

PRODUCT DEVELOPMENT

The mRNA therapeutics pipeline: Data Byte

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Having made its mark as a vaccine modality for COVID-19, other mRNA vaccines for infectious diseases are sure to follow. The technology's potential is much broader than prophylaxis, however. An analysis of active clinical trials listed in ClinicalTrials.gov finds at least 21 mRNA-based therapeutic programs in testing to treat a range of diseases, with cancer by far seeing the most activity.

Of the 21 mRNA therapies, 14 (66%) are designed to treat cancer; these are in testing for at least 10 indications. Moderna Inc. (NASDAQ:MRNA), BioNTech SE (NASDAQ:BNTX) and eTheRNA immunotherapies N.V. are the major players, with eight, five and two cancer mRNA therapies, respectively.

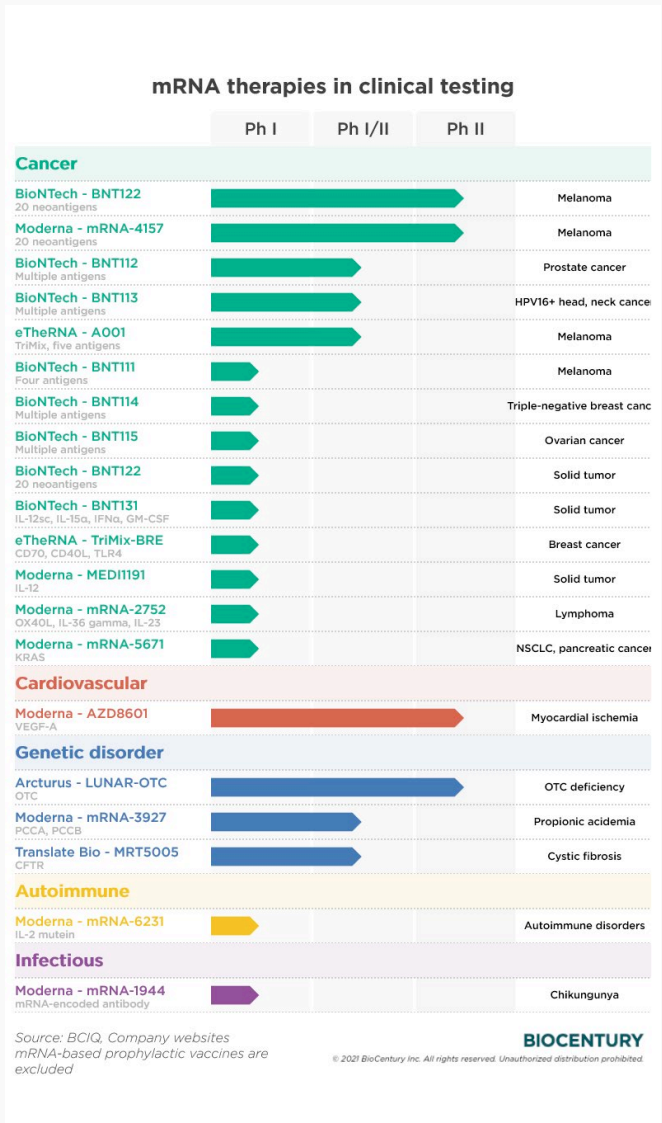
The two most advanced cancer programs are both in Phase II testing for melanoma. Moderna's mRNA-4157, a personalized cancer vaccine that can encode 20 neoepitopes, is in testing with Keytruda pembrolizumab from Merck & Co. Inc. (NYSE:MRK). BioNTech and the Genentech Inc. unit of Roche (SIX:ROG; OTCQX:RHHBY) are developing BNT122, an individualized neoantigen specific immunotherapy (iNeST) that contains up to 20 patient-specific neoantigens encoded as mRNAs.

BioNTech is also developing cancer therapies using its FixVac technology, which employs shared cancer antigens instead of personalized neoantigens.

eTheRNA's TriMix platform combines therapeutic mRNA molecules that encode CD70, CD40L and TLR4. So far, the biotech has used TriMix to generate dendritic cell vaccines *ex vivo*. It intends to focus on enabling *in vivo* delivery for its next programs.

BioNTech's iNeST and FixVac technologies both use lipoplex formulation to deliver the mRNAs to dendritic cells in lymphoid organs such as spleen; whereas the mRNAs in BNT131, which is being developed by BioNTech and Sanofi (Euronext:SAN; NASDAQ:SNY) to produce cytokines, are delivered intratumorally.

Several of Moderna's therapies are also delivered intratumorally.



There are six non-cancer mRNA therapeutic programs in clinical trials for genetic, cardiac, autoimmune and infectious diseases. The most advanced are LUNAR-OTC from Arcturus Therapeutics Holdings Inc. (NASDAQ:ARCT) and AZD8601 from Moderna and AstraZeneca plc (LSE:AZN; NASDAQ:AZN).

Arcturus expects interim results from a Phase II trial of LUNAR-OTC to treat the ornithine transcarbamylase deficiency, a urea cycle disorder, in 2H22. The enzyme replacement therapy delivers mRNA to periportal hepatocytes using the company's LUNAR lipid-delivery platform.

Moderna and AstraZeneca are developing AZD8601 for myocardial ischemia. When injected locally into heart or skin tissue, the therapy is

expected to regenerate blood vessels and improve blood supply through expression of VEGF-A.

Moderna's mRNA-1944 is an mRNA-encoded antibody treatment for Chikungunya. Encoding antibody therapies as genes or mRNA simplifies manufacturing by having the patient make the product; the concept has been making quiet progress in drug development.

Behind the mRNA-based therapeutic programs in clinical trials are at least 21 other candidates in preclinical testing. Newer players in this field include ethris GmbH, NanoGhost, RNACure Biopharma, Strand Therapeutics Inc. and Versameb AG.

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