Incyte Announces Results of Phase 3 Clinical Trials Evaluating Ruxolitinib Cream 1.5% (Opzelura®) in Patients with Prurigo Nodularis (PN) at 2025 American Academy of Dermatology Annual Meeting

March 8, 2025

- *Full data from the Phase 3 TRuE-PN1 study, presented today in a late-breaking oral presentation, showed the study met all primary and key secondary endpoints*
- *Topline data from a separate Phase 3 study, TRuE-PN2, showed that while the primary endpoint did not reach statistical significance, the primary and all key secondary endpoints were in favor of ruxolitinib cream 1.5% versus vehicle*
- *These Phase 3 data will inform planned discussions with regulatory authorities on submission*

WILMINGTON, Del.--(BUSINESS WIRE)--Mar. 8, 2025-- Incyte (Nasdaq:INCY) today announced results from its pivotal Phase 3 TRuE-PN clinical trial program –TRuE-PN1 and TRuE-PN2 studies – evaluating the safety and efficacy of twice-daily ruxolitinib cream 1.5% (Opzelura®), a topical JAK1/2 inhibitor, in adult patients (≥18 years) with prurigo nodularis (PN). The positive TRuE-PN1 data were presented as a late-breaking oral presentation (Session: S028 – Late-Breaking Research: Session 1) today at the 2025 American Academy of Dermatology (AAD) Annual Meeting, being held March 7–11, 2025, in Orlando.

The TRuE-PN1 study met its primary endpoint demonstrating that significantly more PN patients who applied ruxolitinib cream 1.5% versus vehicle control achieved a ≥4-point improvement from baseline in Worst-Itch Numeric Rating Scale (WI-NRS4) at Week 12 (44.6% vs 20.6%; *P*=0.0003). Significant itch improvements were observed with ruxolitinib cream 1.5% versus vehicle control at Day 7 (22.4% vs 8.0%; *P*=0.0064), with numerical improvements versus vehicle control reported at earlier timepoints. Additionally, the TRuE-PN1 study met all key secondary endpoints, including:

- Significantly more patients who applied ruxolitinib cream 1.5% versus vehicle control achieved an Investigator's Global Assessment for Stage of Chronic Prurigo Treatment Success (IGA-CPG-S-TS) at Week 12 (15.8% vs 3.9%; *P*=0.0048).
- As a result, significantly more patients who applied ruxolitinib cream 1.5% versus vehicle control achieved overall treatment success (11.9% vs 2.9%; *P*=0.0164), defined by patients achieving both WI-NRS4 response and an IGA-CPG-S-TS at Week 12; and,
- Significantly more patients treated with ruxolitinib cream 1.5% versus vehicle control also achieved WI-NRS4 at Week 4 (29.7% vs 12.7%, *P*=0.0034).

"PN is a challenging condition characterized by intensely itchy nodules that significantly impact patients' quality of life," said Jim Lee, M.D., Ph.D., Group Vice President, Inflammation and Autoimmunity, Incyte. "These positive results display improvement in itch reduction and skin clearance, reinforcing the potential of ruxolitinib cream to become an effective topical treatment option that will help people living with PN."

Additionally, topline data from the Phase 3 TRuE-PN2 clinical trial demonstrated a strong positive trend across all key secondary endpoints, particularly for IGA-CPG-S-TS at Week 12 and WI-NRS4 at Day 7 (nominal P-value <0.05 for both). While the primary endpoint was in favor of ruxolitinib cream 1.5% versus vehicle, it did not reach statistical significance due to high placebo response. Data from the TRuE-PN2 study will be submitted for presentation at an upcoming scientific meeting.

The overall safety profile of ruxolitinib cream 1.5% in the TRuE-PN clinical trial program is consistent with previous data, and no new safety signals were observed.

"This program includes the first clinical trials evaluating a topical JAK inhibitor for the treatment of patients with PN, a condition associated with the formation of cutaneous nodules across the body that cause persistent itch and discomfort," said Shawn Kwatra, M.D., Joseph W. Burnett Endowed Professor and Chair of Dermatology at University of Maryland School of Medicine and Chief of Service Dermatology at the University of Maryland Medical Center. "In TRuE-PN1, ruxolitinib cream 1.5% demonstrated its ability to significantly improve itch and PN lesions, and I believe it has the potential to be a much-needed novel approach for PN patients."

The findings from the TRuE-PN1 and TRuE-PN2 studies will inform planned discussions with regulatory authorities to determine next steps.

Ruxolitinib cream 1.5% (Opzelura®) was approved by the FDA for the topical treatment of nonsegmental vitiligo in patients 12 years of age and older and 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 in 2022 and 2021, respectively.

More information regarding the 2025 AAD Annual Meeting can be found at: https://www.aad.org/member/meetings-education/am25.

About TRuE-PN
The TRuE-PN clinical trial program includes two Phase 3 studies, TRuE-PN1 (NCT05755438) and TRuE-PN2 (NCT05764161), evaluating the safety and efficacy of twice-daily ruxolitinib cream 1.5% in patients with prurigo nodularis (PN). Both studies include a 12-week double-blind, vehicle-controlled treatment period, followed by a 40-week open-label extension and 30-day safety follow-up.

The studies have each enrolled approximately 180 patients (age ≥18 years) diagnosed with PN and meet certain criteria: ≥6 pruriginous lesions on ≥2 different body areas (such as right and left leg) at screening and baseline having a treatment area <20% body surface area (BSA); Investigator's

Global Assessment for Stage of Chronic Prurigo Treatment Success (IGA-CPG-S) score of ≥2 at screening and baseline; and baseline PN-related Worst-Itch Numeric Rating Scale (WI-NRS) score ≥7.

The primary endpoint for both studies is the reduction in the WI-NRS4 response at week 12, defined as achieving a ≥4-point improvement (reduction) in WI-NRS score from baseline. Key secondary endpoints include: overall treatment success (both WI-NRS4 response and IGA-CPG-S-TS) at Week 12, IGA-CPG-S-TS at Week 12 and WI-NRS4 response at Day 7 and Week 4. Additional secondary endpoints include: WI-NRS4 at each post-baseline visit up to 52 weeks and change from baseline in WI-NRS score. The studies also track the frequency, duration and severity of adverse events associated with the use of ruxolitinib cream.

For more information on the TRuE-PN studies, please visit https://clinicaltrials.gov/study/NCT05755438 and https://clinicaltrials.gov/study/NCT05764161.

About Prurigo Nodularis

Prurigo nodularis (PN) is a chronic inflammatory skin disease characterized by an intense itch and thickened red bumps on the arms, legs and trunk.[1] There are approximately 200,000 individuals in the U.S. living with PN.[2] It can affect people of any age, though is most common among those 40-69 years old.[3,4,5,6] Due to the result of persistent, intense scratching and rubbing of the skin, PN results in itchy bumps on the skin called "nodules," these often have a substantial impact on a patient's sleep and overall quality of life.[1,7]

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.

IMPORTANT SAFETY INFORMATION

OPZELURA is for use on the skin only. Do not use OPZELURA in your eyes, mouth, or vagina.

OPZELURA may cause serious side effects, including:

Serious Infections: OPZELURA contains ruxolitinib. Ruxolitinib belongs to a class of medicines called Janus kinase (JAK) inhibitors. JAK inhibitors are medicines that affect your immune system. JAK inhibitors can lower the ability of your immune system to fight infections. Some people have had serious infections while taking JAK inhibitors by mouth, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses that can spread throughout the body. Some people have been hospitalized or died from these infections. Some people have had serious infections of their lungs while taking OPZELURA. Your healthcare provider should watch you closely for signs and symptoms of TB during treatment with OPZELURA.

OPZELURA should not be used in people with an active, serious infection, including localized infections. You should not start using OPZELURA if you have any kind of infection unless your healthcare provider tells you it is okay. You may be at a higher risk of developing shingles (herpes zoster) while using OPZELURA.

Increased risk of death due to any reason (all causes): Increased risk of death has happened in people 50 years of age and older who have at least 1 heart disease (cardiovascular) risk factor and are taking a medicine in the class of medicines called JAK inhibitors by mouth.

Cancer and immune system problems: OPZELURA may increase your risk of certain cancers by changing the way your immune system works. Lymphoma and other cancers have happened in people taking a medicine in the class of medicines called JAK inhibitors by mouth. People taking JAK inhibitors by mouth have a higher risk of certain cancers including lymphoma and lung cancer, especially if they are a current or past smoker. Some people have had skin cancers while using OPZELURA. Your healthcare provider will regularly check your skin during your treatment with OPZELURA. Limit the amount of time you spend in the sunlight. Wear protective clothing when you are in the sun and use a broad-spectrum sunscreen.

Increased risk of major cardiovascular events: Increased risk of major cardiovascular events such as heart attack, stroke, or death have happened in people 50 years of age and older who have at least 1 heart disease (cardiovascular) risk factor and taking a medicine in the class of medicines called JAK inhibitors by mouth, especially in current or past smokers.

Blood clots: Blood clots in the veins of your legs (deep vein thrombosis, DVT) or lungs (pulmonary embolism, PE) can happen in some people taking OPZELURA. This may be life-threatening. Blood clots in the vein of the legs (deep vein thrombosis, DVT) and lungs (pulmonary embolism, PE) have happened more often in people who are 50 years of age and older and with at least 1 heart disease (cardiovascular) risk factor taking a medicine in the class of medicines called JAK inhibitors by mouth.

Low blood cell counts: OPZELURA may cause low platelet counts (thrombocytopenia), low red blood cell counts (anemia), and low white blood cell counts (neutropenia). If needed, your healthcare provider will do a blood test to check your blood cell counts during your treatment with OPZELURA and may stop your treatment if signs or symptoms of low blood cell counts happen.

Cholesterol increases: Cholesterol increase has happened in people when ruxolitinib is taken by mouth. Tell your healthcare provider if you have high cholesterol or triglycerides.

Before starting OPZELURA, tell your healthcare provider if you:

- have an infection, are being treated for one, or have had an infection that does not go away or keeps coming back
- have diabetes, chronic lung disease, HIV, or a weak immune system
- have TB or have been in close contact with someone with TB
- have had shingles (herpes zoster)
- have or have had hepatitis B or C
- live, have lived in, or have traveled to certain parts of the country (such as the Ohio and Mississippi River valleys and the Southwest) where there is an increased chance for getting certain kinds of fungal infections. These infections may happen or become more severe if you use OPZELURA. Ask your healthcare provider if you do not know if you have lived in an area where these infections are common.
- think you have an infection or have symptoms of an infection such as: fever, sweating, or chills, muscle aches, cough or shortness of breath, blood in your phlegm, weight loss, warm, red, or painful skin or sores on your body, diarrhea or stomach pain, burning when you urinate or urinating more often than usual, feeling very tired
- have ever had any type of cancer, or are a current or past smoker
- have had a heart attack, other heart problems, or a stroke
- have had blood clots in the veins of your legs or lungs in the past
- have high cholesterol or triglycerides
- have or have had low white or red blood cell counts
- are pregnant or plan to become pregnant. It is not known if OPZELURA will harm your unborn baby. There is a pregnancy exposure registry for individuals who use OPZELURA during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. If you become exposed to OPZELURA during pregnancy, you and your healthcare provider should report exposure to Incyte Corporation at 1-855-463-3463.
- are breastfeeding or plan to breastfeed. It is not known if OPZELURA passes into your breast milk. Do not breastfeed during treatment with OPZELURA and for about 4 weeks after the last dose.

After starting OPZELURA:

- Call your healthcare provider right away if you have any symptoms of an infection. OPZELURA can make you more likely to get infections or make worse any infections that you have.
- Get emergency help right away if you have any symptoms of a heart attack or stroke while using OPZELURA, including:
    - discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back
    - severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
    - pain or discomfort in your arms, back, neck, jaw, or stomach
    - shortness of breath with or without chest discomfort
    - breaking out in a cold sweat
    - nausea or vomiting
    - feeling lightheaded
    - weakness in one part or on one side of your body
    - slurred speech
- Tell your healthcare provider right away if you have any signs and symptoms of blood clots during treatment with OPZELURA, including: swelling, pain, or tenderness in one or both legs, sudden, unexplained chest or upper back pain, or shortness of breath or difficulty breathing.
- Tell your healthcare provider right away if you develop or have worsening of any symptoms of low blood cell counts, such as: unusual bleeding, bruising, tiredness, shortness of breath, or fever.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of OPZELURA in people treated for atopic dermatitis include: common cold (nasopharyngitis), diarrhea, bronchitis, ear infection, increase in a type of white blood cell (eosinophil) count, hives, inflamed hair pores (folliculitis), swelling of the tonsils (tonsillitis), and runny nose (rhinorrhea).

The most common side effects of OPZELURA in people treated for nonsegmental vitiligo include: acne at the application site, itching at the application site, common cold (nasopharyngitis), headache, urinary tract infection, redness at the application site, and fever.

These are not all of the possible side effects of OPZELURA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Incyte Corporation at 1-855-463-3463.

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

INDICATIONS AND USAGE
OPZELURA is a prescription medicine used on the skin (topical) for:

- short-term and non-continuous chronic treatment of mild to moderate eczema (atopic dermatitis) in non-immunocompromised adults and children 12 years of age and older whose disease is not well controlled with topical prescription therapies or when those therapies are not recommended

- the treatment of a type of vitiligo called nonsegmental vitiligo in adults and children 12 years of age and older

The use of OPZELURA along with therapeutic biologics, other JAK inhibitors, or strong immunosuppressants such as azathioprine or cyclosporine is not recommended.

It is not known if OPZELURA is safe and effective in children less than 12 years of age with atopic dermatitis or nonsegmental vitiligo.

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.

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, whether or when ruxolitinib cream may provide a successful treatment option for patients with PN and plans with respect to discussions with regulatory authorities and regulatory submissions, 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 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, 2024. Incyte disclaims any intent or obligation to update these forward-looking statements.

[1] National Organization for Rare Disorders. Prurigo Nodularis. https://rarediseases.org/rare-diseases/prurigo-nodularis/. Accessed on January 28, 2025.

[2] Huang AH, et al. *JID*. 2020;140:480-483

[3] Huang AH, et al. *J Am Acad Dermatol*. 2020;83:1559-1565

[4] Wongvibulsin S, et al. *J Invest Dermatol*. 2021;141:2530-2533

[5] Boozalis E, et al. *J Am Acad Dermatol*. 2018;79:714-719

[6] Whang KA, et al. *Medicines (Basel)*. 2019;6:88

[7] Yale Medicine. Prurigo Nodularis. https://www.yalemedicine.org/conditions/prurigo-nodularis-overview. Accessed January 28, 2025.

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