# An Advanced Non-Viral Gene Delivery Technology Enables Secretion of FVIII from Skeletal Muscle

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# Forward-Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements,” within the meaning of Section 27A of the Securities Act of 1933, as amended. All statements, other than statements of historical facts, included in this presentation regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “target,” “design,” “estimate,” “predict,” “opportunity,” “proposition,” “strategy,” “potential,” “plan” or the negative of these terms and similar expressions intended to identify forward-looking statements.

You should not place undue reliance on these forward-looking statements. Forward-looking statements include, but are not limited to, statements about: the timing and success of preclinical studies and clinical trials; the ability to obtain and maintain regulatory approval of our product candidates; the FDA's acceptance of our BLA for INO-3107 with a PDUFA target action date set for October 30, 2026; the potential benefits of INO-3107; the scope, progress and expansion of developing and commercializing our product candidates; our anticipated growth strategies; our ability to establish and maintain development partnershipsand other factors that are described in the “Risk Factors” and “Management's Discussion and Analysis of Financial Condition and Results of Operations” sections of our Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, which has been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov.

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# Company Overview

## Groundbreaking Late-Stage DNA Medicines Platform Company

**FOUNDATION**

Nasdaq Listed
**INO**

Philadelphia, PA (Headquarters)
**>150**
**Employees**

San Diego, CA (R&D and Device Manufacturing)
**51,000 sq.ft.**
**Fully-Integrated cGMP Manufacturing Site**

**PLATFORM**

**Customizable in vivo protein expression using INOVIO's proprietary DNA medicines platform**

**Commercial Ready**

- First-in-class candidate nearing commercialization
- BLA Accepted: Dec. 2025*
- PDUFA Date: Oct. 30, 2026
- Platform component CE Marked in Europe

**Flexible, Validated, and Customizable**

- Wide range of proteins can be expressed in vivo
- Robust clinical PoC and immunological data
- Stable at room temperature without the need for lipids, viral vectors, or adjuvants

**PROGRAMS IN DEVELOPMENT**

**Broad Spectrum of Therapeutic Opportunities**

- Proven ability to target and impact disease
- Pipeline of HPV-related disease, immuno-oncology, and rare disease products

**8**
**Clinical Trials**

Ongoing clinical studies ranging from Phase 1 to Phase 3

**3**
**Next-Gen Programs**

- Factor VIII Program – Hem A
- 2 undisclosed rare disease targets

*INOVIO plans to request meeting with FDA to discuss next steps to remain eligible under accelerated approval pathway.

# INOVIO Pipeline

| PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | REGISTRATION |
|---|---|---|---|---|
| DMAbs<br>Various Targets | INO-5401<br>BRCA 1/2 Mutation | VGX-3100<br>Anal Dysplasia | | INO-3107 *<br>RRP |
| DPROTs<br>Various targets | INO-4201<br>Ebola Booster | INO-3112<br>Head & Neck Cancer | | |
| DLNPs<br>Various targets | INO-6172<br>HIV | INO-5401<br>Glioblastoma | | |
| | INO-6160<br>HIV | | | |
| | DMAbs<br>COVID-19 | | | |

**OUT-LICENSED**

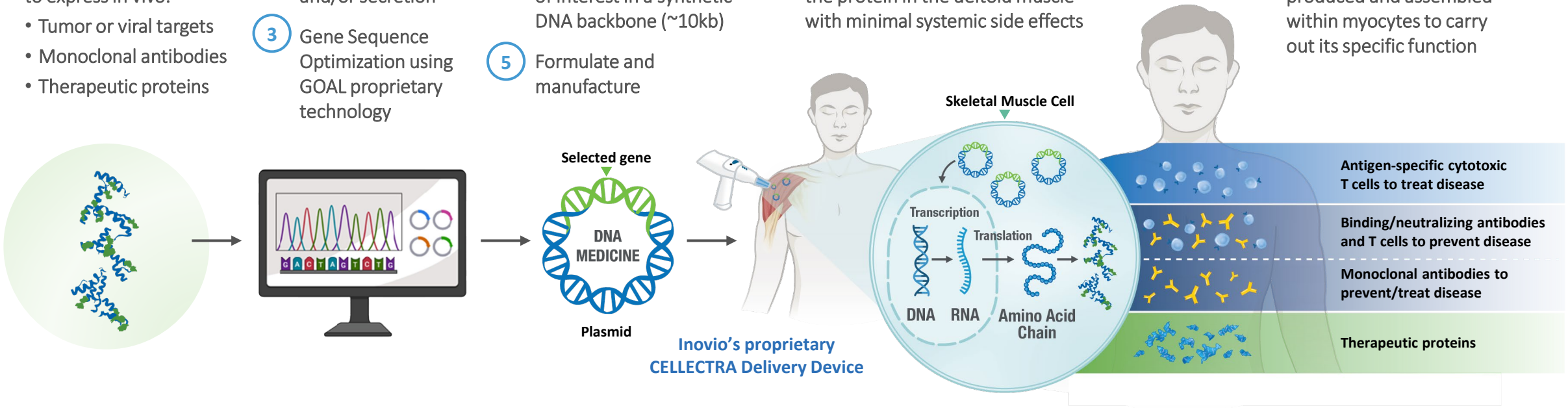
| | | | VGX-3100 **<br>Cervical Dysplasia (HSIL) | |
|---|---|---|---|---|

HPV-RELATED DISEASES  IMMUNO-ONCOLOGY  INFECTIOUS DISEASES  VARIOUS DISEASE TARGETS

*Rolling submission of BLA completed in October 2025, seeking accelerated approval from FDA ** VGX-3100 to Apollo Bio for China

# Customized *In Vivo*-Generated Proteins, Long-Lasting Systemic Therapeutic Benefits

1. Determine and select the protein of interest to express in vivo:
   - Tumor or viral targets
   - Monoclonal antibodies
   - Therapeutic proteins
2. Bioengineering for in vivo expression and/or secretion
3. Gene Sequence Optimization using GOAL proprietary technology
4. Insert sequence for each selected protein of interest in a synthetic DNA backbone (~10kb)
5. Formulate and manufacture
6. DNA is administered via CELLECTRA device to enable local expression of the genes coding for the protein in the deltoid muscle with minimal systemic side effects
7. The protein encoded by the DNA plasmid is produced and assembled within myocytes to carry out its specific function




## 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

# DNA Medicine Platform

CELLECTRA Delivery enhances
uptake of DNA medicine

INOVIO

# CELLECTRA® Delivery Device Enhances Uptake of DNA Medicine

**CELLECTRA 5PSP**


## Track record of success in the clinic:

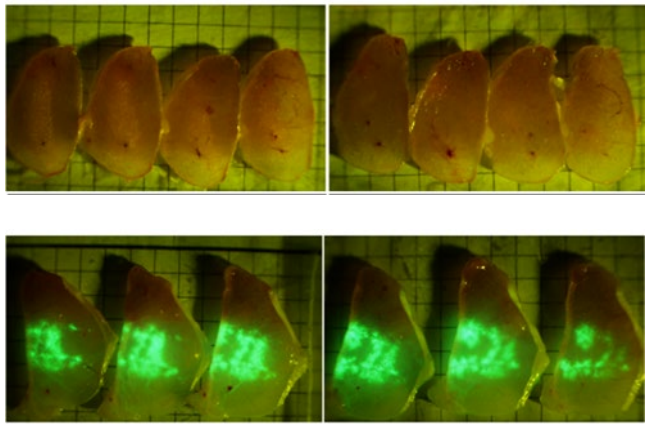
- Nearly 6,000 subjects & 19,000 doses given by both investigational/ commercial-ready CELLECTRA devices
- 2 generations: CELLECTRA 2000, followed by CELLECTRA 5PSP developed to support commercial launch
- 2000 & 5PSP are CE Marked in the EU
- Regulatory authorizations for clinical trials conducted in 36 countries across 6 continents (N.S. America, Europe, Africa, Asia, Australia)
- Temporary discomfort associated with administration followed by highly tolerable safety profile

# INOVIO's Proprietary Platform Technology Permits Enhanced Gene Delivery

**GFP gene expression in rabbit muscle**

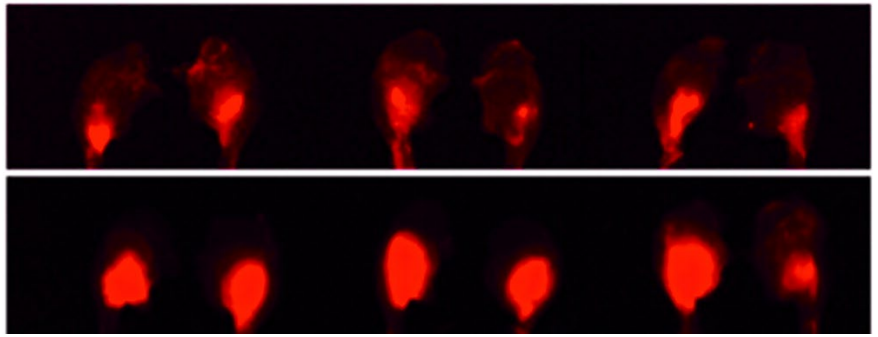
No - EP

With EP



*Sardesai & Weiner Curr Opin Immunol. 2011*

**RFP gene expression in mouse muscle**



EP + PBS formulation

EP + enhanced formulation

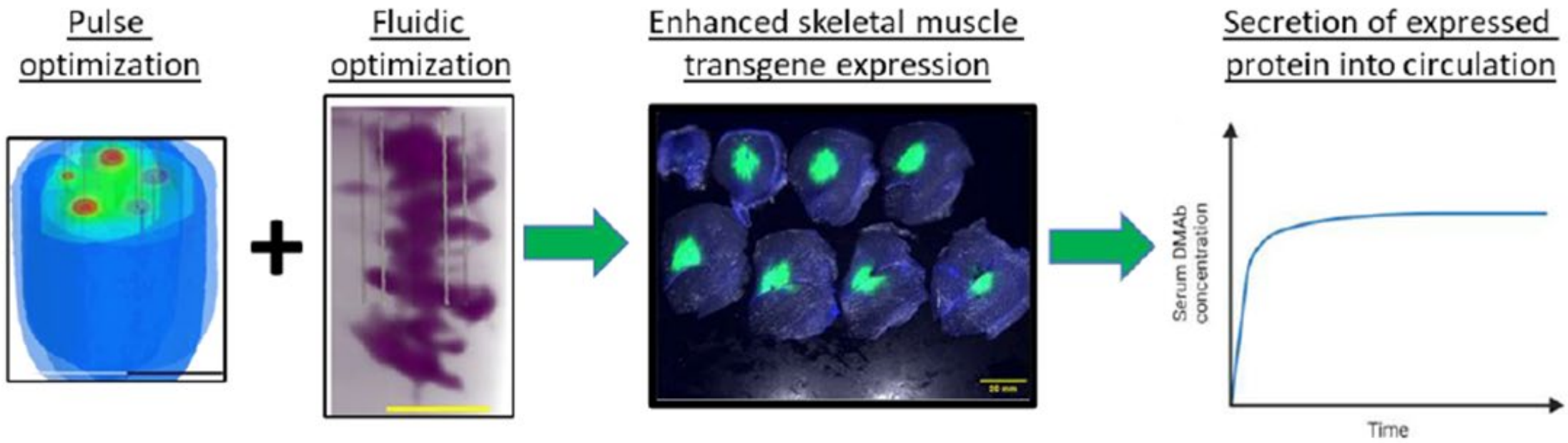
*Schommer et al. Hum Gene Ther. 2019*


+


=

**Increased gene expression levels > 1,000 fold**

# Further Pulse and Fluidic Optimization Leading to Enhanced Expression




The EP electrical field parameters and injected fluid distribution have been optimized to align to permit enhanced transgene expression in the muscle (shown as GFP reporter gene expression in NZW rabbit muscle)

# Utilization of Enhanced Delivery Technology to Develop a DMAb as a Medical Countermeasure

*Human Clinical Data – Proof of Concept*

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# Phase 1 Proof-of-Concept Trial Evaluating DMAbs for COVID-19

- Dose escalation study to evaluate the safety, tolerability and pharmacokinetic profile of mAb AZD5396 and mAb AZD8076 following EP delivery of optimized pDNA AZD5396 and pDNA AZD8076
- Healthy Volunteer Study
- Supported by the Joint Program Executive Office (JPEO) in collaboration with the Defense Health Agency (DHA)
- *Published in Nature Medicine, Tebas et al 2025*

# SARS-CoV-2-DMAB01 Clinical Study Design

- Phase 1 open-label, single-center, dose escalation study focusing on safety and PK
  - Design allows for exploration of dose response; multiple doses & examines durability
  - Funded by DARPA, DoD
- MAbs COV2-2130 (2130) and COV2-2196 (2196), the precursors of AZ's EVUSHELD (AZD7442) were selected to be designed as DMAbs, AZD5396 and AZD8076
  - The MAbs neutralize non-overlapping epitopes on the viral spike receptor binding domain
- Recombinant human hyaluronidase (Hylenex®) is used when dose is prepared to increase plasmid transfection efficiency & plasmid administered with side-port needle & unique EP parameters

| Cohort | n | Dose Each dMAb AZD5396 and AZD8076 | Doses per dMAb | Dose Schedule (Day, D) | Total Dose per dMAb | Total Combined Dose dMAbs |
|---|---|---|---|---|---|---|
| A1 | 4 | 0.5 mg | 1 | D0 | 0.5 mg | **1 mg** |
| A2 | 3 | 1 mg | 1 | D0 | 1 mg | **2 mg** |
| B | 6 | 0.5 mg | 2 | D0, D3 | 1 mg | **2 mg** |
| C | 6 | 1 mg | 2 | D0, D3 | 2 mg | **4 mg** |
| D | 5 | 0.25 mg | 2 | D0, D3 | 0.5 mg | **1 mg** |
| E | 5 | 2 mg | 2 | D0, D3 | 4 mg | **8 mg** |
| F | 5 | 0.5 mg | 2 | D0, D3 | 1 mg | **2 mg** |
| G | 5 | 0.5 mg | 4 | D0, D3 D28, D31 | 2 mg | **4 mg** |

Source: Protocol for dMAb-AZD5396 and dMAb-AZD8076. Version 6.7; IB for dMAb-AZD5396 and dMAb-AZD8076. Version 6.1

# Treatment Administration is Well Tolerated

## Number of Subjects with Elicited Local Reactions by Maximum Severity Grade Per Person in the First 7 Days After Last Dose

| | None | Mild | Moderate | Severe | Total |
|---|---|---|---|---|---|
| Pain | 2 | 27 | 15 | 0 | **44** |
| Pruritis | 40 | 4 | 0 | 0 | **44** |
| Erythema | 25 | 16 | 3 | 0 | **44** |
| Swelling | 40 | 3 | 1 | 0 | **44** |
| Scab | 4 | 40 | 0 | 0 | **44** |
| Infection | 44 | 0 | 0 | 0 | **44** |
| Other events | 32 | 7 | 5 | 0 | **44** |

**Other Events:** soreness with movement; muscle soreness; numbness at injection site (left deltoid); hematoma after the electroporation (the swelling was 3.0 cm after 30 min)

# Minimal Systemic Adverse Events Reported

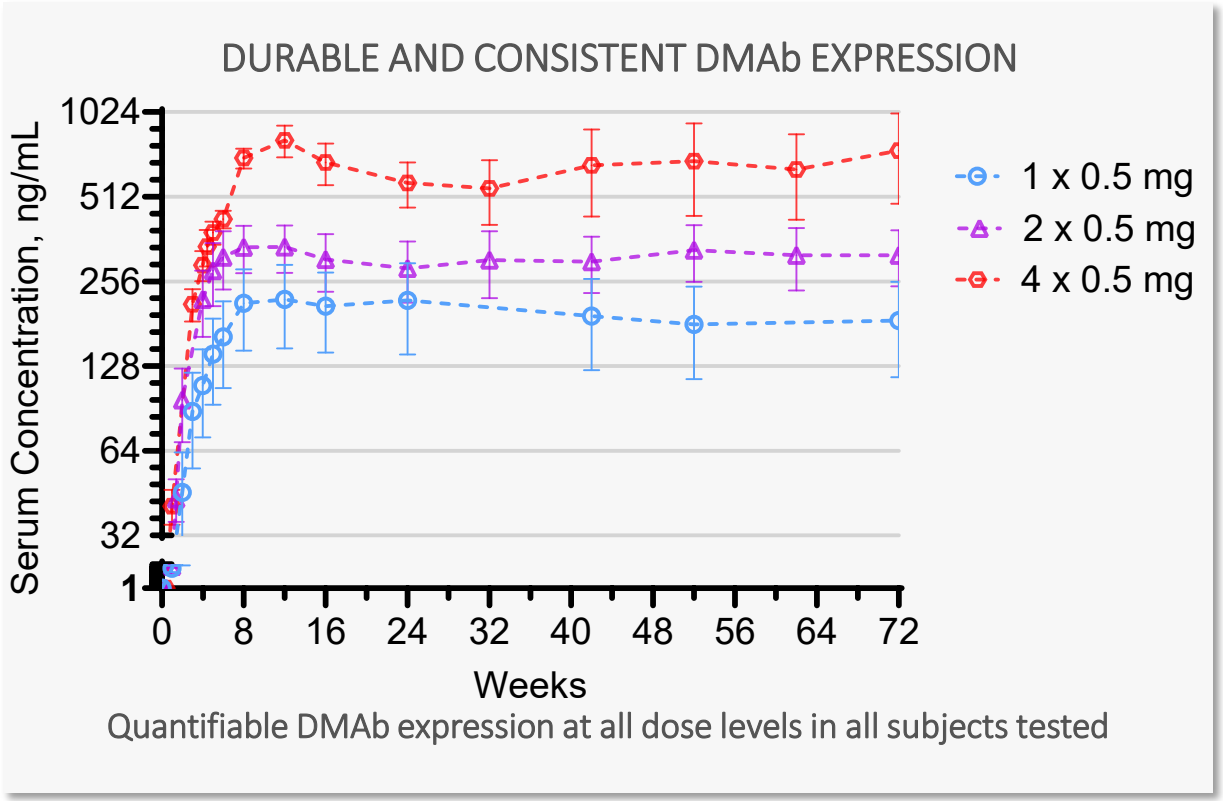
## Elicited Adverse Events for the First 10 Days After Final Dose

| | Subj[a] | Event | Mild | Moderate | Severe | Day 0 | Day 3 | Day 7 | Day 10 |
|---|---|---|---|---|---|---|---|---|---|
| Hypotension | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| Hyperhidrosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Erythema (systemic) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Headache | 3 | 4 | 4 | 0 | 0 | 1 | 2 | 1 | 0 |
| Dizziness | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Myalgia (pain in muscle) | 4 | 4 | 2 | 2 | 0 | 2 | 1 | 0 | 1 |
| Arthralgia (pain in joints) | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Fever | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Peripheral Edema | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other[b] | 2 | 2 | 2 | 0 | 0 | 2 | 0 | 0 | 0 |
| **Total** | **9** | **12** | **10** | **2** | **0** | **5** | **3** | **2** | **2** |

[a]Table columns show the total number (n) of subjects, events, number of events by severity grade, and number of events by observed visit day of reaction.
[b]Nausea during injection; tiredness

# Phase 1 Trial: Key Takeaways From Data

- **Long-lasting in vivo antibody production**: DMAb levels remained stable for 72 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 and neutralized, confirming functional activity through week 72
- **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



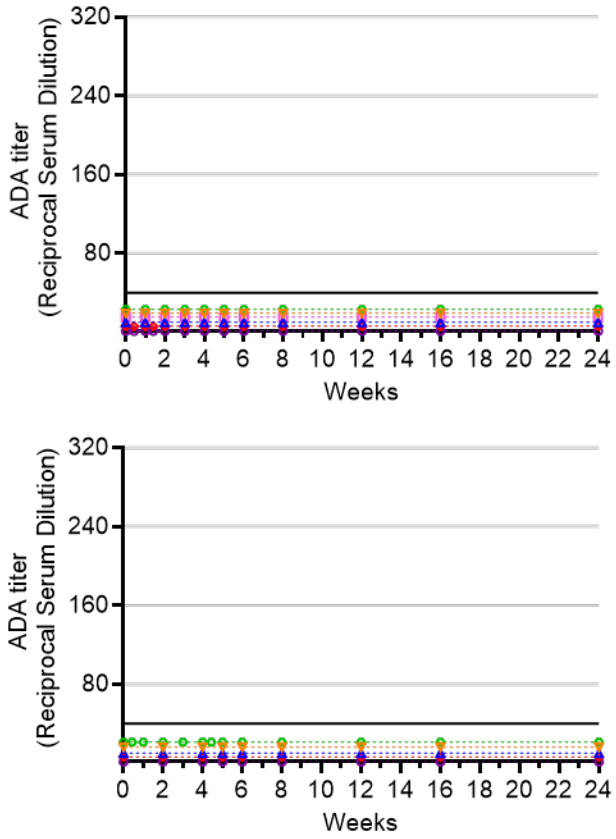
# No Anti-drug Antibodies (ADA) Detected

No ADAs were detected in against the expressed DMAbs, AZD5396 or AZD8076 in any of the 39 participants

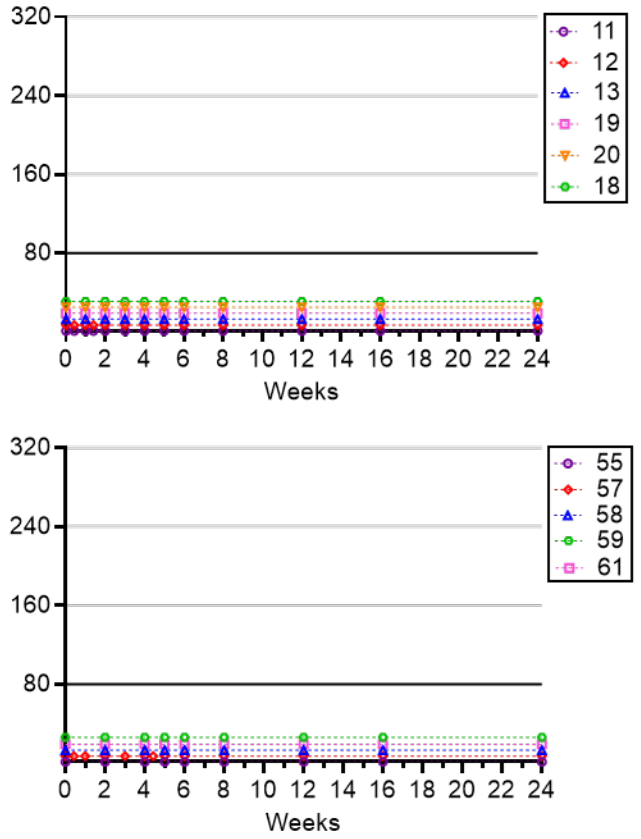
**Cohort B: 2 x 0.5 mg**

**Redosing**
**Cohort G: 4 x 0.5 mg**

**AZD5396 ADA**




**AZD8076 ADA**







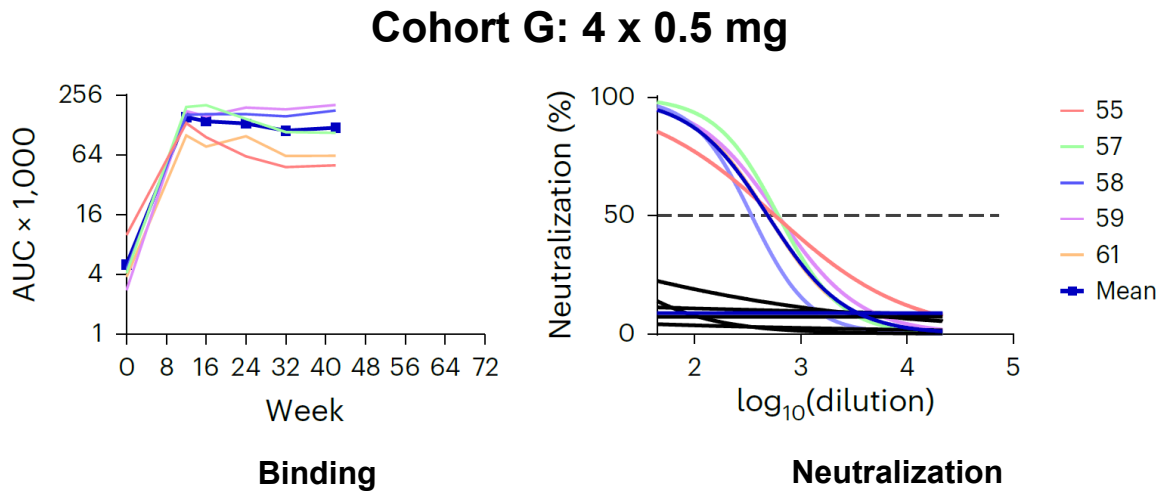



*Tebas P et al. Nat Med. 2025*

# mAbs Isolated for Human Serum Displayed Functionality

DMAbs isolated from participants serum displayed antigen binding and neutralization activity

- Isolated DMAbs bound to SARS-CoV-2 Spike RBD antigen
- Isolated DMAbs neutralized SARS-CoV-2 pseudoviruses at potency values matching the Evushield parental mAbs




*Tebas P et al. Nat Med. 2025*

# DMAb/DPROT™ Technology Has Potential as a New Treatment Paradigm in Rare Disease

- Platform has demonstrated ability for long-term protein secretion
  - Clinical PoC published in Nature Medicine[1]
- Safety data supports its future tolerability profile
- Highly differentiated from existing platforms
  - Ability to re-dose will enable clinical titration
- Development timeline from concept to first in human ~ 2 years
  - Pre-clinical package largely draws on platform applicable data
- Based on existing POC data, platform may be suitable for the treatment of many rare diseases & other therapeutic indications are under developments

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.

# Advancing DPROT Pre-clinical Candidates

- Hemophilia A

# Hemophilia A Overview

## Diagnosis

- Inherited X-linked recessive bleeding disorder due to deficiency of **Factor VIII** (FVIII)
- 'Mild', 'moderate', or 'severe' based on FVIII in blood (as % of normal)

## Epidemiology and disease impact

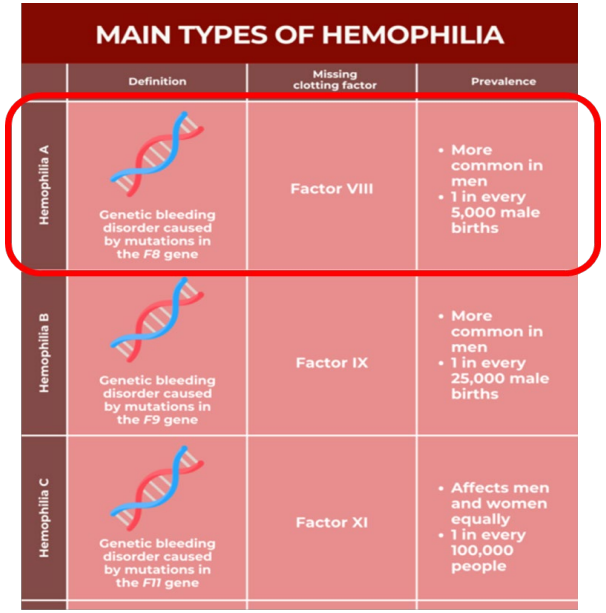
- **~66,000 patients** with hemophilia A in the eight major markets (2024)
- Nearly **46% diagnosed with severe hemophilia**
  - Associated with life threatening spontaneous bleeding into joints after minor trauma; bleeding can occur in various anatomical sites

## Disease management of severe hemophilia

- The overarching goal is to prevent and control bleeding episodes, prevent joint damage, and improve the quality of life for patients

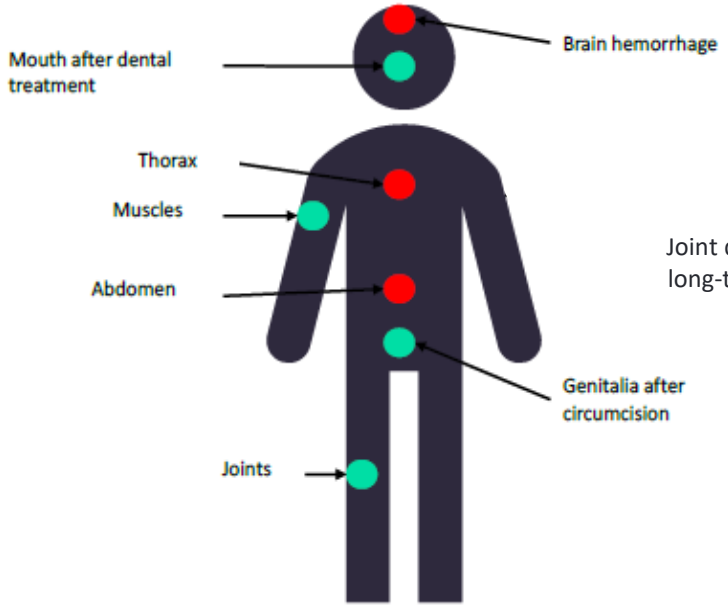
## Treatment options for severe hemophilia

- Clotting Factors Concentrates (CFC): rFVIII products
- Non-Factor Therapy: Emicizumab, (HEMLIBRA®, Roche)
- Gene therapy: Valoctocogene, ROCTOVIAN® (approved June 2023)




Bionews

Common Areas of Bleeding




Joint damage exacerbates long-term disease burden

Source: GlobalData; For more detailed epidemiology figures, please visit the "*Hemophilia A and B: Epidemiology Forecast to 2030*" report on the Pharmaceutical Intelligence Center.

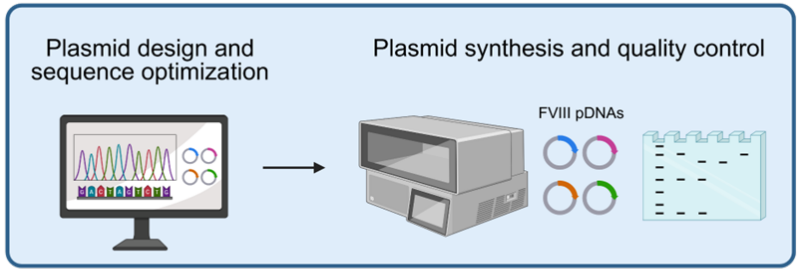
# An Alternative to Viral-based Delivery for Long-Term In Vivo Protein Expression is Still Needed

- Long-term in vivo protein expression remains a sought-after goal for genetic disorders such as Hemophilia
- Significant treatment improvements have been made, but hurdles remain
  - Pre-existing immunity against viral-based vectors
  - Generation of anti-viral vector immunity after in vivo delivery preventing re-dosing
  - Waning protein expression over time which requires re-dosing
  - Safety and tolerability
- Historically non-viral platforms have been hampered by the lack of efficient delivery system
- Inovio's DMAB/DPROT technology could provide potential solutions for those shortcomings

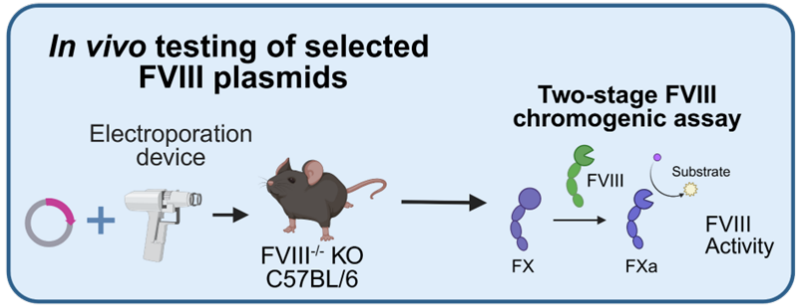
# FVIII DPROT Preclinical Program Overview

Program goal: to identify and characterize a functional FVIII DPROT with enhanced *in vivo* expression and function.

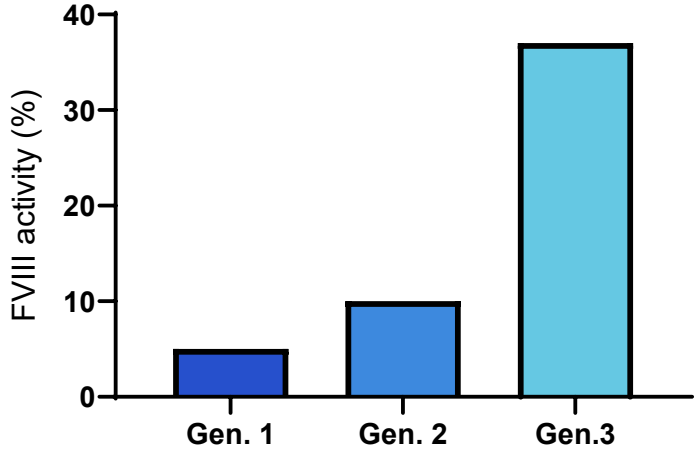
1. Plasmid design & synthesis




2. In vivo screening



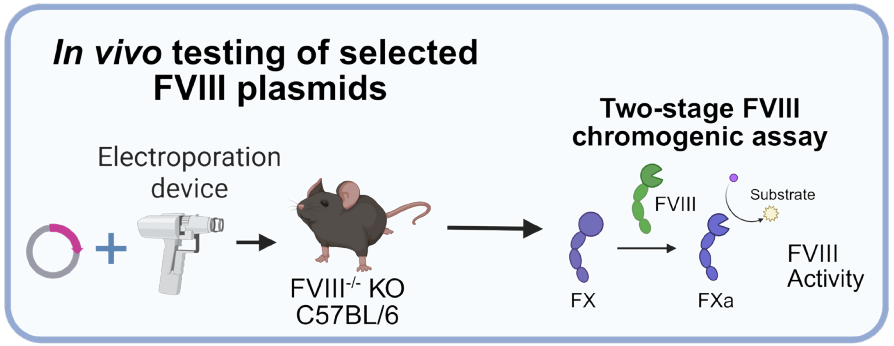

Iterative FVIII design process



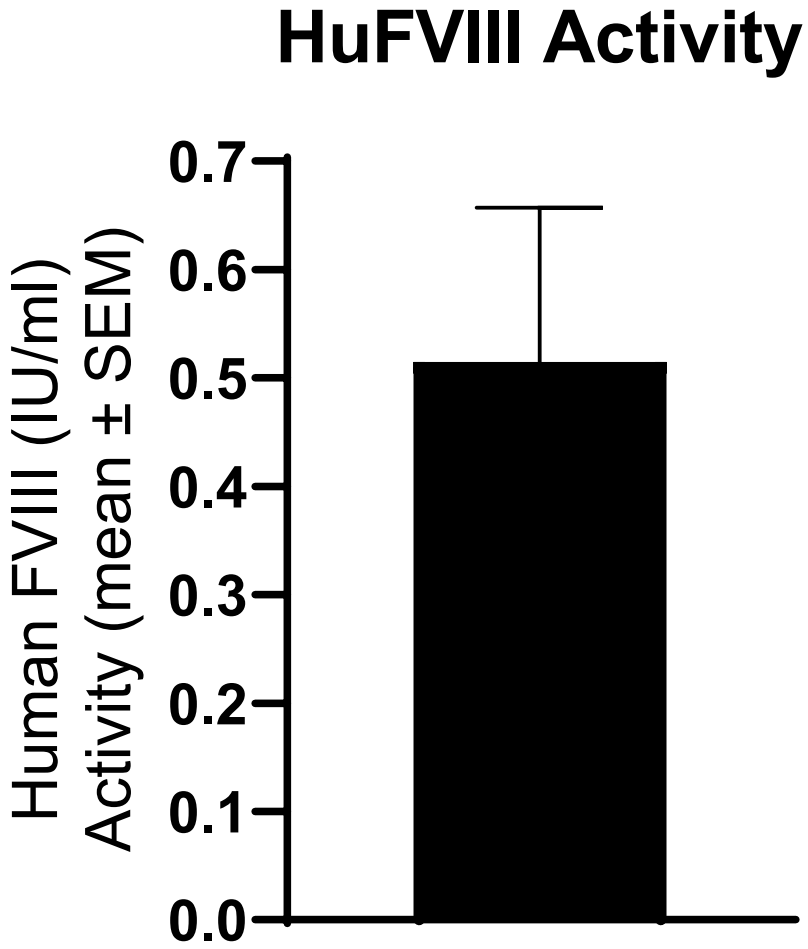

Subsequent rational design iterations produced FVIII constructs with increased levels of activity

Through rational design a candidate DPROT construct, pGX9436 was selected for further development

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

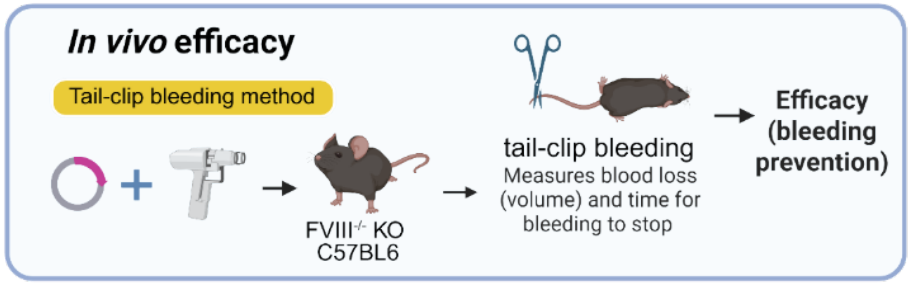


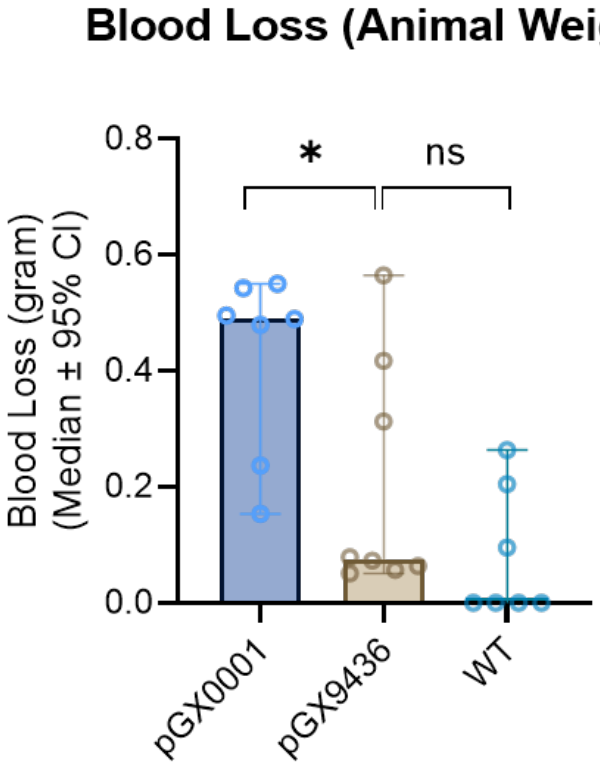

- Demonstrates ectopic expression of huFVIII can be achieved in skeletal muscle cells: activity reaching 50%
- Confirms complex proteins such as huFVIII can be effectively produced and assembled in myocytes

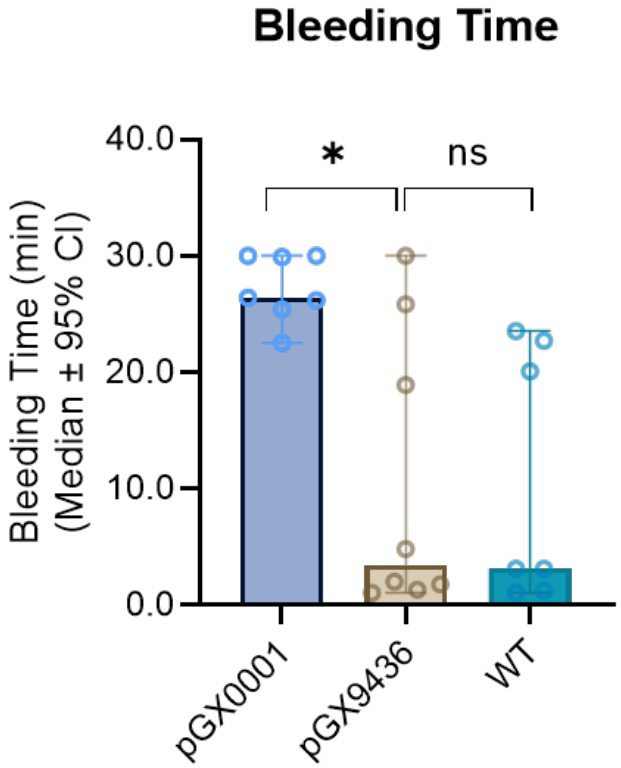


# Inovio DPROT Approach for Hemophilia A: Phenotypic Correction of Bleeding in FVIII KO Mice

Mouse tail clip model




- *pDNA-treated FVIII knockout mice showed significantly reduced bleeding time and blood loss compared to control (pGX0001-treated) knockout mice.*
- *Bleeding control in pDNA-treated knockout mice was comparable to that observed in wild-type mice.*

# DMAb/DPROT™ Technology Has Potential as a New Treatment Paradigm for Hem A and Other Rare Diseases

- Platform allows for rapid design, production and testing of new candidates
- Facility infrastructure and team background expertise has been applied to multiple DPROT targets with rapid preclinical success
- FVIII DPROT displayed functionality in relevant disease models
- Based on existing POC data, platform may be suitable for the treatment of many rare diseases & other therapeutic indications are under developments
  - Seeking partnerships to accelerate Hemophilia A and other non-disclosed programs

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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