Hyloris Expands Cardiovascular Pipeline with Breakthrough Extended-Release Milrinone Capsule in Late-Stage Heart Failure

Patient-friendly alternative to continuous IV administration – proven safety and efficacy

Targeting orphan, late-stage heart failure indication with high unmet medical needs

Liège, Belgium – 8 October 2021 – Hyloris Pharmaceuticals SA (Euronext Brussels: HYL), a specialty biopharma company committed to addressing unmet medical needs through reinventing existing medications, today announces that it has acquired the global rights from the Baker Heart and Diabetes Institute ("the Baker Institute"), Melbourne, Australia, to CRD-102 (and related intellectual property), a novel, clinical-stage, extended-release Milrinone capsule in late-stage heart failure (HF) patients with an implanted left ventricular assist device (LVAD[1]) who have developed right HF. CRD-102 is the second innovative product candidate that has been added to the portfolio this year, further delivering on Hyloris' promise to expand the R&D pipeline with 4 new product candidates in 2021.

Milrinone is a positive inotrope, a group of heart failure drugs that strengthen the heart's contractions so it can pump more blood with fewer heartbeats. Milrinone IV is currently approved for use as an intermittent or continuous infusion for treatment of up to 48 hours for acute decompensated heart failure. Longer term off-label use exceeding 48 hours of treatment duration has also been reported, requiring nursing support and limiting the patient's quality of life by IV administration. Continuous IV use however exposes patients to an increased risk of common IV equipment complications, such as central line-associated bloodstream infections. Milrinone IV was approved in 1987 and in 2020 more than 12 million vials and infusion bags were sold, of which over 2 million in the U.S. alone.

Prof. Dr. David Kaye, Heart Failure Specialist, Head of the Heart Failure Research Group at the Baker Institute and Director of the Department of Cardiology at the Alfred Hospital, Melbourne, Australia, commented: "*Patients with end-stage HF, a serious, debilitating disease, experience extreme difficulties breathing, have a very poor quality of life and suffer from multiple, severe co-morbidities. The current standard of care is predominantly palliative and despite recent advantages with new heart failure therapies, the effectiveness of these is most pronounced in mild to moderate heart failure. CRD-102 has the potential to address the current unmet needs of late-stage LVAD patients by offering a patient-friendly and convenient oral treatment option as compared to repeated, continuous IV infusions, which is the current gold standard in many countries. Its efficacy and safety have been established in earlier Phase 1 and Phase 2 studies[2], and if these results can be repeated in pivotal studies, CRD-102 would have important potential in this underserved patient population.*"

Stijn Van Rompay, Chief Executive Officer of Hyloris, added: "*We are very pleased to partner with the Baker Institute and believe that CRD-102 has the potential to dramatically change the lives of patients living with late-stage HF, more notably, patients with an LVAD who have developed right HF, a severe orphan HF indication. Earlier studies have demonstrated that treatment with CRD-102 resulted in improved quality of life and functional status of late-stage HF patients, and CRD-102 was well-tolerated with no increased incidences of arrhythmias being reported. CRD-102 perfectly fits within our portfolio of value-added cardiovascular products and our strategy for self-commercialisation in the U.S. We are now preparing the next stages of development and anticipate the start of the pivotal clinical study in LVAD patients with right HF towards end 2022 or early 2023.*"

[1] A left ventricular assist device (LVAD) is a battery-operated, mechanical surgically implanted pump, which helps the left ventricle (main pumping chamber of the heart) pump blood to the rest of the body. It is used as a bridge to a heart transplantation or as destination therapy
[2] Nanayakkara et al. Am J Cardiol. 2018; Nanayakkara et al. J. Am. Heart Assoc. 2020; LVAD study results: publication pending

Under the terms of the agreement, Hyloris will be responsible for the further development, manufacturing, regulatory affairs, and commercialisation of CRD-102. In return, Hyloris will pay an upfront payment of $50,000 to the Baker Institute plus sales-based milestone payments and tiered, single to double digit net profit shares in markets where Hyloris intends to self-commercialise CRD-102. In markets where Hyloris intends to seek commercial partnerships, the Baker Institute is eligible to receive tiered, single to double digit net profit shares on net sub-license income.

About CRD-102 and earlier clinical studies in Stage IV HF patients[3]

CRD-102 is a novel, patented, extended-release Milrinone capsule that has been developed for patient-friendly, twice a day convenient oral dosing and provides a steady and predictable exposure of Milrinone. Hyloris will initially pursue a new, longer term use indication in patients with left ventricular assist devices (LVAD) who have developed right heart failure. Orphan drug status[4] has been granted by the FDA in this latter indication and formulation patent claims have been issued in the U.S., Japan and China, and are pending in Europe. In a single dose PK study, patients treated with extended release (ER) Milrinone at a dose of 14mg twice daily, exhibited stable plasma levels within the therapeutic range. An open label safety and tolerability study of ER Milrinone 14mg twice daily in advanced (n=26) left heart failure patients with a history of recurrent hospitalisation generated >5 years patient exposure data and included a prolonged open-label compassionate use phase. ER Milrinone was well tolerated, with no effect on heart rate or blood pressure and was associated with improved functional activity as defined by NYHA Classification.[5] ER Milrinone treatment was also associated with significant improvements in both quality of life (Minnesota Living with Heart Failure Score) and functional capacity (6-minute walk distance) with a trend towards improved renal function.

About Heart Failure (HF)[6] and Standard of Care

Heart failure is a severe and chronic condition in which the heart muscle is unable to pump enough blood to meet the body's need for blood and oxygen. HF usually develops because the heart has been damaged by a heart attack, or because of other conditions such as cardiomyopathy, a disease of the heart muscle. It is the most rapidly growing cardiovascular disorder in the U.S. with 870,000 new cases every year. HF is the most common cause of hospitalisation in people aged over 65 years of age, with about 1 million hospitalisations in the U.S. per year, and 20% readmissions following discharge. The average life expectancy is less than 5 years for 50% of all patients and 90% of patients with advanced HF die within 1 year following diagnosis. Current standard of care depends on disease severity and treatment of advanced HF is predominantly palliative and includes the use of positive inotropes (such as Milrinone IV), digoxin and opioids, as well as LVADs in some cases, which are used either longer-term or as a bridge to heart transplantation. In 2020, there were about 20,000 patients with an LVAD implant in the U.S. and 30% of these patients developed right HF. Over the next coming years, the LVAD patient population is expected to grow at an average annual growth rate of 6% in the U.S.[7]

[3] Nanayakkara et al, American Journal of Cardiology, 2018
[4] FDA's Orphan Drug Designation Program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases and disorders that affect < 200,000 people in the U.S. Orphan designation qualifies the sponsor of the drug for various development incentives, including eligibility for 7 years of market exclusivity upon approval, exemption from FDA application fees, tax credits for qualified clinical trials, and other potential assistance in the development process.
[5] The New York Heart Association (NYHA) Classification provides a way of classifying the extent of heart failure. It classifies patients in one of four categories based on their limitations during physical activity; the limitations/symptoms in regard to normal breathing and varying degrees in shortness of breath and or angina pain.
[6] Centers for Disease Control (CDC); Virani et al, Update report American Heart Association (AHA), Circulation, 2020; Heart Disease and Stroke Statistics, AHA; Argiriou et al, Journal of Thoratic Disease, 2014
[7] Grand View Research, Inc., 2021; Triangle Insights, 2016

About Baker Heart and Diabetes Institute

Baker Heart and Diabetes Institute is an independent, internationally renowned medical research facility, with a history spanning 95 years. The Institute's work extends from the laboratory to wide-scale community studies with a focus on the diagnosis, prevention and treatment of cardiovascular disease, diabetes, and their complications. www.baker.edu.au

About Hyloris Pharmaceuticals

Hyloris is a specialty biopharma company focused on innovating, reinventing, and optimising existing medications to address important healthcare needs and deliver relevant improvements for patients, healthcare professionals and payors. Hyloris has built a broad, patented portfolio of 13 reformulated and repurposed value-added medicines that have the potential to offer significant advantages over available alternatives. Outside of its core strategic focus, the Company also has 3 high barrier generic products in development and registration phase. Two products are currently in initial phases of commercialisation with partners: Sotalol IV for the treatment of atrial fibrillation, and Maxigesic® IV, a non-opioid post-operative pain treatment. The Company's development strategy primarily focuses on the FDA's 505(b)2 regulatory pathway, which is specifically designed for pharmaceuticals for which safety and efficacy of the molecule have already been established. This pathway can reduce the clinical burden required to bring a product to market, and significantly shorten the development timelines and reduce costs and risks. Hyloris is based in Liège, Belgium. For more information, visit www.hyloris.com and follow-us on LinkedIn.

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Disclaimer and forward-looking statements

Hyloris means "high yield, lower risk", which relates to the 505(b)(2) regulatory pathway for product approval on which the Issuer focuses, but in no way relates or applies to an investment in the Shares.
Certain statements in this press release are "forward-looking statements." These forward-looking statements can be identified using forward-looking terminology, including the words "believes", "estimates," "anticipates", "expects", "intends", "may", "will", "plans", "continue", "ongoing", "potential", "predict", "project", "target", "seek" or "should", and include statements the Company makes concerning the intended results of its strategy. These statements relate to future events or the Company's future financial performance and involve known and unknown risks, uncertainties, and other factors, many of which are beyond the Company's control, that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. The Company undertakes no obligation to publicly update or revise forward-looking statements, except as may be required by law.