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New Phase 2 Data Demonstrate Potential Benefit of Nipocalimab for Pregnant Individuals at High Risk of Early-Onset Severe Haemolytic Disease of the Foetus and Newborn (HDFN)

92 percent of pregnancies treated with nipocalimab resulted in a live birth, with 54 percent delivering at or after 32 weeks without intrauterine transfusions[1]

BEERSE, BELGIUM, 26 JUNE 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced positive results from the proof-of-concept Phase 2 open-label UNITY clinical trial for the treatment of pregnant individuals at high risk of early-onset severe (EOS) haemolytic disease of the foetus and newborn (HDFN).[1] A statistically significant (54 percent [n=7/13]) proportion of participants who received nipocalimab achieved the primary endpoint of a live birth at or after gestational age of 32 weeks without intrauterine transfusions (IUTs)[1,a] compared to the historic reference point of 10 percent, which was derived from published and unpublished data (for reference, please see Editor's note b).[2-5,b] Among the seven participants who achieved the primary endpoint, the median gestational age at delivery was 37 and 1/7 weeks.[6] This study demonstrates the potential for nipocalimab to help address the underlying disease mechanism of EOS HDFN.[1] If

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approved, nipocalimab would be the first anti-neonatal Fc receptor (FcRn) treatment and the first approved non-surgical intervention for pregnancies at high risk of HDFN in the European Union.[7] These data will be presented for the first time at the Fetal Medicine Foundation World Congress in Valencia, Spain on 26 June, 2023.[1]

Nipocalimab is currently the only therapy reported in clinical development for the treatment of alloimmunised[c] pregnant individuals at high risk of severe HDFN,[7] a serious and rare condition which occurs when the blood types of a pregnant individual and the foetus are incompatible, potentially causing life-threatening anaemia in the foetus or infant.[8]

"Pregnancies affected by HDFN currently experience a high treatment burden, such as repeated, invasive IUTs that require access to specialty care and put the life of the foetus at risk," said Kenneth J. Moise Jr., M.D., Professor, Department of Women's Health and Director, Comprehensive Fetal Care Center, at Dell Medical School of the University of Texas at Austin and lead study investigator.[d] "I find these data encouraging, as they suggest the possibility of providing families with an effective, non-surgical HDFN treatment option if approved."

In the UNITY clinical trial, 12 of 13 participants experienced a live birth.[1] Additional results show:

- In pregnancies that met the primary endpoint of a live birth at gestational age of or after 32 weeks without IUTs (54 percent; n=7/13), one infant required a simple (blood) transfusion.[6,e] In pregnancies requiring an IUT (n=6/13), all live-born infants (n=5/5) required a simple transfusion.[1] Among the 12 live-born infants, one infant required an exchange (blood) transfusion.[1,f]
- The median gestational age at the first IUT was 28 and 3/7 weeks (range: 24 1/7 – 31 5/7 weeks) for those with live births.[1]
- There were no reports of foetal hydrops.[1,g]

Nipocalimab was generally well tolerated across all the dose groups studied in pregnant individuals at high risk for EOS HDFN:

- One pregnancy resulted in foetal demise due to complications following an IUT performed at gestational age 22 and 5/7 weeks.[1] These complications were considered unrelated to nipocalimab.[1] There were no maternal or infant deaths.[1]
- The most frequently reported adverse events (AEs) were events that are not uncommonly reported in pregnancy or underlying HDFN.[1]
- In the majority of participants, serious adverse events (SAEs [n=4]) were primarily related to HDFN or to various pregnancy-associated conditions and occurred with no discernible pattern or relationship to treatment with nipocalimab. Two participants who experienced live births demonstrated SAEs possibly related to nipocalimab.[1] One participant experienced a subchorionic haematoma,[h] foetal growth restriction and foetal heart rate deceleration.[1] The other participant experienced premature separation of the placenta.[1]
- Neonatal and infant serum immunoglobulin G (IgG) approximated normal physiological nadirs at 24 weeks of age.[1] Overall, in neonates/infants with maternal nipocalimab exposure, there were no unusual/unexpected childhood illnesses and infections reported in neonates/infants are generally those that are commonly seen during the neonatal period through infancy.[1]

Nipocalimab was shown to demonstrate an acceptable benefit-risk profile given the favourable efficacy results in the study, the significant unmet medical need with a potential for foetal/neonatal morbidity or mortality, and was overall well tolerated, supporting further clinical development for the treatment of HDFN.[1]

"Despite advances in prenatal and neonatal care, people affected by an HDFN-pregnancy still experience a high treatment burden and babies may still require medical intervention after birth," said Ludovic de Beaucoudrey, Ph.D., Senior Director, Therapeutic Area Lead, Immunology, Janssen-Cilag Limited. "We are motivated by this urgency to deliver a new treatment option and remain committed

to building on the orphan designation granted to nipocalimab by the European Medicines Agency, further exploring the potential of this medicine as we strive to make meaningful progress in addressing HDFN."

"There is a significant unmet need to help address the serious and life-threatening health consequences of HDFN. Our aspiration is to transform the existing paradigm for families who endure the consequences of HDFN by seeking approval of a targeted, and effective therapy," said Katie Abouzahr, M.D., Vice President, Autoantibody Portfolio and Maternal Fetal Disease Area Leader, Janssen Research & Development, LLC. "These Phase 2 UNITY data in high-risk pregnancies demonstrated the important role that nipocalimab, an FcRn blocking antibody, may play in preventing the transfer of maternal alloantibodies through the placenta, thereby offering a potential treatment option for this devastating disease."

Nipocalimab was granted orphan medicinal product designation by the European Medicines Agency (EMA) in October 2019 for the prevention of HDFN and Fast Track designation in July 2019 and orphan drug status in June 2020 by the U.S. Food and Drug Administration (FDA).[7,9,10]

Editor's Notes

a. Intrauterine transfusion: an invasive, technically complex surgical procedure performed by specialists to inject blood (red blood cells) from a donor to the foetus, usually through the umbilical cord, that may be associated with complications that could lead to morbidity, foetal mortality and premature birth.[11,12]
b. Historical reference point used in this study is based on data from published literature (n=51); and academic research centres with expertise in managing EOS-HDFN, including the Fetal Center at Children's Memorial Hermann Hospital in Houston, Texas, U.S. (n=2); The Department of Maternal Fetal Medicine at Ohio State University in Columbus, Ohio, U.S. (n=4); and The University of Toronto Fetal Medicine program at Mount Sinai Hospital in Toronto, Canada (n=12).[2-5] Across these 69 cases, all patients with prior

EOS-HDFN pregnancies required an IUT in subsequent at-risk pregnancies. A conservative benchmark of 10 percent of patients not requiring an IUT was chosen to account for uncertainties in the accuracy and representation of the underlying data.[2]

c. Alloimmunised: an immune response to foreign antigens upon exposure to genetically different cells or tissues.[13]
d. Dr. Kenneth Moise is a paid consultant for Janssen. He has not been compensated for any media work.
e. Simple transfusion: a procedure wherein a patient receives blood from another blood donor.[14] Neonates impacted by HDFN receive transfusions to treat severe anaemia.[7]
f. Exchange transfusion: a procedure that removes most of the patient's blood (which contains the antigen-positive red blood cells) and replaces it with fresh donor blood or plasma that has a normal bilirubin level.[15] Exchange transfusions are used in HDFN for neonates whose bilirubin levels continue to rise to treatable levels.[15] Exchange transfusions are an invasive procedure with potentially severe side effects and risk of mortality.[15]
g. Foetal hydrops: a condition in which large amounts of fluid build-up in a baby's tissues and organs, causing extensive swelling (oedema), and can be life-threatening.[16] About half of unborn babies with hydrops do not survive.[16] Foetal hydrops is a complication of HDFN, occurring when the mother's immune system causes a baby's red blood cells to break down.[16]
h. Subchorionic haematoma: bleeding that occurs beneath the placental chorion membranes which enclose the embryo in the uterus.[17] It is believed to happen when the chorion membranes partially detach from the uterine wall.[17]

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About UNITY

UNITY (NCT03842189) is a global, multicentre, open-label, non-blinded Phase 2 clinical trial designed to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of nipocalimab for the treatment of pregnant individuals at high

risk for EOS HDFN.[18] The trial enrolled RhD (D) or Kell (K) alloimmunised pregnant individuals with singleton pregnancies at high risk for EOS HDFN with an obstetric history of severe foetal anaemia, foetal hydrops, or a stillbirth at ≤24 weeks gestation.[1] In the trial, 13 participants with 14 pregnancies were enrolled.[1] One pregnancy was included in the safety analysis but was not included in the efficacy analysis due to early elective abortion for a genetic disorder unrelated to HDFN at gestational age 17 weeks.[1] Due to complications following an IUT that was performed at gestational age 22 and 5/7 weeks, one pregnancy resulted in foetal demise considered by the trial investigator to be unrelated to nipocalimab.[1] Participants received once-weekly intravenous infusions.[1] The primary endpoint was live birth at or after gestational age of 32 weeks, without a need for an IUT throughout the entire pregnancy.[1] Safety was monitored for 24 weeks post-delivery for the 13 maternal individuals enrolled, and up to 96 weeks post-birth for infants.[1]

About HDFN

Haemolytic disease of the foetus and newborn (HDFN) is a rare disease where maternal alloantibodies produced in a pregnant person's immune system cross the placenta and attack foetal red blood cells — causing foetal red blood cell haemolysis, leading to anaemia.[8] The symptoms of HDFN can range from mild to life threatening; some cases can involve neonatal jaundice or hyperbilirubinaemia, and severe cases can result in life-threatening foetal anaemia requiring intervention to prevent development of foetal hydrops.[19] With every pregnancy with an antigen-positive foetus, disease severity increases, with an earlier gestational age of HDFN onset due to repeated alloimmunisation.[20] There are currently no approved non-surgical interventions for pregnancies at high risk of EOS HDFN in the European Union,[7] and pregnancies affected by severe HDFN may necessitate repeated IUTs.[21] IUTs are invasive, technically complex surgical procedures performed by specialists at specialised medical centres, and these procedures may be associated with an increased rate of foetal mortality and premature birth.[11,12] The most difficult to treat cases of HDFN are those that develop before 24 weeks gestational age, defined here as early-onset, due to the IUT-related higher procedural complication rate and related mortality.[22] HDFN is categorised as a rare disease and the severe form is

even rarer.[7,8] According to the EMA, in the European Union, it is estimated that the number of patients at risk of HDFN is approximately 3.6 people in 10,000.[7]

About nipocalimab

Nipocalimab is an investigational, high-affinity, fully human, aglycosylated, effectorless, monoclonal antibody that is believed to selectively block FcRn to reduce levels of circulating IgG antibodies, including autoantibodies and alloantibodies that underlie multiple conditions.[23] Nipocalimab is the only anti-FcRn being studied across three key segments in the autoantibody space: maternal-foetal diseases mediated by maternal alloantibodies (e.g., HDFN); rare autoantibody diseases (e.g., generalised myasthenia gravis in adults and children, chronic inflammatory demyelinating polyneuropathy, warm autoimmune haemolytic anaemia, and idiopathic inflammatory myopathies); and prevalent rheumatological diseases (e.g., rheumatoid arthritis, Sjögren's disease, and systemic lupus erythematosus).[18,24-31] Blockade of FcRn by nipocalimab has the potential to reduce overall autoantibody levels while maintaining immune function. FcRn blockade is also believed to prevent placental transfer of maternal alloantibodies to the foetus.[18,32]

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 & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of nipocalimab. 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 January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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