

Flagship Pioneering Announces the Launch of Repertoire Immune Medicines with Industry Veteran John G. Cox as Chief Executive Officer

*Repertoire Immune Medicines harnesses our immune system's intrinsic ability to cure disease
by decoding relevant Antigen-TCR codes and deploying them as breakthrough immune medicines
in immuno-oncology, autoimmune disorders and infectious diseases*

Cambridge, MA, March 12, 2020 – [Flagship Pioneering](#), a life sciences innovation enterprise, announced the launch of Repertoire Immune Medicines, a clinical-stage biotechnology company tapping the curative powers of our immune system to prevent, treat and cure cancer, autoimmune disorders and infectious diseases.

Repertoire Immune Medicines was formed by combining two Flagship companies – the innovative and proprietary immune decoding platforms of Cogen Immune Medicines and the immuno-oncology platforms of Torque Therapeutics to create a fully integrated Immune Medicines company. At the helm is Chief Executive Officer John Cox, who most recently led the spin-off of Bioverativ (BIIV) from Biogen (BIIB), and its growth and successful acquisition by Sanofi (SNY).

During the last 4 years, these two Flagship Pioneering originated companies each advanced novel and complementary platforms – protected by over 30 patent families. Through their combination, Repertoire Immune Medicines now has the unique capability to decipher human subject-derived antigen-T cell receptor (TCR) codes from healthy or diseased tissues in the context of the major MHC (HLA) types. These complexes dictate T cell activation or exhaustion, and their immunological codes can be used to design and clinically test a multitude of unprecedented therapeutic products based on precedented and specific mechanisms of T cell killing of antigen presenting tumor cells or infected cells.

“Repertoire is pioneering a new class of therapies based on high throughput, high content interrogation of the intrinsic ability of T cells to prevent, or cure diseases,” said Noubar Afeyan, Ph.D., Chief Executive Officer of Flagship Pioneering and Co-Founder and Chairman of the Board of Repertoire Immune Medicine. He continued, “our products will be designed to leverage the highly evolved, potent and clinically-validated mechanism of the natural immune synapse to provide immune security to patients. With these ambitious goals in mind, we are pleased to have a proven leader, John Cox, as CEO to realize our shared vision to dramatically improve outcomes for those in need or at risk.”

Repertoire has developed a suite of DECODE™ technologies that allows in-depth characterization of the immune synapse with unprecedented precision. The company leverages its functional response technologies to thoroughly understand the presentation of antigens in disease, de-orphan T cell receptors in the context of single-cell phenotypes, and curate vast amounts of data to enable deep-learning computational prediction models. By coupling single cell technologies with cellular and acellular antigen libraries, the company decodes CD4+ and CD8+ TCR-antigen specificity across selected T cell subsets from patients and from healthy individuals.

“I am pleased to work with the Flagship Pioneering team to integrate these two pioneering companies into a fully formed immune medicines business,” said John Cox, Chief Executive Officer of Repertoire

Immune Medicines. “Advancing rationally designed immune medicines into the clinic and eventually to commercialization offers tremendous potential for patients and long-term value for our shareholders.”

Three DECODE discovery technologies are at the core of the company’s immune synapse deciphering platform:

- MCR: proprietary cell-based reporter assays to experimentally quantify MHC-specific peptide display and de-orphan TCR clonotypes across virtually unlimited peptide-MHC libraries
- CIPHER: proprietary MHC multimer-based assays to detect and measure TCR clonotypes, peptide-MHC reactivity and phenotypes on a single-cell level
- CAPTAN: internally developed deep-learning computational tools to classify platform hits and leverage large datasets to predict TCR reactivity beyond what is currently possible

Decoding immune synapses relevant to a particular disease allows Repertoire to deploy the molecular codes to rationally design new immune medicines as disease-fighting TCRs and disease-associated antigens in its therapeutic products.

Repertoire’s DEPLOY™ technologies form a product-based platform that includes:

- PRIME: a proprietary dendritic cell priming technology to naturally expand a patient’s own tumor reactive T cells in an HLA independent manner against antigens found on solid tumors. PRIME™ T cells are natural, multiclonal CD8+ and CD4+ cells featuring an optimized phenotype and high antigen-specific reactivity to multiple tumor antigens.
- TETHER: a proprietary immunomodulator platform for T cell-directed immune activation. Using the TETHER platform primed T cells are linked to immunomodulators using Repertoire’s proprietary tethering technologies, to safely direct powerful immune activators, such as cytokines or toll-like receptor agonists, to solid tumors.
- STREAM: an autologous, high-yielding and scale-able T cell biomanufacturing platform featuring a modular production system to support rapid, on-demand manufacturing without the complexity of genetic engineering. The STREAM platform enables the rapid deployment of novel immune-coded T cell therapies to patients.

Repertoire is currently engaged in its first dose escalation safety trial with an autologous T cell product TRQ15-01, which leverages its proprietary PRIME platform to prepare the patient’s T cells and its proprietary TETHER platform to link an IL-15 nanogel immune modulator to the T cells.

The journey for Repertoire Immune Medicines commenced when Flagship Labs’ scientists contemplated how to rationally and efficiently direct the power of our T cells for therapeutics and cures. One origination group, led by David Berry, M.D., Ph.D., General Partner of Flagship Pioneering, focused on systematically unlocking antigen specific immune control. In parallel, another Flagship origination group, led by Doug Cole, M.D., General Partner of Flagship Pioneering, and based on the cytokine binding work from Prof. Darrell Irvine’s lab at MIT, focused on using autologous T cells to direct potent immune modulators to the tumor microenvironment.

To date, the combined companies raised over \$220M to create and develop the DECODE discovery platform and DEPLOY product platform, and to initiate its first clinical trial of PRIME & TETHER T cells in cancer. Repertoire's rapid advancement reflects its creative, dedicated and diverse team of over 120 professionals possessing expertise in immunology, experimental medicine, physics, computational science, material sciences, process engineering, bioengineering, protein design and applied mathematics.

ABOUT REPERTOIRE IMMUNE MEDICINES

Repertoire Immune Medicines, a Flagship Pioneering company, is a clinical stage biotechnology company working to unleash the remarkable power of the human immune system to prevent, treat or cure cancer, autoimmune conditions and infectious diseases. The company is founded on the premise that the repertoire of TCR-antigen codes that drive health and disease represents one of the greatest opportunities for innovation in medical science. The company harnesses and deploys the intrinsic ability of T cells to prevent and cure disease. Repertoire scientists created and developed a suite of technologies for its DECODE discovery and DEPLOY product platforms that allow in-depth characterization of the immune synapse and the ability to rationally design, and clinically develop, multi-clonal immune medicines. The company is currently conducting experimental medicine clinical trials using autologous T cells primed against cancer antigens and tethered to IL-15. To learn more about Repertoire Immune Medicine, please visit our website: www.repertoire.com.

ABOUT FLAGSHIP PIONEERING

Flagship Pioneering conceives, creates, resources, and develops first-in-category life sciences companies to transform human health and sustainability. Since its launch in 2000, the firm has applied a unique hypothesis-driven innovation process to originate and foster more than 100 scientific ventures, resulting in over \$30 billion in aggregate value. To date, Flagship is backed by more than \$3.3 billion of aggregate capital commitments, of which over \$1.7 billion has been deployed toward the founding and growth of its pioneering companies alongside more than \$10 billion of follow-on investments from other institutions. The current Flagship ecosystem comprises 37 transformative companies, including: Axcella Health (NASDAQ: AXLA), Denali Therapeutics (NASDAQ: DNLI), Evelo Biosciences (NASDAQ: EVLO), Foghorn Therapeutics, Indigo Agriculture, Kaleido Biosciences (NASDAQ: KLDO), Moderna (NASDAQ: MRNA), Rubius Therapeutics (NASDAQ: RUBY), Seres Therapeutics (NASDAQ: MCRB), and Syros Pharmaceuticals (NASDAQ: SYRS). To learn more about Flagship Pioneering, please visit our website: www.FlagshipPioneering.com.

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