Johnson&Johnson

Media contact:
Bridget Kimmel
Mobile: (215) 688-6033
bkimmel@its.jnj.com

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

Johnson & Johnson's nipocalimab granted U.S. FDA Breakthrough Therapy Designation for the treatment of individuals at high risk for severe hemolytic disease of the fetus and newborn (HDFN)

Breakthrough Therapy Designation for nipocalimab based on results from the Phase 2 UNITY clinical trial for HDFN

Phase 3 clinical trial enrollment underway, representing the only therapy reported to be under clinical development for this serious, life-threatening and rare condition

Spring House, Pa. (February 9, 2024) – Johnson & Johnson today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) for nipocalimab for the treatment of alloimmunized[a] pregnant individuals at high risk of severe hemolytic disease of the fetus and newborn (HDFN). Nipocalimab is currently the only therapy reported to be in clinical development for the treatment of alloimmunized pregnant individuals at risk of severe HDFN, a serious and rare condition that occurs when the blood types of a pregnant individual and the fetus are incompatible, potentially causing life-threatening anemia in the fetus or infant.[1]

"Nipocalimab represents a novel approach for the treatment of patients at risk of severe HDFN who need proven, safe, non-surgical solutions to help address the serious health consequences of this condition," said Katie Abouzahr, M.D., Vice President, Autoantibody and Maternal Fetal Immunology Disease Area Leader, Johnson & Johnson. "We are committed to addressing the substantial unmet need in this devastating disease."

The data from the proof-of-concept Phase 2 open-label UNITY clinical trial provided support for the BTD.[2] The trial met the primary endpoint, with the majority of pregnant patients who received nipocalimab achieving a live birth at or after the gestational age of 32 weeks, without the need for an intrauterine transfusion (IUT) throughout their entire pregnancy.[3] Severe or serious adverse events were generally low and consistent with events associated with pregnancy, HDFN, and gestational age at birth.[3]

Nipocalimab was granted Fast Track designation in July 2019, orphan drug status in June 2020 by the FDA, and orphan medicinal product designation by the European Medicines Agency in October 2019 for the HDFN indication.

The FDA grants BTD to expedite the development and regulatory review of an investigational medicine that is intended to treat a serious or life-threatening condition and is based on preliminary clinical evidence that demonstrates the drug may have substantial improvement in at least one clinically significant endpoint over available therapies. The AZALEA Phase 3 pivotal trial is currently enrolling pregnant individuals who are at risk for severe HDFN who have a history of severe HDFN in a prior pregnancy(ies).[2]

Editor's Notes:

a. Alloimmunized: an immune response to foreign antigens upon exposure to genetically different cells or tissues.[4]

About the UNITY trial

UNITY (NCT03842189) is a global, multicenter, 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.[5] The trial enrolled RhD (D) or Kell (K) alloimmunized pregnant individuals with singleton pregnancies at high risk for EOS HDFN due to an obstetric history of severe fetal anemia, fetal hydrops, or a stillbirth at ≤24 weeks gestation.[3] The primary endpoint was live birth at or after gestational age of 32 weeks, without a need for an IUT throughout the entire pregnancy.[3] Safety was monitored for 24 weeks post-delivery for the 13 maternal individuals enrolled, and up to 96 weeks post-birth for infants.[3] Participants received once-weekly intravenous infusions.[3] The trial met the primary endpoint, with 54% of pregnant patients who received nipocalimab achieving a live birth at or after the gestational age (GA) of 32 weeks, without the need for an intrauterine transfusion throughout their entire pregnancy.

About HDFN

Hemolytic disease of the fetus and newborn (HDFN) is a rare disease (and in its severe form, even rarer) that arises in pregnancies with maternal-fetal incompatibility in certain red blood cell types. Alloantibodies produced by the maternal immune system against fetal red blood cells cross the placenta during pregnancy and attack fetal red blood cells causing fetal anemia or persist after birth in the neonate to cause neonatal hyperbilirubinemia and anemia.[1] The symptoms of HDFN can range from mild jaundice, to neurotoxic hyperbilirubinema in the neonate, to life-threatening fetal anemia requiring invasive intervention.[6] The potential for in utero onset at increasingly earlier gestational age with increasing risk of severe outcomes may occur with each incompatible pregnancy due to pregnancy-related alloimmunization.[7] Currently no non-surgical interventions are approved for pregnancies at high risk of early-onset severe (EOS) HDFN in the U.S. Pregnancies affected by severe HDFN may necessitate repeated intrauterine transfusions (IUTs).[8] IUTs are invasive, technically complex surgical procedures performed by specialists at specialized medical centers, and these procedures may be associated with an increased rate of fetal mortality and premature birth.[9,10] The most difficult to treat cases of HDFN are those that develop before 24 weeks gestational age, defined here as EOS, due to high rates of IUT-related complications associated with mortality.[11] According to the *American Journal of Obstetrics and Gynecology*, in the U.S., it is estimated that up to 80 of every 100,000 pregnancies are affected by HDFN each year.[12]

About Nipocalimab

Nipocalimab is an investigational, high-affinity, fully human, aglycosylated, effectorless, monoclonal antibody that aims to selectively block FcRn to reduce levels of circulating immunoglobulin G (IgG) antibodies, including autoantibodies and alloantibodies that underlie multiple conditions.[13] Nipocalimab is the only anti-FcRn being studied across three key segments in the autoantibody space: Rare Autoantibody diseases (e.g., generalized myasthenia gravis in adults and children, chronic inflammatory demyelinating polyneuropathy, warm autoimmune hemolytic anemia, and idiopathic inflammatory myopathies); Maternal Fetal diseases mediated by maternal alloantibodies (e.g., HDFN); and Prevalent Rheumatology (e.g., rheumatoid arthritis, Sjögren's disease, and systemic lupus erythematosus).[5,14,15,16,17,18,19,20,21] Blockade of FcRn has the potential to reduce overall autoantibody levels while preserving immune function without causing broad immunosuppression. Blockade of IgG binding to FcRn in the placenta is also believed to prevent transplacental transfer of maternal alloantibodies to the fetus.[5,22]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed.

Janssen Research & Development, LLC and Janssen Biotech, Inc. are both Johnson & Johnson companies.

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 materialize, 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 behavior 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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