

SQZ Biotechnologies

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SQZ Biotechnologies seeks to expand the universe of cell therapies

Potential game-changing Cell Squeeze technology opens up cell therapy to diverse cells and cargoes in immuno-oncology and beyond.

Immune cell-based therapies have become a critical weapon against cancer and can drive durable patient benefit yet the arsenal of therapies is limited by current cell engineering methods to certain cell types and biological approaches. These cell therapies can also be costly and time-consuming to produce. SQZ Biotechnologies has taken a unique approach to overcome these limitations, creating a novel platform technology that can accommodate a wide range of cells and cargo enabling development opportunities in immuno-oncology (IO) and beyond (Fig. 1).

According to CEO, Armon Sharei, “We have shown we can engineer virtually any cell—including T, B, NK, and red blood cells—with many cargo types, from nucleic acids to peptides to small molecules.” Sharei continued, “We address the fundamental challenge of engineering desired cell functions and can do it in a scalable way, opening up a universe of potential cell therapies that were not previously possible.”

A clinical stage company, SQZ Biotech recently shared interim results from a phase 1 trial in HPV-positive cancers at ASCO, a second IND filing in IO has been accepted, and the preclinical pipeline includes additional programs in oncology, autoimmunity, and infectious disease. The company also envisions a Point-of-Care manufacturing platform to help speed development and make cell and gene therapies accessible to more patients.

Advantages of Cell Squeeze

SQZ Biotech’s proprietary Cell Squeeze technology leverages mechanical deformation rather than viruses, electricity or lipids to cross cell membranes and deliver desired molecules into cells without disrupting their function. A solution of cells and cargo are passed through a narrow passage in a microfluidic chip at high speed, temporarily disrupting the cell membrane and allowing cargo to enter the cytosol before subsequently closing. The platform has the capacity to quickly and consistently deliver a wide range of cargo—DNA, RNA, CRISPR as well as other proteins and peptides—and multiple cargoes simultaneously to engineer several cell properties in a single therapy. “The practical advantages of our technology could alter the landscape for cell therapies, significantly expanding their therapeutic range and accessibility,” said Sharei.

SQZ Biotechnologies’ pipeline includes multiple programs in immuno-oncology, with an initial focus on engineering APCs to activate and direct immune responses. The first investigational therapy to reach the clinic, SQZ APCs are peripheral blood

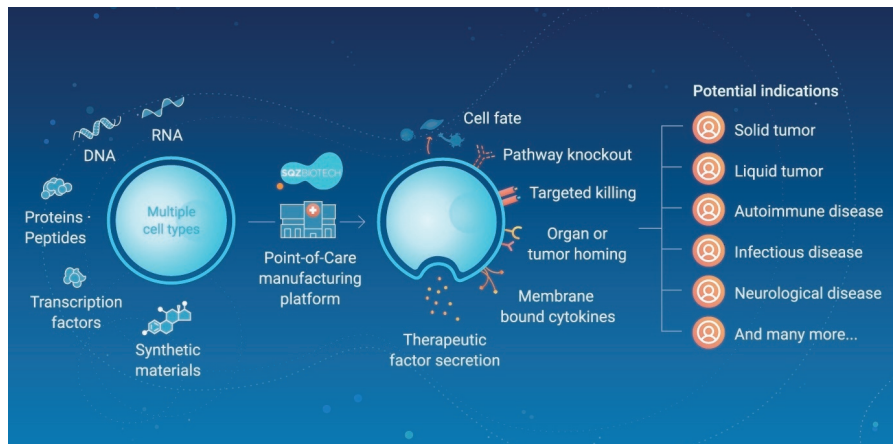


Fig. 1 | SQZ Biotechnologies’ cell engineering capabilities may advance a broad range of therapeutic indications. The company’s Point-of-Care manufacturing platform in development could significantly alter the patient treatment landscape.

mononuclear cells (PBMCs) loaded with tumor-specific HPV peptide antigens. In partnership with Roche, SQZ APCs are being tested in patients with head and neck, cervical, or anal cancer. As reported recently, initial results showed that the HPV-specific SQZ APC monotherapy—which is administered without patient pre-conditioning—was safe and well-tolerated, fast to manufacture, and demonstrated early signs of immune activity. After completion of the monotherapy cohort, the company expects to progress toward the combination phase with immune checkpoint inhibitors. A next-generation APC IO product, ‘enhanced APCs’ or eAPCs, incorporates mRNA encoding multiple activating signals and antigens and is progressing toward the clinic.

Advancing programs to IND

An IND for a second IO therapy against HPV-positive solid tumors, SQZ AACs, has been approved with initial results expected in 2022. SQZ activating antigen carriers (AACs) are derived from red blood cells (RBCs) that are loaded with antigens and adjuvants. AACs are rapidly taken up in the lymphoid organs by professional APCs, which are potent CD8⁺ T cell activators. AACs loaded with HPV antigen are designed to access this pathway and activate a robust tumor killing response against HPV-positive solid tumors. SQZ sees potential to apply its platform in IO to engineer multiple immune cells, including TCR, TIL, and CAR therapies, offering a practical and cost-effective option.

Just as natural or engineered APCs can stimulate

immune responses, given the right inputs they can also dial down immunity and induce tolerance. SQZ is developing a therapy called SQZ TACs, for Tolerizing Antigen Carriers, for patients with autoimmune disease. TACs deliver antigen to endogenous antigen presenting cells without an inflammatory element, leading to Ag-specific T cell deletion, increased immunosuppressive T regulatory cells, and bystander Ag suppression.

A pipeline program in infectious disease, using SQZ eAPC to treat chronic HBV, is also underway, and the company envisions future applications in regenerative medicine, intervening therapeutically with transcription factors cargo to redirect cell fate. The company recently presented preclinical data showing that it can generate neurons from induced human pluripotent stem cells (iPSCs) through the single delivery of an mRNA encoding a fate-specifying transcription factor.

By solving the fundamental challenge of broadly engineering cells at scale and providing a decentralized platform for cell therapy production, SQZ aims to unleash the full potential of cell therapies in oncology and beyond.

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