FOR IMMEDIATE RELEASE

FDA Approves Bracco Diagnostics Inc.'s ProHance® (Gadoteridol) Injection, 279.3 mg/mL, for Pediatric Patients Younger than Two Years

Monroe Township, NJ, December 23, 2020 – Bracco Diagnostics Inc., the U.S subsidiary of Bracco Imaging S.p.A., a leading global company in the diagnostic imaging business, today announced that the U.S. Food and Drug Administration (FDA) has approved ProHance® (Gadoteridol) Injection, 279.3 mg/mL for intravenous use with magnetic resonance imaging (MRI) in pediatric patients under two years old, including term neonates, to visualize areas with disrupted blood brain barrier and/or abnormal vascularity throughout the brain, spine and associated tissues.

ProHance was previously approved for this use in patient populations over the age of two.

"Term neonates, our youngest patients, are special and this approval is an important milestone in providing them with the specialized care they need," said Vittorio Puppo, President and CEO of Bracco Diagnostics Inc. "Bracco is dedicated to providing healthcare providers with safe and effective contrast media to help them meet the challenges presented by this unique patient population, and ultimately improve diagnosis. The inclusion of term neonates to the label reinforces the safety of ProHance, the fastest growing GBCA on the market today."

The approval of the extended label was based on a study of pediatric patients undergoing magnetic resonance imaging (MRI) of the central nervous system (CNS) showing that ProHance at the standard dose (0.10 mmol/kg) was effective in improving the three co-primary visualization endpoints: lesion border delineation, visualization of lesion internal morphology, and lesion contrast enhancement. Pharmacokinetic (PK) simulations and safety evaluations indicate that these data in pediatric patients under two years of age were similar to those of adults.

The retrospective study enrolled 125 pediatric patients with ages ranging from term neonates to 24 months old; 17 were less than 1 month of age, 40 were between 1 month and 6 months of age, 29 were between 6 months and 12 months of age, and 39 were between 12 months and 24 months of age. Three independent, blinded radiologists evaluated the paired pre- and post-contrast MRI image sets and all three reported improvement in the paired image sets for each of the three co-primary endpoints.

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Indications and Usage for ProHance® (Gadoteridol) Injection, 279.3 mg/mL and ProHance® Multipack™ (Gadoteridol) Injection, 279.3 mg/mL

CENTRAL NERVOUS SYSTEM
ProHance® (Gadoteridol) Injection, 279.3 mg/mL is indicated for use in MRI in adults and pediatric patients including term neonates to visualize lesions with disrupted blood brain barrier and/or abnormal vascularity in the brain (intracranial lesions), spine and associated tissues.

EXTRACRANIAL/EXTRASPINAL HEAD AND NECK
ProHance (Gadoteridol) Injection, 279.3 mg/mL is indicated for use in MRI in adults to visualize lesions in the head and neck.

IMPORTANT SAFETY INFORMATION:

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **chronic, severe kidney disease (GFR <30 mL/min/1.73m^2), or**
  - **acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended ProHance dose and allow a sufficient period of time for elimination of the drug from the body prior to re-administration.**

CONTRAINDICATIONS
Contraindicated in patients with known allergic or hypersensitivity reactions to ProHance

WARNINGS AND PRECAUTIONS
Nephrogenic Systemic Fibrosis: NSF has occurred in patients with impaired elimination of GBCAs. Higher than recommended dosing or repeated dosing appears to increase risk.
Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of administration and resolved with prompt emergency treatment. Prior to ProHance administration, ensure the availability of trained personnel and medications to treat hypersensitivity reactions. Consider these risks, especially in patients with a history of hypersensitivity reactions or a history of asthma or other allergic disorders.

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Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver, and spleen. Linear GBCAs cause more retention than macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established, but they have been established in the skin and other organs in patients with impaired renal function.
Acute Kidney Injury: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.

ADVERSE REACTIONS
The most commonly reported adverse reactions are nausea and taste perversion with an incidence ≥ 0.9%.

USE IN SPECIFIC POPULATIONS
Pregnancy: GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. Use only if imaging is essential during pregnancy and cannot be delayed.
Lactation: There are no data on the presence in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.
Pediatric Use: The safety and effectiveness of ProHance have been established for use with MRI to visualize lesions with abnormal blood brain barrier or abnormal vascularity of the brain, spine, and associated tissues in pediatric patients from birth, including term neonates, to 17 years of age. Adverse reactions in pediatric patients were similar to those reported in adults. No case of NSF associated with ProHance or any other GBCA has been identified in pediatric patients ages 6 years and younger.

Please see full Prescribing Information and Patient Medication Guide for additional important safety information for/regarding ProHance® (Gadoteridol) Injection, 279.3 mg/mL and ProHance® Multipack™ (Gadoteridol) Injection, 279.3 mg/mL at https://imaging.bracco.com/sites/braccoimaging.com/files/technica_sheet_pdf/us-ProHance-PI-DEC2020-4718378.pdf

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

ProHance is manufactured for Bracco Diagnostics Inc. by BIPSO GmbH – 78224 Singen (Germany).

For additional information about Bracco's products, and for full prescribing information, please visit http://imaging.bracco.com/us-en.

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About Bracco Imaging S.p.A.

Bracco Imaging S.p.A., part of the Bracco Group, is a world-leading diagnostic imaging provider, headquartered in Milan, Italy.

Bracco Imaging offers a product and solution portfolio for all key diagnostic imaging modalities: X-ray imaging (including Computed Tomography-CT, Interventional Radiology, and Cardiac Catheterization), magnetic resonance imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers and novel PET imaging agents. Our continually evolving portfolio is completed by a range of medical devices, advanced administration systems and dose-management software. The Company operates in over 100 markets worldwide, either directly or indirectly, through subsidiaries, joint ventures, licenses and distribution partnership agreements. Bracco Imaging has a strong presence in key geographies: North America, China, Europe, Japan, Brazil, Mexico and South Korea.

Bracco Imaging's manufacturing plants operate in full compliance with the best practices and sustainable eco-friendly production processes. Manufacturing sites are based in Italy, Switzerland, Germany, Canada, China, Japan, and the USA.

Bracco Imaging has a well-skilled and innovative Research and Development (R&D) organization with an efficient process-oriented approach and track record in the diagnostic imaging industry. R&D activities are located in three centers based in Italy, Switzerland and the USA. To learn more about Bracco Imaging, visit **www.braccoimaging.com**.

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