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BMS Inserts Cash Into Prime Medicine's Gene-Editing Ambitions

by Andrew McConaghie

An upfront payment of $110m from BMS has come just in time for Prime Medicine, but its real test will be the first Phase I data, expected early next year.

Next-generation gene editing company *Prime Medicine* has signed a research partnership with *Bristol Myers Squibb* to work on *ex vivo* T-cell therapies, providing it with some much-needed cash and a chance to demonstrate the potential of its platform.

The Cambridge, MA-based biotech unveiled the big pharma partnership and its $110m upfront payment (half of which is an equity investment) alongside news that it was slimming down its pipeline to focus on only the most high-value projects.

Prime sees its technology as a next generation of gene editing, having more versatility and precision than first-generation CRISPR gene editing, as pioneered by companies such as *CRISPR Therapeutics*, and base editing, being developed by *Beam Therapeutics* and others. It claims its platform is the only one that can edit, correct, insert and delete DNA sequences in any target tissue.

Key Takeaways

- Prime Medicine believes it has the most versatile gene-editing platform, and has just received a vote of confidence via the BMS deal.
- Investors are nevertheless more focused on the results from its first Phase I readout, expected in 2025.

However, since its foundation in 2019, it has still not brought any of its gene-editing techniques into the clinic, and following its IPO around two years ago, it has lost three

quarters of its market cap (now worth just $549m).

This erosion of investor confidence has been coupled with a high cash burn meaning that before the deal, Prime was set to run out of money in 2025. Now, the upfront payment and anticipated cost savings from the R&D cuts will help extend its cash runway into the first half of 2026.

The BMS deal also includes $185m worth of potential preclinical milestones. Speaking at a Chardan investor conference on 30 September, CEO Keith Gottesdiener said these would be "incremental infusions" to help the firm move forward. The deal also includes a further $1.2bn of clinical development milestones and over $2.1bn in potential commercialization milestones and royalties on net sales.

Under the pact, Prime will provide strategic advice on gene editing and develop reagents from which a next generation of *ex vivo* T-cell therapies can be produced. BMS will be responsible for all other stages of development, manufacturing and commercialization. The partners have not disclosed precise targets but indicated these could be in immunological diseases and cancer, and provide a next generation of CAR-Ts to follow BMS's existing products. (Also see "*BMS Fast Tracks CAR-T Manufacturing With Cellares Deal*" - Scrip, 22 Apr, 2024.)

Whole Gene Correction Technology

Prime's platform can make small, medium and large edits, and the latter are made via its prime assisted site-specific integrase gene editing (PASSIGE) technology. This allows a gene-sized unit of up to five or ten kilobases to be inserted very precisely into a specific DNA location, allowing numerous disease-related mutations to be replaced in a single gene-sized sequence. Such an approach will be used in the BMS collaboration, and Prime claims the technology, which is also non-viral and one-step, is unmatched in other gene-editing platforms.

The BMS collaboration also gives Prime's technology a chance to shine in areas of high unmet need beyond the rare genetic diseases in its own internal pipeline. "There is tremendous opportunity for PASSIGE and Prime Editing to revolutionize the field of cell therapy, and we look forward to expanding our reach over time through both internal and partnered efforts," Gottesdiener added.

Despite the funding boost, the company has still had to shelve some preclinical programs in order to focus on the most high-value assets. It has decided to prioritize two programs for the treatment of chronic granulomatous disease (CGD), which the company believes together have potential to address the vast majority of people living with the genetic condition in which phagocyte white blood cells are unable to kill certain types of bacteria and fungi.

The first of these is PM359, an *ex vivo* autologous hematopoietic stem cell (HSC) product for the treatment of p47phox CGD, which affects around a quarter of patients. This is now in a Phase I/II

study in adult and pediatric patients, with initial results expected next year.

The second candidate is an *ex vivo* HSC product for X-linked CGD, which the company has just unveiled as a companion to PM359. This will use the PASSIGE technology, and is expected to address over 90% of known mutations in the *CYBB* gene with a single approach. Mutations in *CYBB* occur in approximately two thirds of patients with CGD.

Prime intends to take advantage of the crossover between the two programs, including the IND filing, chemistry, manufacturing and controls work and clinical trial, to help accelerate the X-CGD program.

The company also expects new preclinical data from a lipid nanoparticle "Prime Editor in Wilson's Disease" program in the fourth quarter of 2024, and is also working on two preclinical programs in cystic fibrosis.

The R&D cuts mean the company will stop work on its "hotspot correction" technique in retinitis pigmentosa/rhodopsin and a large-scale deletion approach in Friedreich's Ataxia.

Gottesdiener said at the investor conference that the markets continued to "lump in" gene editing companies like Prime in with very early preclinical companies. He also said investors were currently not differentiating among the various gene-editing companies, but reiterated his belief that Prime's technology had greater potential than others, and said he expected to win over skeptics with future data.

"We're not a preclinical company anymore, but I'll feel better when I actually have clinical data in hand, and can look people in the eye and say that," he said.

On the day of the announcement, the company's NASDAQ-listed shares rose by 12%, but the next day lost nearly all its gains, nearing the $3.50 per share it started on. Investors clearly now see the company's first Phase I data readout in 2025 as the next big catalyst.