Incyte and Syndax Announce New England Journal of Medicine Publication of Data from Pivotal AGAVE-201 Trial of Niktimvo™ (axatilimab-csfr) in Chronic Graft-Versus-Host Disease

September 18, 2024

– Trial met its primary endpoint across all dose cohorts with 74% of patients at the 0.3 mg/kg every 2 weeks dose achieving a complete or partial response within the first six months of treatment –

– Niktimvo approved by U.S. FDA for the treatment of chronic graft-versus-host disease after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg –

– Niktimvo added to latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for the treatment of chronic GVHD –

WILMINGTON, Del. and WALTHAM, Mass., Sept. 18, 2024 /PRNewswire/ -- Incyte (Nasdaq:INCY) and Syndax Pharmaceuticals (Nasdaq:SNDX) today announced that results from the pivotal Phase 2 AGAVE-201 trial of Niktimvo™ (axatilimab-csfr), an anti-CSF-1R antibody, in adult and pediatric patients with recurrent/refractory active chronic graft-versus-host disease (GVHD) who had received at least two prior lines of systemic therapy were published in *The New England Journal of Medicine.*[1] The publication, entitled "Axatilimab in Recurrent or Refractory Chronic Graft-Versus-Host Disease" can be found online here.

"Niktimvo is the first FDA approved treatment that targets the disease-modifying macrophages involved in both the fibrotic and inflammatory processes driving chronic GVHD," said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. "Following the launch of this new medicine, clinicians will be able to offer patients an agent that targets a distinct pathway and has demonstrated broad and durable responses in patients with chronic GVHD who progressed after at least two prior lines of therapy."

"The publication of the pivotal AGAVE-201 data in *The New England Journal of Medicine* underscores the importance of this dataset and the practice-changing potential of Niktimvo," said Neil Gallagher, M.D., Ph.D., President, Head of Research and Development at Syndax. "Together with the Incyte team, we look forward to delivering this important new medicine to patients with chronic GVHD and exploring its potential application in earlier lines of chronic GVHD treatment and other diseases."

The AGAVE-201 pivotal trial enrolled 241 patients with recurrent or refractory chronic GVHD who had received two or more prior systemic therapies, with 74% having previously received ruxolitinib, 31% having previously received ibrutinib and 23% having previously received belumosudil. Patients were enrolled across 121 sites in 16 countries.

The results show that the trial met the primary endpoint across all cohorts receiving Niktimvo 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. Patients in the 0.3 mg/kg every two weeks cohort (n=80) achieved the highest overall response rate (ORR) of 74% within the first six months of treatment (95% CI: 63-83). Patients in this cohort experienced a median time to response to Niktimvo of 1.7 months (range: 0.9-8.1). Among the patients who had a response in the 0.3 mg/kg dose cohort, an estimated 60% of patients maintained a response at 12 months (measured from first response until new systemic therapy or death, based on the Kaplan Meier estimate).

"Results from the AGAVE-201 trial show rapid, durable responses in all organs studied and patient subgroups, with clinically meaningful symptom burden reduction reported by most of these heavily-pretreated patients who had not responded to previous lines of treatment," said Daniel Wolff, M.D., Ph.D., Head, Senior Physician, and Professor at University Hospital Regensburg. "As patients with chronic GVHD often cycle through the currently available therapies in the pursuit of relief from this debilitating disease, with nearly 50% of patients requiring more than two lines of therapy, I am pleased that Niktimvo will soon be available for these patients in need."

Clinically meaningful reduction in chronic GVHD symptoms (>5-point reduction in the modified Lee Symptom Scale) was reported by 60% of patients in the 0.3 mg/kg dose cohort. In the same cohort, organ-specific responses, including complete responses (CRs), were seen across all organs studied, including lower gastrointestinal (GI), upper GI, esophagus, joints/fascia, mouth, lungs, liver, eyes and skin. Additionally, responses were notable in fibrosis-dominated organs, including the esophagus (78%), joints and fascia (76%), lungs (47%) and skin (26%). Responses were observed across key patient subgroups, including objective response rates ≥75% in the 0.3 mg/kg cohort who received prior ibrutinib, ruxolitinib, and/or belumosudil.

The most common treatment-emergent adverse events (TEAEs) were consistent with the on-target effects of CSF-1R inhibition and with what was previously observed with Niktimvo treatment. TEAEs in greater than 20% of patients in the overall population (n=239) include transient laboratory abnormalities of increases in aspartate aminotransferase (AST), blood creatine kinase, lipase, lactate dehydrogenase, and alanine aminotransferase (ALT), as well as fatigue, and infections. In the 0.3 mg/kg dose cohort, grade ≥3 adverse events were reported in 49% of patients, with 6% experiencing TEAEs leading to discontinuation of treatment, based on the data cut that was analyzed for publication.

On August 14, 2024, Incyte and Syndax announced the U.S. Food and Drug Administration's (FDA) approval of Niktimvo for the treatment of chronic GVHD after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg (88.2 lbs), with a recommended dosage of 0.3 mg/kg, up to a maximum dose of 35 mg, as an intravenous infusion over 30 minutes every two weeks until progression or unacceptable toxicity. On August 30, 2024, axatilimab-csfr (Niktimvo) was added to the latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 2A recommendation for the treatment of chronic GVHD after the failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg.[2] Treatments are classified as category 2A when there is uniform NCCN consensus that the intervention is appropriate, based on lower level evidence. The updated NCCN guidelines are available at www.nccn.org.

In the United States, Niktimvo will be co-commercialized by Incyte and Syndax Pharmaceuticals. Incyte has exclusive commercialization rights for Niktimvo outside of the U.S. The Companies anticipate launching Niktimvo in the U.S. no later than early first quarter 2025.

About AGAVE-201

The global 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 (cGVHD) whose disease had progressed after two or more 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, 1.0 mg/kg every two weeks or 3.0 mg/kg every four weeks. The trial's primary endpoint was the proportion of patients in each dose group who achieved an objective response as defined by 2014 NIH Consensus Criteria for cGVHD by cycle 7 day 1. Secondary endpoints included 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://www.clinicaltrials.gov/study/NCT04710576.

About Niktimvo™ (axatilimab-csfr)
Niktimvo (axatilimab-csfr) is a first-in-class anti-CSF-1R antibody approved for use in the U.S. for the treatment of chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg (88.2 lbs).

In 2016, Syndax licensed exclusive worldwide rights to develop and commercialize Niktimvo from UCB. In September 2021, Syndax and Incyte entered into an exclusive worldwide co-development and co-commercialization license agreement for Niktimvo in cGVHD and any future indications.

Axatilimab is being studied in frontline combination trials in chronic GVHD – a Phase 2 combination trial with ruxolitinib (NCT06388564) and a Phase 3 combination trial with steroids are expected to initiate by year end. Axatilimab is also being studied in an ongoing Phase 2 trial in patients with idiopathic pulmonary fibrosis (NCT06132256).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
Infusion-Related Reactions
Niktimvo™ (axatilimab-csfr) can cause infusion-related reactions. Infusion-related reactions, including hypersensitivity reactions, occurred in 18% of patients who received Niktimvo in the clinical trial (AGAVE-201), with Grade 3 or 4 reactions in 1.3%.

Premedicate with an antihistamine and an antipyretic for patients who have previously experienced an infusion-related reaction to Niktimvo. Monitor patients for signs and symptoms of infusion-related reactions, including fever, chills, rash, flushing, dyspnea, and hypertension. Interrupt or slow the rate of infusion or permanently discontinue Niktimvo based on severity of the reaction.

Embryo-Fetal Toxicity
Based on its mechanism of action, Niktimvo may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with Niktimvo and for 30 days after the last dose.

ADVERSE REACTIONS
Serious adverse reactions occurred in 44% of patients who received Niktimvo (N=79). Serious adverse reactions in >2 patients included infection (pathogen unspecified) (14%), viral infection (14%) and respiratory failure (5.1%). Permanent discontinuation of Niktimvo due to an adverse reaction occurred in 10% of patients and dose reduction due to adverse reaction occurred in 8% of patients. Dose interruptions due to an adverse reaction occurred in 44% of patients. The adverse reactions leading to dose interruption in >2 patients were viral infection, infection (pathogen unspecified), bacterial infection, musculoskeletal pain, and pyrexia.

The most common (≥15%) adverse reactions, including laboratory abnormalities, were increased aspartate aminotransferase (AST), infection (pathogen unspecified), increased alanine aminotransferase (ALT), decreased phosphate, decreased hemoglobin, viral infection, increased gamma glutamyl transferase (GGT), musculoskeletal pain, increased lipase, fatigue, increased amylase, increased calcium, increased creatine phosphokinase (CPK), increased alkaline phosphatase (ALP), nausea, headache, diarrhea, cough, bacterial infection, pyrexia, and dyspnea.

Clinically relevant adverse reactions in <10% of patients who received Niktimvo included:

- *Eye disorders:* periorbital edema
- *Skin and subcutaneous skin disorders:* pruritus
- *Vascular disorders:* hypertension

Immunogenicity: Anti-Drug Antibody–Associated Adverse Reactions
Across treatment arms in patients with cGVHD who received Niktimvo in clinical trials, among the patients who developed anti-drug antibodies (ADAs), hypersensitivity reactions occurred in 26% (13/50) of patients with neutralizing antibodies (NAb) and in 4% (2/45) of those without NAb.

USE IN SPECIFIC POPULATIONS
Lactation
Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 30 days after the last dose of Niktimvo.

Females and Males of Reproductive Potential
Pregnancy Testing
Verify pregnancy status in females of reproductive potential prior to initiating Niktimvo.

Contraception
Females
Advise females of reproductive potential to use effective contraception during treatment with Niktimvo and for 30 days after the last dose of Niktimvo.

DOSAGE AND ADMINISTRATION
Dosage Modifications for Adverse Reactions
Monitor aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), creatine phosphokinase (CPK), amylase, and lipase prior to the start of Niktimvo therapy, every 2 weeks for the first month, and every 1 to 2 months thereafter until abnormalities are resolved. See Table 1 in the Prescribing Information for more recommendations.

Please see the full Prescribing Information for Niktimvo.

About Incyte

A global biopharmaceutical company on a mission to *Solve On*., Incyte follows the science to find solutions for patients with unmet medical needs. Through the discovery, development and commercialization of proprietary therapeutics, Incyte has established a portfolio of first-in-class medicines for patients and a strong pipeline of products in Oncology and Inflammation & Autoimmunity. Headquartered in Wilmington, Delaware, Incyte has operations in North America, Europe and Asia.

For additional information on Incyte, please visit Incyte.com or follow us on social media: LinkedIn, X, Instagram, Facebook, YouTube.

About Syndax
Syndax Pharmaceuticals is a commercial stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include revumenib, a highly selective menin inhibitor, and Niktimvo™ (axatilimab-csfr), a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor. Syndax is working to unlock the full potential of its pipeline and is conducting several clinical trials across the continuum of treatment for both revumenib and Niktimvo. For more information, please visit www.syndax.com/ or follow the Company on X (formerly Twitter) and LinkedIn.

Incyte Forward-Looking Statements
Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding whether and when Niktimvo might provide a successful treatment option for patients with chronic GVHD and statements regarding the potential for axatilimab to treat other conditions, 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 U.S.; 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 on form 10-K for the year ended December 31, 2023 and its report on form 10-Q for the quarter ended June 30, 2024. Incyte disclaims any intent or obligation to update these forward-looking statements.

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 acceptance of Syndax and its partners' products in the marketplace, sales, marketing, manufacturing and distribution requirements, 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.

[1] Wolff D, et al. Axatilimab in Recurrent or Refractory Chronic Graft-versus-Host Disease. *N Engl J Med* 2024;391:1002-14. DOI: 10.1056/NEJMoa2401537.

[2] NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Cell Transplantation (HCT). Version 2.2024 – August 30, 2024. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Incyte Contacts:
Media
media@incyte.com

Investors
ir@incyte.com

Syndax Contact:
Sharon Klahre
sklahre@syndax.com
Tel 781.684.9827

SNDX-G

View original content:https://www.prnewswire.com/news-releases/incyte-and-syndax-announce-new-england-journal-of-medicine-publication-of-data-from-pivotal-agave-201-trial-of-niktimvo-axatilimab-csfr-in-chronic-graft-versus-host-disease-302252402.html

SOURCE Syndax Pharmaceuticals, Inc.