Generation Bio Announces Breakthrough in its Non-Viral Genetic Medicine Platform with Novel “Immune-Quiet” DNA

October 18, 2023

– Immune-quiet DNA (iqDNA) is a novel variant of closed-ended DNA (ceDNA) that evades host innate immune detection in both mice and non-human primates (NHPs) with a systemic cytokine profile and tolerability comparable to mRNA

– Company is advancing iqDNA in lieu of prior ceDNA constructs across all programs, including its lead program in hemophilia A

– Company is extending cash runway guidance into 2026 through collaboration income and expense control while increasing investment in its iqDNA and cell-targeted lipid nanoparticle (ctLNP) platforms

– Company will present data on iqDNA and ctLNP platforms at upcoming scientific meetings today and on October 26, and will host a webcast R&D event on November 1

CAMBRIDGE, Mass., Oct. 18, 2023 (GLOBE NEWSWIRE) -- Generation Bio Co. (Nasdaq:GBIO), a biotechnology company developing genetic medicines for people living with rare and prevalent diseases, today announced the development of a proprietary, novel DNA called immune-quiet DNA (iqDNA). iqDNA is an optimized variant of the company’s closed-ended DNA (ceDNA) that upon systemic administration with Generation Bio’s lipid nanoparticle (LNP) delivery has shown cytokine levels and tolerability comparable to chemically modified messenger RNA (mRNA) in mice and non-human primates (NHPs).

Generation Bio’s non-viral genetic medicine platform aims to advance durable, redosable, and titratable therapies to reach potentially hundreds of millions of patients worldwide. The company has made deep investments in its three proprietary platform technologies, comprising novel DNA cargos, rapid enzymatic synthesis (RES) manufacturing, and cell-targeted LNP (ctLNP) delivery.

“Developing solutions that allow genetic medicines to avoid innate immune stimulation is a shared and fundamental requirement for enabling non-viral therapeutics, as exemplified by the development of modified mRNA to enable a global modality,” said Matt Stanton, Ph.D., chief scientific officer of Generation Bio. “Our development of iqDNA is a similar step toward realizing the full potential of non-viral DNA therapeutics. I’m excited to further advance our platform as we seek to create safe and effective medicines that could marry the scalability and drug-like properties of mRNA with the durability of DNA-based genetic medicines.”

Systemic dosing in mouse and NHP studies demonstrates that iqDNA delivered via LNP evades detection by the key innate immune pathways that are reactive to DNA. Figure 1 below shows a comparison of IL-6 levels, representative of all cytokines measured, in a cohort of NHPs that received an infusion of ceDNA, iqDNA, or mRNA, each delivered using the same LNP at 1 mg/kg and containing luciferase as a reporter gene.

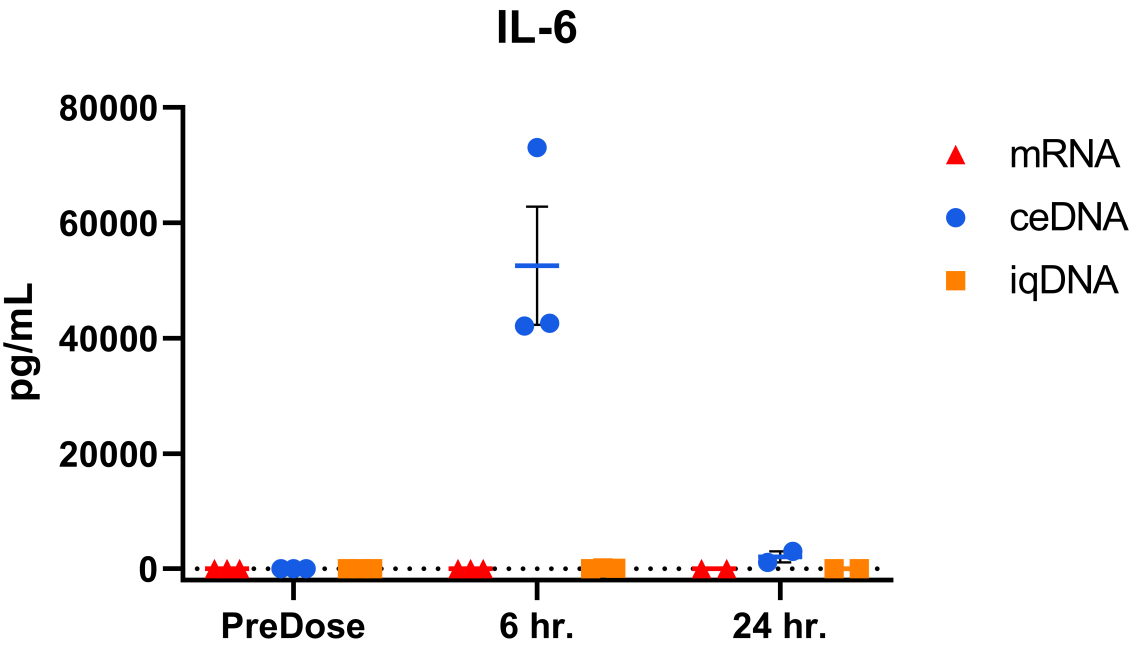

Figure 1: IV infusion 1 mg/kg

Importantly, companion mouse studies demonstrate that iqDNA conserves the key features of ceDNA that afford therapeutic benefit, including expression.

Due to the superior tolerability profile of iqDNA, Generation Bio is discontinuing development of prior ceDNA constructs and is advancing iqDNA as the

cargo for its lead program in hemophilia A as well as for all other programs. Scaling of iqDNA factor VIII for NHP testing is underway, leveraging existing RES systems and processes.

“The identification of iqDNA is the culmination of six years of work at Generation Bio to address the central challenge of immune activation for DNA-based genetic medicines,” said Geoff McDonough, M.D., chief executive officer of Generation Bio. “We expect that iqDNA will significantly enhance the tolerability profile of our lead program in hemophilia A allowing us to leverage our broad portfolio of LNPs to advance this and our other programs.”

Dr. McDonough continued: “In parallel with cargo optimization, we have made substantial investments in the translation of our ctLNP delivery system from mice to NHPs, initially motivated by avoiding the innate immune stimulation caused by off-target delivery of ceDNA to immune cells. This led to the development of our stealth LNP plus targeting technology, which unlocks the potential for reaching non-liver cell types and tissues. Our collaboration with Moderna aims to create highly specific *in vivo* delivery to T cells and other immune cell types with both iqDNA and mRNA cargos. We are excited to share updates on our iqDNA and ctLNP platforms as we make progress across our liver and non-liver programs.”

Cash runway extended into 2026

Generation Bio believes it has sufficient cash to extend the funding of its operations into 2026 based on income from the Moderna collaboration, including the initial upfront payment, as well as interest income and expense control. Concurrent with extending its cash runway, the company is increasing investment in its iqDNA and ctLNP platforms.

Upcoming events and presentations

- ***AIchE Conference, October 18:*** Dr. Stanton will present the data on iqDNA at the American Institute of Chemical Engineers' (AIchE) 6th International Conference on CRISPR Technologies in Boston, Mass. A copy of this presentation is available on Generation Bio’s website.
- ***ESGCT Annual Congress, October 26:*** On Thursday, October 26 Dr. Stanton will give an oral presentation at the European Society for Gene and Cell Therapy (ESGCT) 30th Annual Congress in Brussels, Belgium. The presentation will cover the development and progress of Generation Bio’s ctLNP platform, including its stealth and targeting delivery system. A copy of the slide presentation will be made available on Generation Bio’s website following the event.
- ***Webcast R&D Event, November 1:*** On Wednesday, November 1 the company will host a webcast-only R&D deep dive and Q&A session to provide further detail on its platform capabilities across iqDNA, RES manufacturing, and ctLNP. Registration information for the webcast can be found on the Events page of Generation Bio’s investor website.

About Generation Bio

Generation Bio is innovating genetic medicines to provide durable, redosable treatments for people living with rare and prevalent diseases. The company’s non-viral genetic medicine platform incorporates a novel immune-quiet DNA called iqDNA; a unique cell-targeted lipid nanoparticle delivery system, or ctLNP; and a highly scalable capsid-free manufacturing process that uses proprietary cell-free rapid enzymatic synthesis, or RES, to produce iqDNA. This approach is designed to enable multi-year durability from a single dose, to deliver large genetic payloads, including multiple genes, to specific tissues and cell types, and to allow titration and redosing to adjust or extend expression levels in each patient. RES has the potential to expand Generation Bio’s manufacturing scale to hundreds of millions of doses to support its mission to extend the reach of genetic medicine to more people, living with more diseases, around the world.

For more information, please visit www.generationbio.com.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the company, including statements about the company’s strategic plans or objectives, cash resources, technology platform, research and clinical development plans, and preclinical data and other statements containing the words “believes,” “anticipates,” “plans,” “expects,” and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the conduct of research activities, the initiation and completion of preclinical studies and clinical trials and clinical development of the company’s product candidates; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; whether results from earlier preclinical studies will be predictive of the results of later preclinical studies and clinical trials; uncertainties regarding our novel technologies, including iqDNA; uncertainties regarding the RES manufacturing process; challenges in the manufacture of genetic medicine products; whether the company’s cash resources are sufficient to fund the company’s operating expenses and capital expenditure requirements for the period anticipated; the impact of the COVID-19 pandemic on the company’s business and operations; as well as the other risks and uncertainties set forth in the “Risk Factors” section of our most recent annual report on Form 10-K and quarterly report on Form 10-Q, which are on file with the Securities and Exchange Commission, and in subsequent filings the company may make with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the company’s views as of the date hereof. The company anticipates that subsequent events and developments will cause the company’s views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the company’s views as of any date subsequent to the date on which they were made.

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/b9bf80f8-5900-471d-

b097-b2167f082be9