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EMERGING COMPANY PROFILE

TAKING RNA EPIGENETICS BY STORM

By Michael Leviten, Senior Writer

Storm Therapeutics Ltd. is the first company to come out of the budding field of RNA epigenetics, and is targeting RNA-modifying enzymes for cancer.

CEO Keith Blundy told BioCentury RNA-modifying enzymes fit into the landscape of epigenetic targets because, like DNA-modifying enzymes, they alter gene expression without changing the genetic code.

“It’s the same paradigm as DNA and histone modification enzymes that have been drugged by small molecules and compounds in the clinic,” he said, adding that Storm is following a similar development path by starting in cancer.

Humans express at least 140 RNA-modifying enzymes, several of which were discovered by Storm’s academic founders Tony Kouzarides and Eric Miska. The enzymes decorate both coding and non-coding RNAs with a variety of chemical moieties — ranging from simple methyl groups to complex sugars — that can modulate their half-life, specificity or translation.

Miska told BioCentury the enzymes could provide an indirect route to controlling a slew of disease targets. Because few of the enzymes are well-characterized and none have been targeted by therapeutics, he thinks the field represents a rich and untapped space reminiscent of chromatin modifiers, as well as the multigene enzyme families that regulate protein degradation.

“We are the first, but I’ll be shocked if others don’t get into this space because it’s exploding in academia and there are some obvious targets,” he told BioCentury.

Miska is a professor of molecular genetics at **University of Cambridge**. Kouzarides is a professor of molecular cancer biology at University of Cambridge and a founder of antibody reagent company **Abcam plc** and cancer company **Chroma Therapeutics Ltd.**

Blundy said Storm is focusing on two classes of RNA-modifying enzymes, RNA methyltransferases and terminal uridylyltransferases (TUTases), and has already advanced two undisclosed targets in drug discovery.

STORM THERAPEUTICS LTD., Cambridge, U.K.

Technology: Small molecule modulators of RNA modifying enzymes

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2016 by Tony Kouzarides, Eric Miska, Oliver Rausch and David Simmons

University collaborators: [University of Cambridge](#), [University of Oxford](#), [University of Texas](#)

Corporate partners: None

Number of employees: 14

Funds raised: £12 million (\$15.8 million)

Investors: Cambridge Innovation Capital, Merck Ventures, Pfizer Ventures, Touchstone Innovations

CEO: Keith Blundy

Patents: None issued

However, he said Kouzarides has a paper under review linking the N6-methyladenosine (m6A)-forming enzyme **METTL3** and about 50 other RNA-modifying enzymes to acute myelogenous leukemia (AML). Storm is also evaluating the platform for breast and lung cancer, and expects it to address a wide range of indications.

Blundy said Storm is expanding on those results by conducting larger CRISPR screens and will validate the targets in mouse models.

Storm is also developing mass spectrometry protocols that can map changes in RNA modifications under different conditions, and functional assays that can link the modifications to changes in RNA levels and activities. Blundy said the company has 50 RNA modifications it can routinely measure. “The number grows by the week,” he said.

“We intend to build a toolbox, so we have proprietary drug discovery programs and we have enzymes in the freezer with substrates, and assays ready to support a new drug discovery program when somebody outside the company develops a good case for a target,” he said.

Blundy said Storm plans to make small molecule therapies and is outsourcing its drug discovery work to **Evotec AG** and other CROs.

The company closed a \$16 million series A round in 2016, led by Merck Ventures and Pfizer Ventures. Blundy said the funding will take Storm through mid-2019 when he expects to have efficacy data from the first programs. The company plans to raise more financing in late 2018, and enter the clinic by 2021. ■

COMPANIES AND INSTITUTIONS MENTIONED

Abcam plc (LSE:ABC), Cambridge, U.K.
Chroma Therapeutics Ltd., Abingdon, U.K.
Evotec AG (Xetra:EVT), Hamburg, Germany
Storm Therapeutics Ltd., Cambridge, U.K.
University of Cambridge, Cambridge, U.K.

TARGETS

METTL3 - Methyltransferase like 3

REFERENCES

Martz, L. "On your marks." *BioCentury Innovations* (2017)

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