



INSTITUT UNIVERSITAIRE
DE CARDIOLOGIE
ET DE PNEUMOLOGIE
DE QUÉBEC



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News release

PULMONARY ARTERIAL HYPERTENSION: FIRST GLOBAL STUDY IN EPIGENETICS TO TREAT THIS DISEASE

Quebec City, on May 30, 2019 — On the margins of the World Pulmonary Arterial Hypertension Day, the Quebec Heart and Lung Institute – Laval University (the Institute) is proud to announce the establishment of the first global study in epigenetics on the treatment of pulmonary arterial hypertension (PAH).

PAH¹ is a complex vascular disease that mainly affects young people between the ages of 20 and 60. These patients' quality of life remains highly precarious, because of its symptoms that are troublesome such as the shortness of breath and the chronic fatigue. Although the current treatments partially improve the symptoms, there is none at this time to cure this severe disease that can be fatal in a few years.

Thanks to an outstanding contribution of \$3.2 million from the Canadian Institutes of Health Research (CIHR), Resverlogix, and the IUCPQ Foundation, the clinical study APPRoACH (APabetalone for PulmonaRy Arterial Hypertension), supported by Resverlogix and seven other centres around the world, will be established. This study will be led by doctors Steeve Provencher, respirologist and researcher at the Institute, co-founder of the PAH Research Group and Associate teaching clinician at the Laval University's Faculty of Medicine, and also Sébastien Bonnet, another researcher at the Institute and co-founder of the PAH Research Group, holder of the Canadian Research Chair in Translational Research in Pulmonary Vascular Diseases as well as a full professor at the Laval University's Faculty of Medicine.

The team of researchers wants to build on a new molecule, apabetalone, which would be capable of modifying the expression of genes that are responsible for the cells to multiply; the latter are accumulating enough to clog the pulmonary arteries. "If we are getting meaningful results in the course of this study, we hope to improve the quality of life and the survival of people around the world with pulmonary arterial hypertension," said Dr. Steeve Provencher.

This research project is the result of the work of over 25 researchers, research professionals and students from the PAH Research Group who have been working for more than 7 years, among other things, through the support of the Canadian Research Chair in Translational Research in Pulmonary

¹ PAH is a rare disease that is defined by the wall thickening of the small arteries located in the lungs. This wall is hardening over time. The resulted narrowing impairs the blood circulation and increases the resistance to its passage. Therefore, the pulmonary artery pressure is rising. This pressure results in an increased effort on the heart, leading to a right heart failure. It is estimated that approximately 1 million people in the world are affected.

Vascular Diseases and Resverlogix, which has worked with the group during the first preclinical study involving apabetalone.

“The Pulmonary Arterial Hypertension Research Group brings together female and male researchers from clinical and fundamental environments within one and the same research program. That’s the one, based on both the clinical investigation and the basic research, that makes this group a highly functioning research team and one-of-a-kind in Canada,” explains Michel J. Tremblay, Associate Vice President, Research, Creation and Innovation. “The CIHR significant funding will enable it to achieve the APPRoACH study, the results of which will have real benefits on the quality of life for patients with pulmonary hypertension.”

The group distinguishes itself by its leadership and manages the feat of being at once, an author of preclinical findings, and a responsible for this new clinical study. The Institute is recognized in Quebec and abroad for the expertise of its medical and research teams in respirology. “With the fact of obtaining this major funding, the Institute demonstrates its innovation capacity, its excellence in research and put forward its role as a world leader in PAH,” said Dr. Denis Richard, Director of the Institute’s Research Centre.

“Through our discovery and ongoing development of apabetalone, and through our ground-breaking work in the field of epigenetics, we are proud to support this important advancement in the potential treatment of PAH,” said Dr. Ewelina Kulikowski, Senior Vice President, Research & Development of Resverlogix. “This work is a shining example of how industry and academia can leverage their respective strengths to advance treatments into new therapeutic areas with significant unmet need.”

The annual research competition of the IUCPQ Foundation allows many researchers to undertake and continue work for the benefit of the population and the people with cardiovascular, respiratory, and obesity-related diseases. “Today’s announcement is a concrete example of the leverage effect the IUCPQ Foundation is having with many researchers in obtaining outside funding to continue their work. So I’m particularly proud when I see the impact that the grants given make in our annual research competition,” said M^{rs}. Josée Giguère, Executive Director of the IUCPQ Foundation.

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ABOUT THE INSTITUTE – IUCPQ.qc.ca

Every year, 15,568² people are hospitalized and 122,952 visits were made on an outpatient basis for 43,690 users. The service area is more than 2 million people, which represents approximately 30% of Quebec’s population. Affiliated with the Laval University, the institution counts on the cooperation and the dedication of over 3,000 employees, physicians, professionals, researchers, managers as well as volunteers for providing quality care and services to both hospitalized and outpatient clientele. In particular, the Institute offers programs of specialized and ultraspecialized care and services to treat cardiovascular and respiratory diseases as well as those related to obesity. The Institute’s physicians as well as health professionals have extensive expertise and contribute advancing the science of medicine. It also has as its mission to assess technologies and intervention methods in health. The Institute’s Research Centre is recognized internationally for the quality of its science.

ABOUT THE RESEARCH CENTRE

The Research Centre’s vision is to play an international significant role in the fight against societal chronic diseases through its model of integrated science in cardiology, in respirology as well as in obesity–type 2 diabetes–metabolism. It counts on the cooperation of 177 researchers and physicians scientists, many of whom are recognized as being leaders in their field. These world-class researchers are among the most productive in Quebec. In addition, the perfect correspondence of the research

² 2017–2018 financial data

components to the Institute's specializations ensures a synergy between clinicians and researchers, thereby allowing a rapid knowledge transfer to the care.

ABOUT THE LAVAL UNIVERSITY

Driven by innovation and the pursuit of excellence, Laval University is one of Canada's leading research universities, ranking 8th with \$356 million in research funding last year. A leader in distance education, it has more than 1,600 professors, nearly 2,200 lecturers and other academic and research staff who share their knowledge with over 43,000 students, 25% of whom are enrolled in graduate studies. The university values diversity and is proud of the members of its community, who come from 120 countries. The oldest francophone university in North America, Laval University has so far trained more than 300,000 people who each contribute in their own way to the advancement of society. www.ulaval.ca

ABOUT RESVERLOGIX

Resverlogix is developing apabetalone (RVX-208), a first-in-class, small molecule that is a selective BET (bromodomain and extra-terminal) inhibitor. BET inhibition is an epigenetic mechanism that can regulate disease-causing genes. Apabetalone is a BET inhibitor selective for the second bromodomain (BD2) within the BET proteins. This selective inhibition of apabetalone on BD2 produces a specific set of biological effects with potentially important benefits for patients with high-risk cardiovascular disease, diabetes mellitus, chronic kidney disease, end-stage renal disease treated with hemodialysis, neurodegenerative disease, Fabry disease, peripheral artery disease and other orphan diseases, while maintaining a well-described safety profile.

Resverlogix common shares trade on the Toronto Stock Exchange (TSX:RVX).

ABOUT THE IUCPQ FOUNDATION

The IUCPQ Foundation's role is to promote and support the IUCPQ-UL's work, whose primary mission is the health of individuals with cardiovascular, respiratory, and obesity-related diseases. In recent years, the foundation contributed over \$25 million by funding the purchase of specialized equipment as well as helping to fund research and education, and this, to the greater benefit of the population in central and eastern Quebec, which represents more than 2.2 million people.

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