Next-Gen Protein Replacement Therapeutics: DNA-Encoded Protein (DPROT) Technology Demonstrates *In Vivo* Production of Functional HuFVIII in Mouse Model

World Federation of Hemophilia April 22nd, 2026

Dr. Mike Sumner, Chief Medical Officer & Head of Development

Forward-Looking Statements

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In addition, the forward-looking statements included in this presentation represent INOVIO's views as of the date hereof. INOVIO anticipates that subsequent events and developments may cause its views to change. However, while INOVIO may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing INOVIO's views as of any date subsequent to the date of this presentation.

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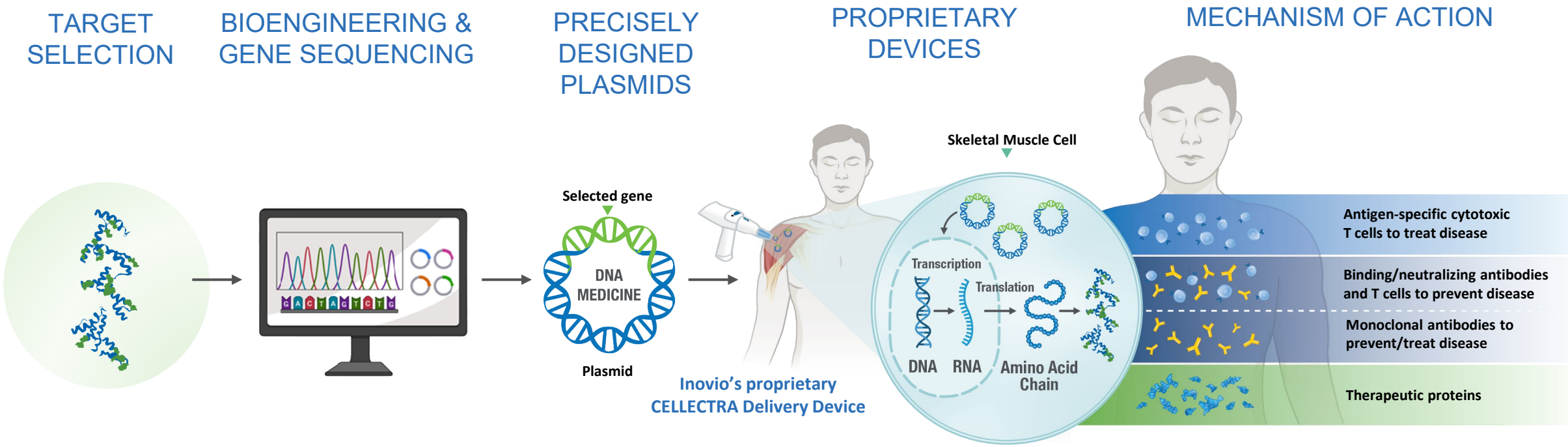
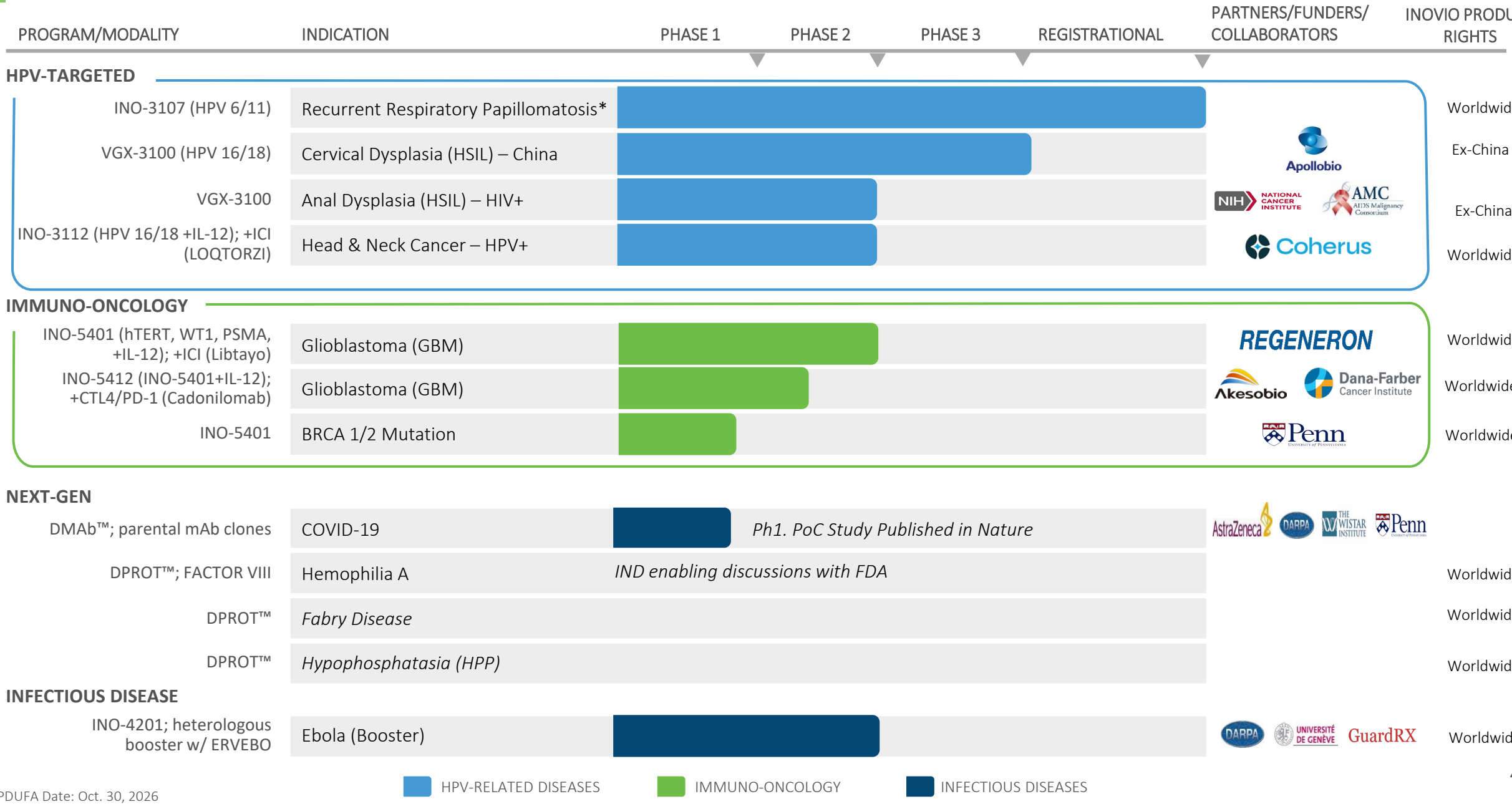
DNA Medicines: Customized *In Vivo*-Generated Proteins



Inovio's DNA medicines platform enables tailored and sustained *in vivo* protein expression that can:

- Induce cytotoxic T cells to target specific cancers or viral infections
- Generate monoclonal antibodies for both prevention and treatment of diseases
- Achieve therapeutic levels of protein expression to support disease control in enzyme/protein replacement diseases

INOVIO Pipeline



* PDUFA Date: Oct. 30, 2026

INOVIO's DNA Medicine DPROT/DMAb* Platform

- Targeted localized delivery utilizing CELLECTRA® device technology
  - Without need for lipid nanoparticles or viral vectors
- Platform supported by comprehensive nonclinical GLP toxicology and biodistribution studies
  - These studies support IND filings for all Inovio DNA products with identical plasmid backbones, without requirement for additional nonclinical GLP safety data
  - No plasmid integration
- Potential for future platform designation with FDA

CELLECTRA® 5PSP

DNA-encoded Protein / DNA-encoded Monoclonal Antibody

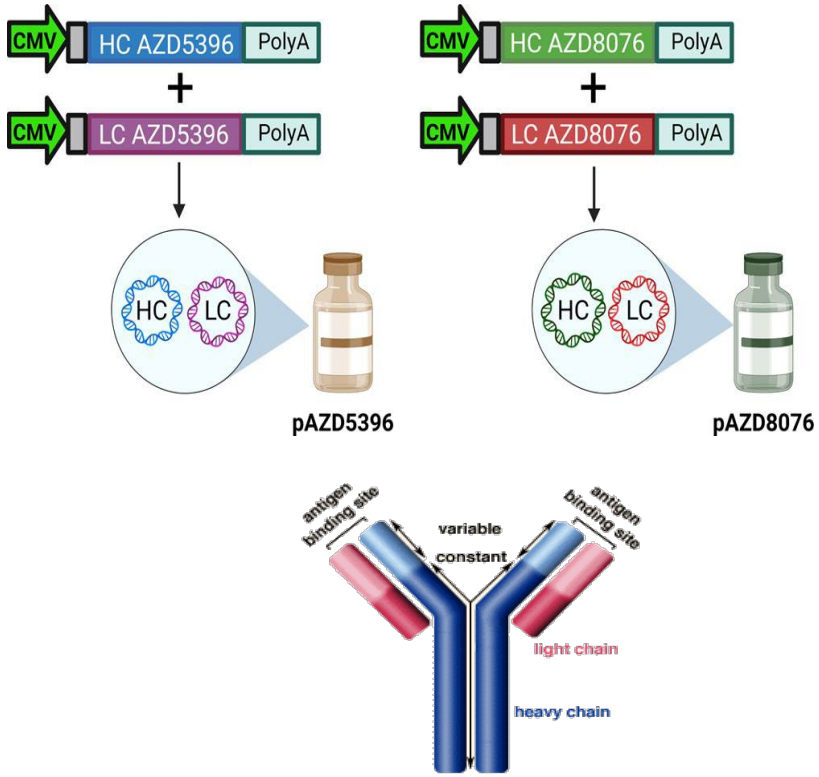
Next-Generation Platform

Proof-of-Concept Clinical Data

INOVIO

Next-Generation DNA Medicine – Clinical Proof-of-Concept

- DARPA funded, Wistar Institute-led proof-of-concept Phase 1 clinical trial in collaboration with AstraZeneca, the University of Pennsylvania and INOVIO to develop anti-SARS-CoV-2-specific DMAbs™
  - Data highlight potential to deliver a broad spectrum of therapeutic proteins that could be used to treat diseases with missing or defective proteins
  - Data published in *Nature Medicine*

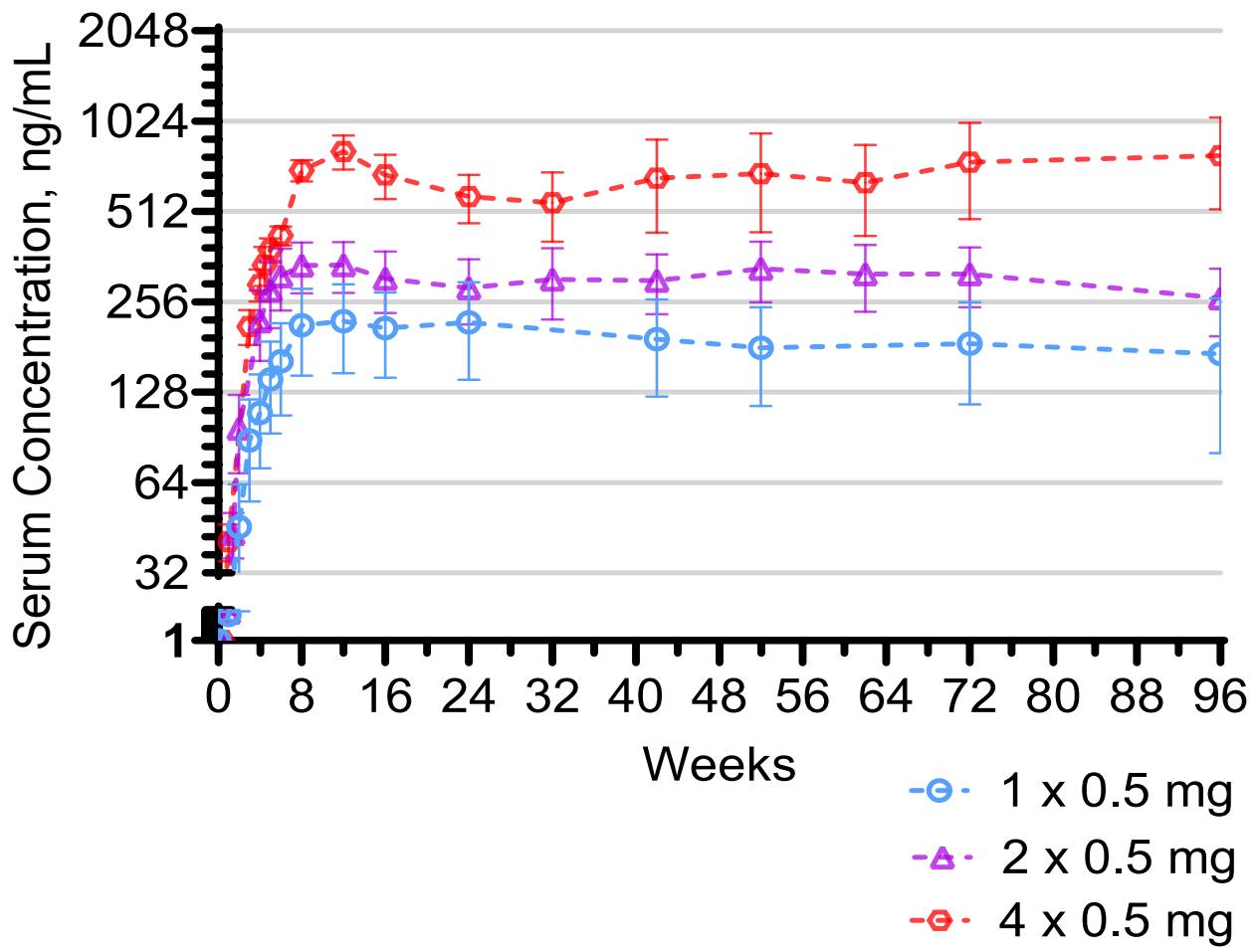


DMAbs were based on parental mAb clones COV2-2130 (2130) and COV2-2196 (2196), the precursors of EVUSHELD AZD7442. Four synthetic DNA constructs were designed for optimal in vivo expression of the heavy (HC) and light chains (LC) of AZD5396 and AZD8076. DNA construct cocktails were each formulated with human recombinant hyaluronidase enzyme.

Tebas P, et al. Safety and pharmacokinetics of SARS-CoV-2 DNA-encoded monoclonal antibodies in healthy adults: a phase 1 trial. Nat Med. 2025

Ongoing Phase 1 Trial with DMAbs™

- **Long-lasting *in vivo* antibody production**: DMAb levels remained stable for 96 weeks in all participants reaching that timepoint
- **No anti-drug antibodies (ADA):** no immune rejection of the DMAbs detected across ~1,000 blood samples
- **Effective target binding**: expressed DMAbs successfully bound to SARS-CoV-2 Spike protein receptor-binding domain, confirming functional activity through week 96
- **Re-dosing at days 28 & 31 achieved DMAb levels over 1 µg/ml:** Redosing appeared to be more effective at increasing DMAb concentrations compared with escalating single doses



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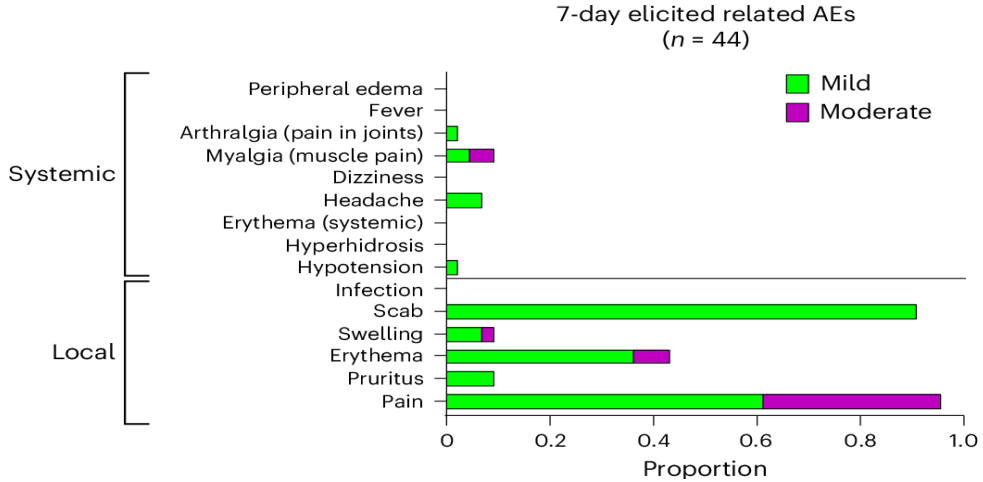
Tebas P. Et al, Conference on Retroviruses and Opportunistic Infections, 2026

Tolerability Profile of DMAb Administered with CELLECTRA® IM

- **Elicited AEs (≤7 days post-dose):** Frequency and severity of treatment- or procedure-related elicited AEs are shown
  - Very low frequency of systemic AE's versus other delivery platforms
- **Pain Assessment:** Pain perception is highly variable, based on perceived benefit, and diminishes within minutes of administration
  - "mild to moderate discomfort that resolves within 5-10 minutes“
    - No meaningful differences observed across repeat administrations

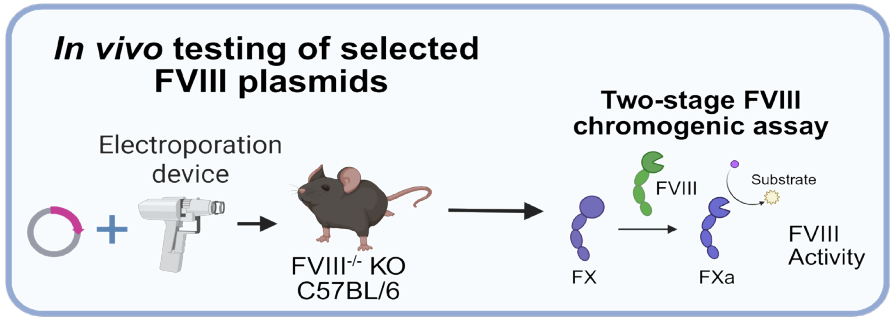


Tebas, P., Patel, A., Agnes, J.T. et al. Safety and pharmacokinetics of SARS-CoV-2 DNA-encoded monoclonal antibodies in healthy adults: a phase 1 trial. Nat Med 31, 4150–4159 (2025). https://doi.org/10.1038/s41591-025-03969-0

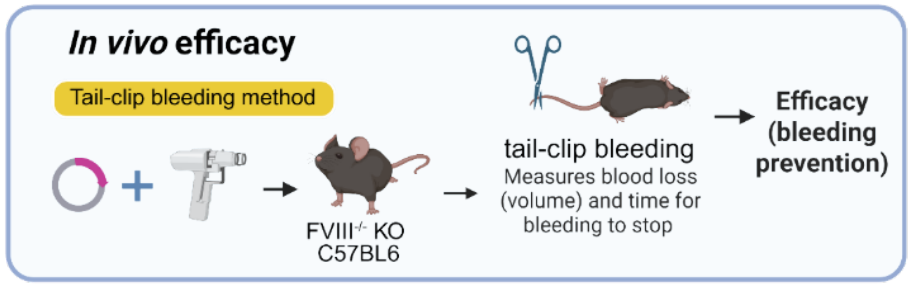
DPROT: An Alternative to Viral-based Delivery for Long-Term *In Vivo* Protein Expression

- Sustained *in vivo* protein expression remains a crucial objective in the treatment of genetic disorders such as hemophilia
- Despite notable progress, several challenges persist:
  - Pre-existing immunity to viral vectors
  - Development of anti-viral vector immunity post *in vivo* administration, restricting the possibility of re-dosing
  - Gradual decline in protein expression over time, necessitating additional dosing
  - Safety and tolerability concerns
- Historically, non-viral delivery platforms have faced limitations due to inefficient delivery mechanisms
- DMAb/DPROT technology presents potential solutions to overcome these challenges
  - Durable expression of therapeutic proteins in pre-clinical models achieved across 3 distinct diseases: FVIII (Hemophilia A); α-Galactosidase A (Fabry Disease) and Tissue Non-specific Alkaline Phosphatase (Hypophosphatasia)
  -

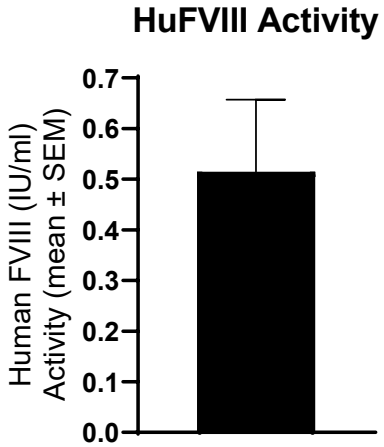
INOVIO DPROT Approach for Hemophilia A: Human FVIII (HuFVIII) is Expressed and Functional in FVIII KO Mice

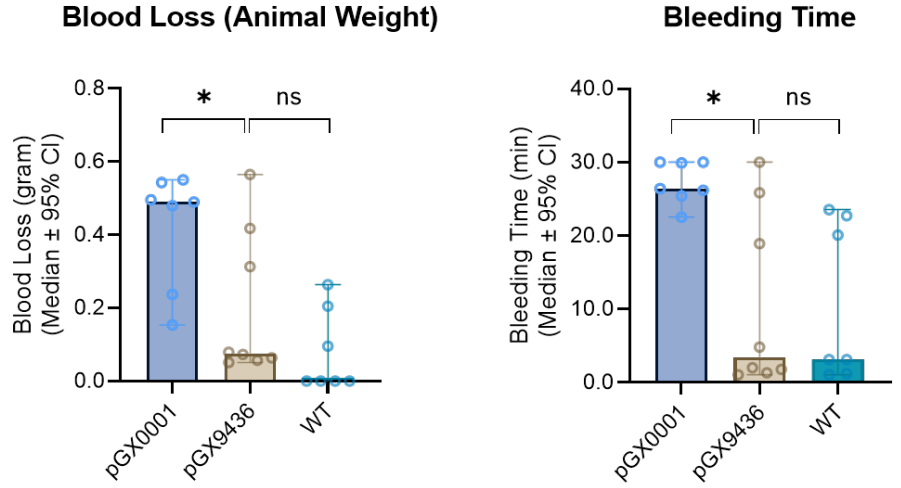


Mouse tail clip model



Confirms complex proteins such as huFVIII can be effectively produced, assembled in myocytes and secreted into the circulation





pDNA/EP -treated FVIII KO mice showed significantly reduced bleeding time and blood loss compared to control (pGX0001-treated) KO mice, with bleeding control in pDNA/EP -treated KO mice comparable to that observed in wild-type mice.

DMAb/DPROT: Potential New Therapeutic Paradigm

- Platform has demonstrated ability to achieve long-term protein expression and secretion
  - Clinical PoC published in *Nature Medicine*[1]
  - Serum levels within therapeutic range for multiple diseases; we expect platform optimization to enable higher serum concentrations to be achieved
- Highly differentiated from existing platforms
  - Ability to re-dose will enable clinical titration and long-term disease management
  - Potential to generate new IP and extend product life cycle
- Safety data supports its future tolerability profile
- Development timeline from concept to first in human ~ 2 years
  - Preclinical package largely draws on platform applicable data
- Based on existing POC data, platform may have broad applicability for many disease states

1. Tebas P, et al. Safety and pharmacokinetics of SARS-CoV-2 DNA-encoded monoclonal antibodies in healthy adults: a phase 1 trial. *Nat Med*. 2025; Epub ahead of print.


Thank you.
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