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News Release

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Bayer starts phase II/III study with vericiguat in children with heart failure

- Phase II/III study VALOR will assess efficacy, safety and pharmacokinetics of vericiguat in pediatric patients
 - VALOR is the pivotal study in pediatric heart failure with vericiguat
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Berlin, June 1, 2023 – Bayer and its development partner MSD (a tradename of Merck & Co., Inc., Rahway, NJ, USA) today announced that the first patient has been enrolled in the Phase II/III VALOR trial. VALOR will investigate the efficacy, safety, and pharmacokinetics of vericiguat (Verquvo™) in pediatric patients aged > 28 days to 18 years with heart failure due to left ventricular systolic dysfunction. VALOR is the pivotal study in pediatric heart failure with vericiguat.

Heart failure can occur at any age and rates in children are increasing.¹ Although the incidence of pediatric heart failure is low at up to 7 per 100,000 children, the impact on the children and adolescents affected is high, with an in-hospital mortality rate of 7–26%.^{1,2} Heart failure symptoms include failure to thrive, shortness of breath or increased respiratory frequency (tachypnea), tiredness and fatigue, fluid retention and reduced ability to do physical tasks.³ Children with heart failure are 24 times more likely to be hospitalized than children without heart failure.¹

“Pediatric heart failure remains a devastating diagnosis for children and their families,” said Professor Joseph Rossano, Co-Director of the Cardiac Center and Chief of the Division of Cardiology at Children's Hospital of Philadelphia and VALOR Steering Committee Chairperson. “Because vericiguat has a distinct mechanism of action and is well tolerated when used with other treatments in adults, it could be an important treatment option in pediatric heart failure, which is a complex and diverse condition.”

“Although heart failure is more common in older adults it is important to be aware that children can be affected too and there are few clinical trials that have been conducted specifically in a pediatric heart failure population,” said Dr. Christian Rommel, Member of the Executive Committee of Bayer’s Pharmaceuticals Division and Head of Research and Development. “With the start of our pediatric study VALOR we want to address this gap and will investigate if vericiguat can be used as a treatment option for pediatric heart failure.”

Vericiguat is a soluble guanylate cyclase (sGC)-stimulator which significantly reduces the risk of cardiovascular death or hospitalization due to heart failure with reduced ejection fraction in adult patients who have had a recent worsening heart failure event.⁴ It specifically restores the deficient NO-sGC-cGMP pathway, which plays a critical role in the progression of heart failure.⁵ In the pivotal study VICTORIA, vericiguat has demonstrated efficacy on top of background heart failure therapy^{4,5} and is recommended for worsening chronic heart failure with reduced ejection fraction across major heart failure guidelines internationally (e.g. ESC-guideline recommendation class IIb).^{6,7,8,9}

VALOR is a randomized, placebo-controlled, double-blind trial which enrolls patients in > 28 days through < 18 years of age with a history of symptomatic chronic heart failure resulting from systemic left ventricular systolic dysfunction and a reduced left ventricular ejection fraction. The primary endpoint is change in plasma concentration of N-terminal pro-brain natriuretic peptide (NTproBNP) from baseline to Week 16. More information can be found online at www.clinicaltrials.gov ([NCT05714085](https://clinicaltrials.gov/ct2/show/study?term=NCT05714085)).

Vericiguat is being jointly developed with MSD (a tradename of Merck & Co., Inc., Rahway, NJ, USA).

About Verquvo™ (vericiguat)

Vericiguat 2.5 mg, 5 mg, and 10 mg is an oral once daily stimulator of soluble guanylate cyclase (sGC), an important enzyme in the NO-sGC-cGMP signaling pathway.¹⁰ When nitric oxide (NO) binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling.¹¹ Heart failure is associated with impaired synthesis of NO and decreased activity of sGC, which may contribute to myocardial and vascular dysfunction.¹⁰ By directly stimulating sGC,

independently of and synergistically with NO, vericiguat augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation. In the EU Verquvo is indicated for symptomatic chronic heart failure in adult patients with reduced ejection fraction who are stabilized after a recent decompensation event requiring intravenous (IV) therapy.

About the Worldwide Collaboration between Bayer and MSD

Since October 2014, Bayer and MSD (known as Merck & Co., Inc. in the U.S. and Canada) have pursued a worldwide collaboration in the field of sGC modulators. The collaboration brings together two leading companies that have stated their intent to fully evaluate this therapeutic class in areas of unmet medical need. The vericiguat program is being co-developed by Bayer and MSD. MSD has the commercial rights to vericiguat in the U.S. and Bayer has the exclusive commercial rights in the rest of world. The companies share equally the costs of the development of vericiguat.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2022, the Group employed around 101,000 people and had sales of 50.7 billion euros. R&D expenses before special items amounted to 6.2 billion euros. For more information, go to www.bayer.com.

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js (2023-0038E)

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¹ Amdani S et al. *JACC*. 2022;17;79(19):1917-28.

² Ahmed H, VanderPluym C. *Cardiovasc Diagn Ther* 2021;11(1):323-335

³ Ferreira JP et al. *Global Heart*. 2019 Sep 1;14(3):197-214

⁴ Armstrong PW, et al. *N Engl J Med* 2020;382:1883–1893

⁵ Tromp J et al. *J Am Coll Cardiol* 2022;10:73–84

⁶ Heidenreich PA, et al. *Circulation*. 2022;145:e895–e1032

⁷ McDonald M et al. *Can J Cardiol* 2021;37:531–546

⁸ Tsutsui H et al. *J Card Fail* 2021;27:1404–1444

⁹ McDonagh TA et al. *Eur Heart J* 2021;42:3599–3726

¹⁰ Ezekowitz JA et al. *JACC Heart Fail*. 2020;8:931-939

¹¹ Pieske B et al. *Eur J Heart Fail*. 2014 Sep: 1026-38