Incyte Announces New Data for Ruxolitinib Cream (Opzelura®) in Children with Atopic Dermatitis

October 13, 2023

- In the TRuE-AD3 trial, children (age ≥2 to <12 years old) with atopic dermatitis (AD) treated with ruxolitinib cream achieved significant efficacy, as defined by the Investigator's Global Assessment-treatment success (IGA-TS), following eight weeks of treatment

- In a second study, treatment with ruxolitinib cream over eight weeks under maximum-use conditions was well tolerated in children (age ≥2 to <12 years)

- Data were shared at the European Academy of Dermatology and Venereology (EADV) Congress 2023

WILMINGTON, Del.--(BUSINESS WIRE)--Oct. 13, 2023-- Incyte (Nasdaq:INCY) today announced expanded results from the pivotal Phase 3 TRuE-AD3 study evaluating the safety and efficacy of ruxolitinib cream (Opzelura®) in children (age ≥2 to <12 years) with atopic dermatitis (AD), the most common type of eczema. These data were presented today in a late-breaking oral presentation (Abstract #6746; Session: D3T01.3I: Late Breaking News) at the European Academy of Dermatology and Venereology (EADV) Congress 2023, held from October 11-14 in Berlin. Additionally, results from a Phase 1 open-label maximum-use trial evaluating the safety and tolerability of ruxolitinib cream in children (age ≥2 to <12 years) treated under maximum-use conditions over an 8-week trial period were featured as an ePoster at the EADV Congress 2023.

Data from the TRuE-AD3 study, which build upon previously announced topline results, showed the study met its primary endpoint with significantly more patients treated with ruxolitinib cream (0.75% and 1.5%) achieving Investigator's Global Assessment Treatment Success (IGA-TS) than patients treated with vehicle control (non-medicated cream). IGA-TS is defined as an IGA score of 0 (clear) or 1 (almost clear) with at least a two-point improvement from baseline at Week 8. In addition, secondary endpoints such as time to NRS4 (≥4-point improvement in itch Numerical Rating Scale [NRS] score) and patients demonstrating at least a 75% improvement in the Eczema Area and Severity Index (EASI75) at Week 8 were also achieved.

"The TRuE-AD3 data presented today at EADV reinforce the strong safety and efficacy profile of ruxolitinib cream and its potential to treat younger age groups," said Jim Lee, M.D., Group Vice President, Inflammation & AutoImmunity, Incyte. "There is still a significant medical need for a nonsteroidal topical treatment that provides rapid and effective control of the signs and symptoms of AD in children."

Additional key findings from the TRuE-AD3 study include:

- Fifty-six percent (56.5%) of patients treated with ruxolitinib cream 1.5% and 36.6% treated with ruxolitinib cream 0.75% achieved IGA-TS at Week 8 (P<=0.0001 for both) compared to 10.8% of patients treated with vehicle.
- More than half (67.2%/51.5%) of patients treated with ruxolitinib cream (1.5% and 0.75% respectively) achieved EASI75 compared to those treated with vehicle at Week 8 (15.4%; P<0.0001 for both).
- In patients 6 to <12 years old, NRS4 was achieved by 43.4% (1.5% treatment arm) and 37.5% (0.75% treatment arm) of patients at Week 8 compared to those treated with vehicle (29.7%).
    - Median time to NRS4 was 13.0/11.0 days (1.5% and 0.75% respectively) compared to 23.0 days for vehicle (hazard ratio, 1.74/1.77; P<0.05 for both).
- The mean steady-state plasma concentrations (Css) of ruxolitinib at Week 8 were 23.2 nM (1.5% ruxolitinib cream) and 11.3 nM (0.75% ruxolitinib cream), which are well below 281 nM (the level above which bone-marrow suppression may be induced[1]), suggesting meaningful systemic JAK inhibition is highly unlikely.
- Ruxolitinib cream was well tolerated with no serious infections, major adverse cardiovascular events (MACE), malignancies or thromboses reported during the 8-week vehicle-controlled period. The most common treatment-related adverse event observed in the ruxolitinib cream arms was application site pain (2.7% vs 0% in vehicle arm).

Results from the maximum-use trial (MUsT) in children (age ≥2 to <12 years) with at least 35% of their body surface area affected by AD showed ruxolitinib cream was well tolerated, with efficacy results consistent with data from an adolescent and adult maximum-use study and a pilot pharmacokinetics (PK)/safety pediatric study[2,3].

Key findings from the MUsT study include:

- About 20% (20.7%) of patients treated with ruxolitinib cream 1.5% reported treatment emergent adverse events (TEAEs) through Week 8; none were serious or led to treatment interruption or discontinuation. No TEAEs suggestive of systemic JAK inhibition were reported.
- The mean (SD) Css of ruxolitinib cream through Week 4 was 98.2 (148) nM, which is well below 281 nM, suggesting meaningful systemic JAK inhibition is highly unlikely.
- Approximately 54% of patients achieved an IGA of 0 or 1 and approximately 73% achieved NRS4 by Week 4.

Opzelura is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate AD in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable.

"AD is a chronic immune-mediated disease that impacts about 13 percent of children in the U.S., yet there remains a need for new treatment options to help this age group manage this difficult to treat skin condition," said Dr. Lawrence Eichenfield, Chief of Pediatric and Adolescent Dermatology at Rady

Children's Hospital San Diego. "As a clinician, I have been extremely pleased with the results achieved by many of my adolescent and adult patients with AD prescribed ruxolitinib cream, and I am excited about the potential to have a safe, well tolerated and effective non-steroidal topical treatment option available to my pediatric patients in the future."

AD – the most common type of eczema – is a chronic skin disease, which in the U.S. affects an estimated 2-3 million patients ages 2-11 and more than 21 million people 12 years of age and older[4,5]. It is characterized by inflammation and itch. Signs and symptoms include irritated and itchy skin that can cause red lesions that may ooze and crust. People with AD are also more susceptible to bacterial, viral and fungal infections[6].

More information regarding the EADV Congress 2023 can be found at https://eadvcongress2023.org/.

About TRuE-AD3

TRuE-AD3 (NCT04921969) is a randomized, double-blind, vehicle-controlled Phase 3 study evaluating the safety and efficacy of ruxolitinib cream compared to vehicle (non-medicated cream) in children with atopic dermatitis (AD). The study enrolled over 300 patients (age ≥2 to <12 years) diagnosed with AD for at least three months and who were candidates for topical therapy.

Patients with an Investigator's Global Assessment (IGA) score of 2 to 3 (a measure of disease severity), and with AD on 3% to 20% of their Body Surface Area (BSA; excluding scalp) were randomized 2:2:1 to receive ruxolitinib cream 0.75% administered twice daily (BID); ruxolitinib cream 1.5% BID; or vehicle (non-medicated cream) BID. Patients who successfully completed an efficacy assessment at Week 8 were offered participation in the 44-week long-term safety treatment extension period with their same treatment group (ruxolitinib cream 0.75% or 1.5% BID). Patients initially randomized to vehicle cream were re-randomized (1:1) in a blinded manner to one of the active treatment groups.

The primary endpoint of TRuE-AD3 is the proportion of patients achieving an Investigator's Global Assessment Treatment Success (IGA-TS), defined as an IGA score of 0 (clear) or 1 (almost clear) with at least a two-point improvement from baseline at Week 8. Secondary endpoints include: the proportion of patients achieving at least a 75% improvement in the Eczema Area and Severity Index (EASI75) – another measurement of disease extent and severity – the proportion of patients (age ≥6 to <12 years) with at least a 4-point improvement in the itch numerical rating scale (NRS4 at Week 8 and time to achieve NRS4). The study is also tracking the frequency, duration and severity of adverse events associated with the use of ruxolitinib cream.

For more information about the study, please visit https://www.clinicaltrials.gov/study/NCT04921969.

About MUsT (NCT05034822)

The MUsT pediatric maximum-use study (NCT05034822) is a Phase 1 open-label trial evaluating the safety, pharmacokinetics (PK), efficacy and patient-reported outcomes (PRO) of ruxolitinib cream after topical application twice daily (BID) in children over a 52-week treatment period.

Children ages ≥2 to <12 years old with an atopic dermatitis (AD) diagnosis for ≥three months, an Investigator's Global Assessment (IGA) score of 3 (moderate) or 4 (severe), with AD on ≥35% of their body surface area (BSA; excluding scalp) and with an itch Numerical Rating Scale (NRS) score of ≥4 (for patients 6 to <12 years of age) were eligible. Patients enrolled applied ruxolitinib cream 1.5% twice daily (BID) to baseline lesions for four weeks (maximum use trial period), then only to active lesions for an additional four weeks (treatment extension period), for a total treatment period of eight weeks. Eligible patients were offered the option to continue into a 44-week long-term safety (LTS) period continuing this regimen as-needed to active lesions. All study patients will have a 30-day safety follow-up visit.

The primary outcome measure of the pediatric maximum-use study is the number of treatment emergent adverse events (TEAEs), defined as any adverse event reported for the first time or worsening of a pre-existing event after first application of ruxolitinib cream. Secondary outcome measures included concentration of ruxolitinib in plasma, steady-state plasma concentration (Css) of ruxolitinib and accumulation ratio of ruxolitinib between plasma concentrations at one hour post application.

For more information about the study, please visit https://clinicaltrials.gov/study/NCT05034822.

About Opzelura® (ruxolitinib) Cream 1.5%

Opzelura, a novel cream formulation of Incyte's selective JAK1/JAK2 inhibitor ruxolitinib, approved by the U.S. Food & Drug Administration for the topical treatment of nonsegmental vitiligo in patients 12 years of age and older, is the first and only treatment for repigmentation approved for use in the United States. Opzelura is also approved in the U.S. for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis (AD) in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable. Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants, such as azathioprine or cyclosporine, is not recommended.

In Europe, Opzelura (ruxolitinib) cream 15mg/g is approved for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age.

Incyte has worldwide rights for the development and commercialization of ruxolitinib cream, marketed in the United States as Opzelura.

Opzelura is a registered trademark of Incyte.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis.**

- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled. Carefully consider the benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA.

Serious lower respiratory tract infections were reported in the clinical development program with topical ruxolitinib.

No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

MORTALITY

In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing an oral JAK inhibitor to tumor necrosis factor (TNF) blocker treatment, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

MALIGNANCIES

Malignancies were reported in patients treated with OPZELURA. Lymphoma and other malignancies have been observed in patients receiving JAK inhibitors used to treat inflammatory conditions. In RA patients treated with an oral JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer (NMSC)) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy when on treatment, and patients who are current or past smokers.

Non-melanoma skin cancers, including basal cell and squamous cell carcinoma, have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate. Exposure to sunlight and UV light should be limited by wearing protective clothing and using broad-spectrum sunscreen.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke), was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue OPZELURA in patients who have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue OPZELURA in patients that have experienced a myocardial infarction or stroke.

THROMBOSIS

Thromboembolic events were observed in trials with OPZELURA. Thrombosis, including pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid OPZELURA in patients at risk. If symptoms of thrombosis occur, discontinue OPZELURA and treat appropriately.

Thrombocytopenia, Anemia, and Neutropenia

Thrombocytopenia, anemia, and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations

Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Adverse Reactions

In nonsegmental vitiligo, the most common adverse reactions (incidence ≥1%) are application site acne (6%), application site pruritus (5%), nasopharyngitis (4%), headache (4%), urinary tract infection (2%), application site erythema (2%), and pyrexia (1%).

Pregnancy

There is a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Lactation

Advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose (approximately 5-6 elimination half-lives).

Please see Full Prescribing Information, including Boxed Warning, and Medication Guide for OPZELURA.

About Incyte Dermatology

Incyte's science-first approach and expertise in immunology has formed the foundation of the company. Today, we are building on this legacy as we discover and develop innovative dermatology treatments to bring solutions to patients in need.

Our research and development efforts in dermatology are initially focused on leveraging our knowledge of the JAK-STAT pathway. We are exploring the potential of JAK inhibition for a number of immune-mediated dermatologic conditions with a high unmet medical need, including atopic dermatitis, vitiligo, hidradenitis suppurativa, lichen planus, lichen sclerosus and prurigo nodularis.

To learn more, visit the Dermatology section of Incyte.com.

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.

Forward-Looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding the presentation of data from Incyte's TRuE-AD3 and MUsT studies, whether or when ruxolitinib cream will be approved or commercially available for use in humans anywhere in the world outside of the already approved indications in specific regions, and Incyte's dermatology program generally 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 FDA, EMA and other regulatory authorities; the efficacy or safety of Incyte's products; the acceptance of Incyte's 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 and its quarterly report on Form 10-Q for the quarter ended June 30, 2023. Incyte disclaims any intent or obligation to update these forward-looking statements.

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[1] Cardama A, et al. *Blood*. 2010;115(15):3109-3117.

[2] Bissonnette R, et al. *Am J Clin Dermatol*. 2022;23(3):355-364.

[3] Leung DYM, et al. *Ann Allergy Asthma Immunol*. 2023;130(4):500-507.e3.

[4] U.S. Census Bureau (2020). 2020 Decennial Census. Retrieved from https://data.census.gov/cedsci/table?q=Populations%20and%20People&tid=DECENNIALPL2020.P1 [data.census.gov].

[5] Data on file.

[6] Boguniewicz M, et al. *Ann Allergy Asthma Immunol.* 2018;120(1):10-22.

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