mRNA's Next Act: Cancer Vaccines and Gene Editing

By Gail Dutton
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The potential for mRNA technology extends far beyond the COVID-19 vaccines that made it a household word. Coming applications include therapeutic vaccines for cancer and other diseases, vaccines for latent conditions such as shingles and herpes, and, eventually, mRNA therapeutics for conditions where immune activation is unnecessary.

“The applications for mRNA are quite broad, because, basically, you are giving information to a cell to make any protein you want,” Pierre Kemula, B.Sc., CFO at **CureVac** told *BioSpace*. “That’s the beauty of mRNA.”

Bespoke Vaccines

Vaccine developers are currently exploring multivalent mRNA vaccines. With influenza, for example, “The idea is that you will be able to make your vaccine a bit later in the season and be closer to the circulating strain of virus. Ultimately, this allows researchers to develop bespoke vaccines that are tailored to specific regional outbreaks,” Kemula said. “The more antigens, the broader the efficacy of the vaccine will be.”

Moderna’s **bivalent booster vaccine** for COVID-19 is another more widely-known example. Two vaccines are in Phase II/III trials now, targeting multiple variants of the SARS-CoV-2 virus. The goal is to start a booster campaign for vulnerable populations this fall, involving at least one of those vaccines.

Notably, multivalent vaccines can also target multiple conditions. For example, Kemula said, "With more antigen, you can do combinations, maybe targeting several things, such as flu and COVID." CureVac's COVID-19 vaccine candidates are co-developed with GSK and have a second-generation vaccine backbone, engineered to address COVID-19 variants as well as a range of other diseases. There are also potential combination vaccines. One candidate, targeting four strains of flu, **entered Phase I** earlier this year.

Moderna's **pipeline** shows another vaccine, mRNA-1230, currently in preclinical development targeting COVID-19, flu and respirational syncytial virus (RSV).

Beyond Immune Activation: "The Holy Grail"

"Today, the sweet spot of mRNA is prophylactic vaccines – the low-hanging fruit – but the future is to transfer that immune activation potential to cancer vaccines," Kemula said.

"The goal of cancer vaccines is to elicit a targeted immune response against the tumor to fight the disease or protect the patient by stabilizing the condition," he explained. "Cancer vaccines have been a challenge for the industry. There's no real cancer vaccine out there."

To that end, CureVac **acquired** Frame Cancer Therapeutics in June. The acquisition offers the ability to identify a broad panel of neoantigens based on structural changes in the cancer genome. "This enables much broader applications. One of the consequences is that – we hope – we'll be able to have a customized vaccine based upon (combining) a few recurring antigens as well as personalized approaches," Kemula said.

Cancer vaccines hold great potential but, currently, "A lot of the oncology research (involving mRNA) is in preclinical Phase I trials, so it will be quite a while before we see them," Margery Fischbein, managing director of the healthcare practice at investment bank Cassel Salpeter & Co. cautioned.

As mRNA therapies advance, "The Holy Grail is to go beyond immune activation," Kemula said. "There's a huge field where you can encode for any protein with mRNA." In theory, it will become possible to inject patients with

mRNA that encodes for certain missing or deficient enzymes and thus help them regain homeostasis and potentially cure the disease.

“One of the challenges is that sizeable quantities of mRNA may need to be injected to treat chronic disease, which may result in tolerability issues,” he noted.

There are easier applications within that space, however, and they probably will be tackled first. “Think of the eye. It’s a privileged organ (meaning the immune system does not initially attack), and its small, so you don’t need to inject so much material and thus don’t have as much of an immune response. That’s probably an area where mRNA could be additive to existing therapies,” Kemula suggested.

Gene editing applications also may have potential. Here, mRNA could be used to express cas9 or other proteins, and eliminate the inability for repeat dosing that currently challenges gene therapies. “mRNA is a transient technology,” Kemula pointed out. “You go in, express a protein, and after some time it’s gone.” In certain genomic medicine applications, that can be an advantage.

For prophylactic vaccines – particularly for COVID-19 – development speed and initial antibodies levels were the most important criteria, allowing mRNA vaccines to protect as many people as possible as quickly as possible. For a durable response, however, the body also needs T cell responses. “It’s just a matter of time before the industry gets there,” Kemula predicted.

With a robust pipeline in mRNA therapeutics and vaccines, Ira Z. Leiderman, managing director of Cassel Salpeter predicted, “more and faster approvals, though not as fast as for the SARS-CoV-2 vaccines.” That prediction is based upon regulators’ presumed comfort level with mRNA technology and the vast numbers of people who have received mRNA vaccines with few issues.

That said, whatever happens depends upon the outcome of clinical trials, many of which are just being planned. “There’s still a lot of learning that has to occur,” Fischbein cautioned.

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- **mRNA in the Spotlight as BioNTech Finally Makes a Splash in CancerThis will open in a new window**
- **Moderna mRNA Portfolio on Track to Hit 2025 Goal with Nipah Virus Trial Launch**