



News Release

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Janssen Receives Positive CHMP Opinion for Long-Acting Regimen for the Treatment of HIV

Regimen is based on co-administration of REKAMBYS® (rilpivirine injection) and ViiV Healthcare's VOCABRIA® (cabotegravir injection) once every month or once every 2-months to treat HIV-1

Long-acting, two-drug regimen reduces treatment intake days from 365 to either 12 or six per year

BEERSE, BELGIUM, 16 OCTOBER, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending Marketing Authorisation for REKAMBYS® (rilpivirine injection) in combination with ViiV Healthcare's VOCABRIA® (cabotegravir injection), for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults. If approved, this will be the first complete long-acting regimen, dosed once-monthly or once every-2-months, for virologically suppressed people living with HIV-1 across the European Economic Area.

"HIV remains one of the greatest global health threats of our time, so approval of the first once-monthly or once every-2-month injectable treatment regimen would mark an important step forward in the fight against this disease," said Paul Stoffels, M.D., Vice Chairman of the Executive Committee, Chief Scientific Officer, Johnson & Johnson. "At Janssen, we are dedicated to changing the course of the HIV epidemic through our relentless pursuit of improved therapies and preventive solutions. If approved by the European Commission, this two-drug, long-acting regimen could mean patients living with HIV, no longer need daily therapy, maintaining viral load suppression with just 12 or six injection days a year."

The CHMP positive opinion is for co-administration of rilpivirine and cabotegravir injections for the treatment of HIV-1 infection in adults who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) and are on a stable antiretroviral regimen without present or past evidence of viral resistance or prior virological failure with agents of the non-nucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitor (INI) class. The CHMP opinion also included Janssen's EDURANT® (rilpivirine tablets) together with cabotegravir

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oral tablets for use as lead-in therapy for one month prior to the commencement of the long-acting injection regimen.

The EU-Marketing Authorisation Application (MAA) for rilpivirine long-acting injections is based on the pivotal Phase 3 ATLAS (Antiretroviral Therapy as Long-Acting Suppression), FLAIR (First Long-Acting Injectable Regimen) and ATLAS-2M studies. The ATLAS and FLAIR studies included more than 1,100 participants from 16 countries.^{1,2} The studies demonstrated that rilpivirine and cabotegravir, when injected intramuscularly once monthly, was as effective as continuing daily, oral, antiretroviral regimens in maintaining viral suppression throughout the 48-week study period.^{1,2}

In both studies, the most common adverse reactions (Grades 1 to 4) observed in $\geq 2\%$ of participants receiving rilpivirine and cabotegravir were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, rash, and diarrhoea.³ Over the 48-week study period, a total of 4% of participants discontinued rilpivirine and cabotegravir due to adverse events.³

The EU-MAA included 48-week data from the pivotal ATLAS-2M study to support the use of rilpivirine injections once every-2-months. Results from the study showed the antiviral activity and safety of long-acting rilpivirine and cabotegravir injections administered once every-2-months was non-inferior to a once-monthly administration in virologically suppressed adults living with HIV-1 infection over a 48-week period.⁴ In the ATLAS-2M study rates of serious adverse events (SAEs) (27/522 [5.2%]) and withdrawals due to adverse events (AEs) (12/522 [2.3%]) at 48 weeks were low and were similar to those experienced in the one month arm (SAEs: 19/523 [3.6%], withdrawals due to AEs 13/523 [2.5%]). The most common AEs were similar between once every-2-months and once a month injections.⁵

At Janssen we are dedicated to driving innovation across the whole continuum of HIV care, through education, prevention, detection and treatment. We believe we have a responsibility to advance our knowledge and capabilities to address all aspects of the HIV epidemic and are deeply committed to the millions of people living with or at-risk of HIV. We are optimistic about the future - we have changed the face of HIV, and we can change it again. The long-acting regimen has been co-developed as part of a collaboration with ViiV Healthcare.

The CHMP positive opinion is one of the final steps before marketing authorisation is granted by the European Commission, which has the authority to approve medicines for use throughout the European Economic Area.

In July, Janssen resubmitted the New Drug Application (NDA) for once-monthly dosing of rilpivirine and cabotegravir to the US Food and Drug Administration (FDA). Further regulatory applications have been submitted and are being reviewed by other regulatory bodies worldwide.

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About ATLAS (NCT02951052)

ATLAS is a Phase 3, open-label, active-controlled, multi-centre, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of a two-drug regimen of LA, injectable rilpivirine and cabotegravir dosed every four weeks compared to continuation of current oral anti-retroviral therapy (ART) of two nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or protease inhibitor (PI) among virally suppressed individuals.⁶ The primary endpoint for ATLAS is the proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL per the FDA Snapshot algorithm at Week 48 (missing,

switch, or discontinuation = failure, intent-to-treat exposed [ITT-E] population). Participants were required to be virally suppressed for six months or longer, on a first or second regimen, with no prior failure.⁶

About ATLAS-2M (NCT03299049)

The ATLAS-2M study is a Phase 3, randomised, open-label, active-controlled, multicentre, parallel-group, non-inferiority study designed to assess the non-inferior antiviral activity and safety of long-acting cabotegravir and rilpivirine administered every eight weeks compared to long-acting cabotegravir and rilpivirine administered every four weeks over a 48-week treatment period in 1,045 adults living with HIV-1.⁷ Participants were required to be virologically suppressed for six months or greater, on first or second regimen, with no prior failure. The primary outcome measure for the study is the proportion of participants with HIV-1 RNA ≥ 50 c/mL at Week 48 using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population).^{1,7}

ATLAS-2M is being conducted at research centres in Australia, Argentina, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden and the United States.

For further information, please see <https://clinicaltrials.gov/ct2/show/NCT03299049>

About FLAIR (NCT02938520)

FLAIR is a Phase 3, randomised, open-label, multi-centre, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of a two-drug regimen of intramuscular, long-acting injectable rilpivirine and cabotegravir in virologically suppressed adults living with HIV, following 20 weeks of induction therapy with ViiV Healthcare's Triumeq® (abacavir / dolutegravir / lamivudine) compared to continuation of the oral dolutegravir-based treatment regimen.⁸ The primary endpoint for FLAIR is the proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL per the FDA Snapshot algorithm at Week 48 (missing, switch, or discontinuation = failure, intent-to-treat exposed [ITT-E] population).⁸

About rilpivirine

Rilpivirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) developed by Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson and marketed as a 25mg tablet under the tradename EDURANT®. Taken once daily, oral rilpivirine is used for the treatment of HIV-1 infection in combination with other antiretroviral agents in antiretroviral treatment-naïve patients 12 years of age and older, with a viral load $\leq 100,000$ HIV RNA copies/mL.⁹ The most common side effects of oral rilpivirine include: depression, headache, trouble sleeping (insomnia) and rash.⁹

Rilpivirine long-acting is an investigational, prolonged-release suspension for intramuscular injection being developed by Janssen Sciences Ireland UC and is not approved by regulatory authorities anywhere in the world. Once-monthly dosing of cabotegravir and rilpivirine has been approved by Health Canada as a co-pack with two injectable medicines (cabotegravir and rilpivirine) under the brand name CABENUVA® for the treatment of HIV-1 infection in adults who are virologically stable and suppressed.¹⁰

About cabotegravir

Cabotegravir is an INI developed by ViiV Healthcare for the treatment of HIV-1 in virologically suppressed adults. It is being evaluated in combination with injectable rilpivirine as a long-acting formulation. The oral formulation of rilpivirine is also approved for the treatment of HIV-1 infection in combination with other antiretroviral agents in antiretroviral treatment-naïve patients 12 years of age and older and weighing at least 35 kg with a viral load $\leq 100,000$ HIV RNA copies/mL.

Important Safety Information (ISI)

Please refer to the full Summary of Product Characteristics for full prescribing information for EDURANT® (rilpivirine): <https://www.medicines.org.uk/emc/product/4968/smpc>

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension. Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen Cilag International NV and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

Cautions Concerning Forward-Looking Statements This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding rilpivirine. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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- 1 Swindells S, Andrade-Villanueva J-F, Richmond G, et al. Long-acting cabotegravir and rilpivirine for maintenance of HIV-1 suppression. N Engl J Med. DOI: 10.1056/NEJMoa1904398.
 - 2 Orkin C, Arasteh K, Hernandez-Mora MG, et al. Long-acting cabotegravir and rilpivirine after oral induction for HIV-1 infection. N Engl J Med. DOI: 10.1056/NEJMoa1909512.
 - 3 Overton ET, Orkin C, Swindell S, et al. Monthly long-acting cabotegravir and rilpivirine is non-inferior to oral ART as maintenance therapy for HIV-1 infection: Week 48 pooled analysis from the phase 3 ATLAS and FLAIR studies. Presented at IAS 2019.
 - 4 Overton ET et. al. Cabotegravir and rilpivirine every 2 months is non inferior to monthly: ATLAS-2M study. Presented at CROI 2020: Available at: <https://www.croiconference.org/abstract/cabotegravir-rilpivirine-every-2-months-is-noninferior-to-monthly-atlas-2m-study/> Last accessed October 2020.
 - 5 Janssen Data on File. CABOTEGRAVIR + RILPIVIRINE_CROI 2020_Abtract 34_Table 20200917. September 2020.

- 6 Swindells S et al. (2019) Long-Acting Cabotegravir + Rilpivirine For Maintenance Therapy: Atlas Week 48 Results. Oral presentation, the Annual Conference on Retroviruses and Opportunistic Infections (CROI).
- 7 Efficacy, Safety and Tolerability Study of Long-acting Cabotegravir Plus Long-acting Rilpivirine (CAB LA + RPV LA) in Human-immunodeficiency Virus-1 (HIV-1) Infected Adults. Available at: <https://clinicaltrials.gov/ct2/show/study/NCT03299049>. Last accessed October 2020.
- 8 Orkin C et al. (2019) Long-Acting Cabotegravir + Rilpivirine For Hiv Maintenance: Flair Week 48 Results. Oral Presentation at the Annual Conference on Retroviruses and Opportunistic Infections (CROI).
- 9 EDURANT® Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/4968/smpc> Last accessed October 2020.
- 10 Drugs. Cabenuva FDA Approval Status. Available at: <https://www.drugs.com/history/cabenuva.html>. Last accessed October 2020.