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LUCA: off-the-shelf mitochondria for wide-ranging applications

BY DANIELLE GOLOVIN, STAFF WRITER

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With a fresh $30.3 million from an oversubscribed series B financing, Tokyo-based LUCA is optimizing its mitochondrial isolation technology to deliver allogeneic mitochondria for restoring energy production in dysfunctional or damaged cells.

LUCA believes its single off-the-shelf product offers a pipeline of opportunities, which it is exploring through both an internal pipeline and several partnerships.

Creating an off-the-shelf mitochondrial product is challenging because the organelle can lose its function during isolation or freeze-thaw cycles. LUCA believes it has solved both problems.

Though the details of its methods are undisclosed, President and CEO Rick Tsai told BioCentury that work by LUCA adviser Yoshihiro Ohta provided the starting point.

Ohta, a professor at Tokyo University of Agriculture and Technology, discovered a method to isolate intact mitochondria by forming pores in the cell's membrane using streptolysin-O, a method his group described as "gentle membrane disruption" in a 2015 Biochemical and Biophysical Research Communications publication. In the paper, the isolated mitochondria retained their double membranes and continued to generate ATP.

"We have gone through many reiterations and the method now is dramatically different," said Tsai.

LUCA has unpublished data showing its isolated mitochondria are readily taken up by cells and result in an over 20% increase in total ATP production in vitro, with additional unpublished data showing the mitochondrial therapy improved heart function in a pig model of myocardial infarction.

Since most heart attack patients are treated with a catheter to open the blocked artery, the cardiologist has opportunity to deliver a dose of LUCA's mitochondria through the catheter to prevent ischemia-reperfusion injury, Tsai said. The company plans to start a clinical trial in the indication in 2024.

Tsai said the company hasn't observed any immune reaction to the therapy so far in animal models, even when using human mitochondria. "Since mitochondria are intracellular organelles, most likely they do not carry antigens like that on

LUCA's research partnerships

Partner	Date	Details
Kyowa Kirin	May 2022	Genetic mitochondrial diseases
Hokkaido University	May 2021	Immune cell therapy
Kyoto University, Hokkaido University, Tokyo University of Science, Tokyo University of Agriculture and Technology	Dec 2020	Acute respiratory distress syndrome (ARDS) caused by COVID-19 infection
Nagoya University	Oct 2020	Cardiac ischemic–reperfusion injury
University of Oxford	Sept 2020	Fetal growth restriction
Osaka University	June 2019	Mitochondrial diseases
Hokkaido University, Tokyo University of Agriculture and Technology	April 2019	Basic mitochondrial research

Source: LUCA Science's website

the cell surface membrane to cause immune reactions," said Tsai.

LUCA is open to expanding into any indication with dysfunctional or damaged mitochondria, and has already struck seven partnerships to do so. The latest is its first with a company. In May, LUCA partnered with Kyowa Kirin Co. Ltd. (Tokyo:4151) to develop a therapy to treat genetic mitochondrial diseases.

LUCA intends to partner with cell therapy companies to reduce immune cell exhaustion or enhance cell function. It already has an academic partnership along these lines with Hokkaido University.

Tsai said LUCA's next-generation products may involve mitochondrial gene edits to alter specific functions of the organelle tailored to indications.

Tsai said investors "liked the fact that we have multiple collaborations showing results in different cell types and animal models," demonstrating the platform's potential.

But it was the pig study and other in vivo work that sealed the deal, CFO Yoshikazu Tokuoka told BioCentury. "Our in vivo study data hooked our leading investors."

The series B financing, announced Monday, was co-led by Japan-based Fast Track Initiative Inc. and DCI Partners and

COMPANY PROFILE
LUCA SCIENCE INC.
Tokyo, Japan

Technology: Mitochondrial isolation and therapeutic platform

Origin of technology: Tokyo University of Agriculture and Technology and non-profit organization Koinobori Associate Inc.

Disease focus: N/A

Clinical status: Preclinical

Founded: 2018 by Masashi Suganuma

Academic collaborators: Hokkaido University, Kyoto University, Nagoya University, University of Oxford, Osaka University, Tokyo University of Agriculture and Technology, Tokyo University of Science

Corporate partners: Kyowa Kirin Co. Ltd. (Tokyo:4151)

Number of employees: 20

Funds raised: About $40 million

Investors: Fast Track Initiative, DCI Partners, 4BIO Capital, Axil Capital Partners, Nissay Capital, Remiges Ventures, Asahi Kasei Pharma, Nippon Venture Capital, QB Capital, SMBC Venture Capital and Cahc co., Ltd.

CEO: Rick Tsai

Patents: Undisclosed

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U.K.-based 4BIO Capital. Existing investors Remiges Ventures and Nippon Venture Capital and new investors Nissay Capital, Asahi Kasei Pharma Corp., QB Capital/NCB Venture Capital and SMBC Venture Capital also participated.

According to BioCentury's BCIQ database, LUCA's raise was the second-largest series B round for a Japanese company, behind a 2014 raise by now-public Solasia Pharma K.K. (Tokyo:4597).

Following the closing of the financing, Philippe Fauchet of 4BIO Capital, Tai Harada of Fast Track Initiative and Shuntaro Kodama of DCI Partners will join LUCA's board.

Axil Capital Partners led LUCA's $9.8 million in a series A round in September 2020, joined by Remiges Ventures, Nippon Venture Capital, Fast Track Initiative and Cahc.

Switzerland-based cellvie Inc. is also using mitochondria to revive cell energy production. That company, which was founded in 2018, is also starting with ischemia-reperfusion injury, but is initially infusing autologous mitochondria. cellvie plans to expand into aging, cardiovascular, renal and transplant indications with an allogeneic product once it solves the problem of how to increase the shelf life of a frozen product.

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