessed through the following:

Conference ID: SNDXSPEC
Domestic Dial-in Number: 800-579-2543
International Dial-in Number: 785-424-1789
Live webcast: https://www.veracast.com/webcasts/syndax/events/specconf.cfm

For those unable to participate in the conference call or webcast, a replay will be available on the Investors section of the Company's website at www.syndax.com approximately 24 hours after the conference call and will be available for 90 days following the call.

About Chronic Graft-Versus-Host Disease
Chronic graft-versus-host disease (GVHD), 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 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 GVHD and IPF. Phase 1/2 data of Axatilimab in chronic GVHD demonstrating its broad activity and tolerability was last presented at the 63rd American Society of Hematology Annual Meeting and data was published in the Journal of Clinical Oncology. Axatilimab was granted Orphan Drug Designation by the U.S. Food and Drug Administration for the treatment of patients with chronic GVHD and IPF. In September 2021, Syndax and Incyte entered into an exclusive worldwide co-development and co-commercialization license agreement for axatilimab. Axatilimab is being developed under an exclusive worldwide license from UCB entered into between Syndax and UCB in 2016.

About AGAVE-201
The global Phase 2 AGAVE-201 dose-ranging trial evaluated the efficacy, safety, and tolerability of axatilimab in 241 adult and pediatric patients with recurrent or refractory active chronic GVHD whose disease had progressed after two prior therapies. Patients were randomized to one of three treatment groups that investigated a distinct dose of axatilimab administered at 0.3 mg/kg every two weeks, 1 mg/kg every two weeks or 3 mg/kg every four weeks. The trial's primary endpoint is the proportion of patients in each dose group who achieved an objective response as defined by 2014 NIH Consensus Criteria for chronic GVHD by cycle 7 day 1. Secondary endpoints include duration of response, percent reduction in daily steroids dose, organ specific response rates and validated quality-of-life assessments using the Modified Lee Symptom Scale.

For more information about AGAVE-201, visit https://clinicaltrials.gov/ct2/show/NCT04710576.

About Syndax Pharmaceuticals, Inc.
Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include revumenib, a highly selective inhibitor of the Menin–KMT2A binding interaction, and axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor. For more information, please visit www.syndax.com or follow the Company on Twitter and LinkedIn.

About Incyte
Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @Incyte.

Syndax 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, the reporting of clinical data for Syndax's product candidates, the potential filing of a BLA by year-end 2023, 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; 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 therein. 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.

Incyte Forward-looking Statements
Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding the AGAVE-201 trial and the potential for axatilimab to become a treatment option for chronic graft-versus-host disease, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are based on Incyte's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; determinations made by the U.S. FDA and other regulatory authorities outside of the United States; the efficacy or safety of Incyte and its partners' products; the acceptance of Incyte and its partners' products in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; and other risks detailed from time to time in Incyte's reports filed with the Securities and Exchange Commission, including its annual report for the year ended December 31, 2022. Incyte disclaims any intent or obligation to

update these forward-looking statements.

References

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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