Novel FVIII Secretion Via Non-Viral Vector DNA Medicine Platform

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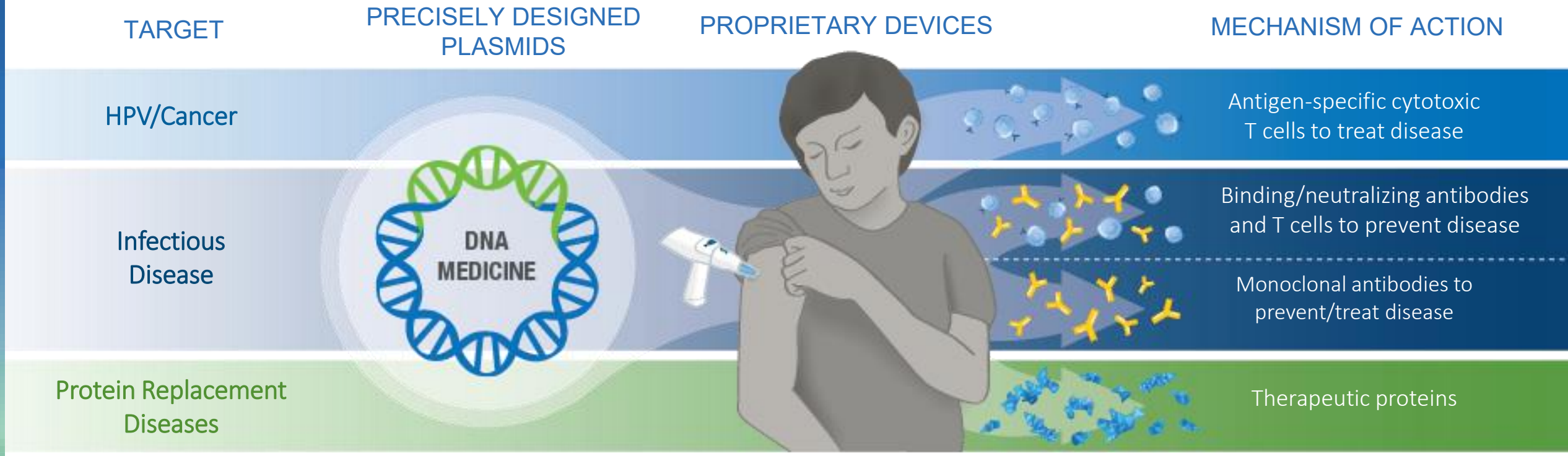
INOVIO's DNA Medicines Platform



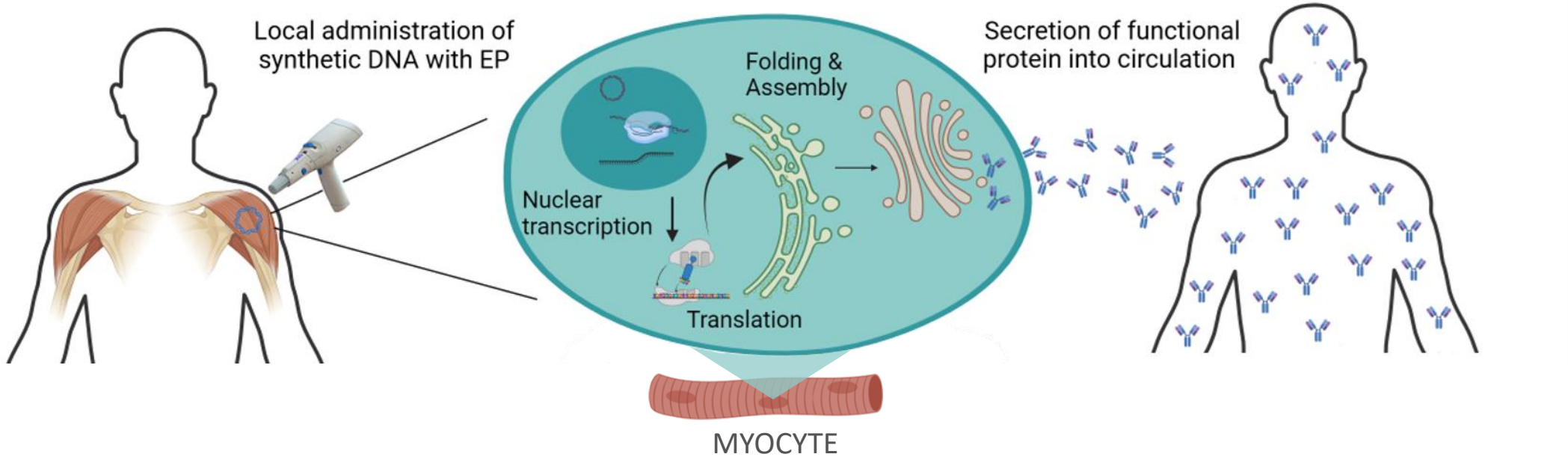
In Vivo Protein Production:

Teaching the body to make its own disease-fighting tools

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 solution for those shortcomings

The Next Generation of DNA Medicine



DMAb/DPROT technology enables in vivo production of proteins (e.g. mAbs or FVIII)

- DNA is administered via CELLECTRA device to enable local expression of the genes coding for the proteins in the deltoid muscle.
- DMAbs/DPROTs are expressed and assembled in myocytes and secreted into the blood where they can circulate in the body.

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

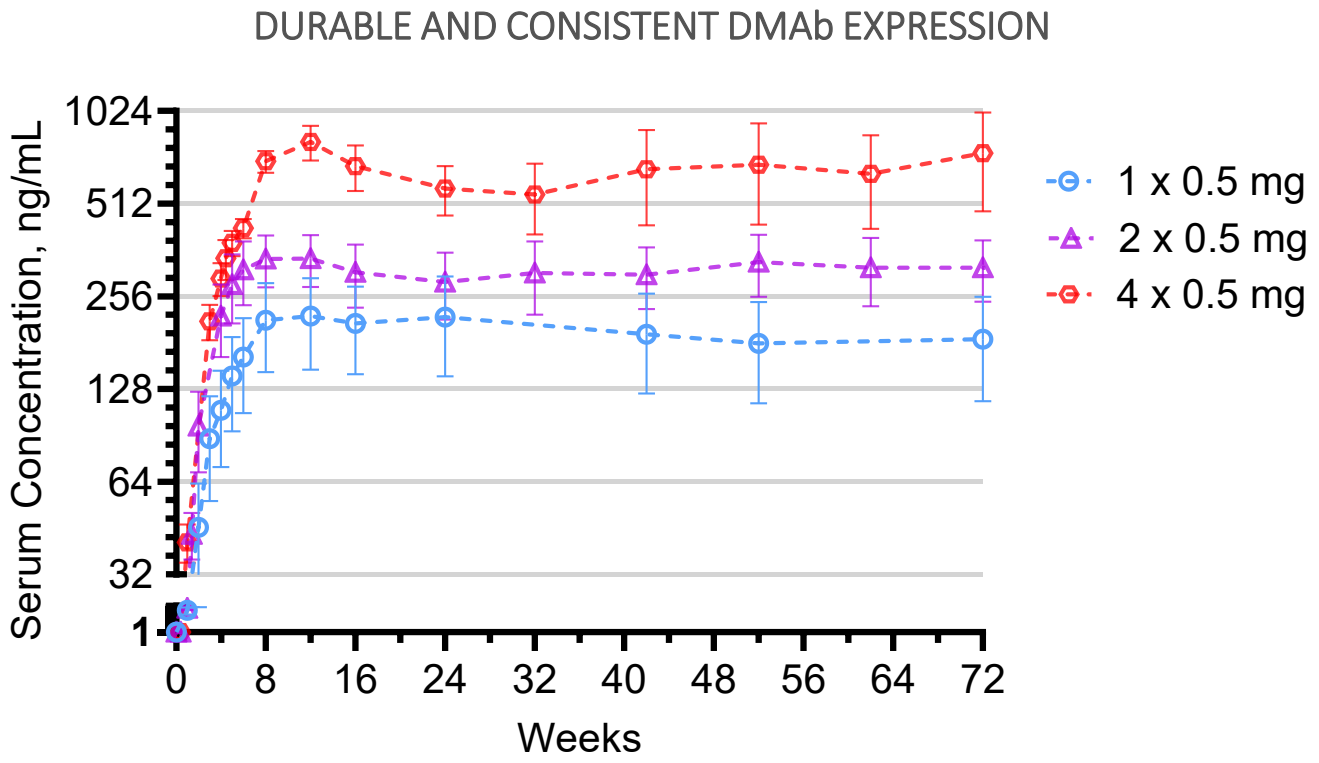
- Dose escalation study to evaluate the safety, tolerability and pharmacokinetic profile of mAb AZD5396 and mAb AZD8076 following EP delivery of optimized DMAb AZD5396 and DMAb AZD8076
- Published in Nature Medicine
- Healthy Volunteer Study, N=44
- Supported by the Joint Program Executive Office (JPEO) in collaboration with the Defense Health Agency (DHA)

INOVIO AstraZeneca Penn University of Pennsylvania THE WISTAR INSTITUTE

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.

Ongoing Phase 1 Trial: Key Takeaways

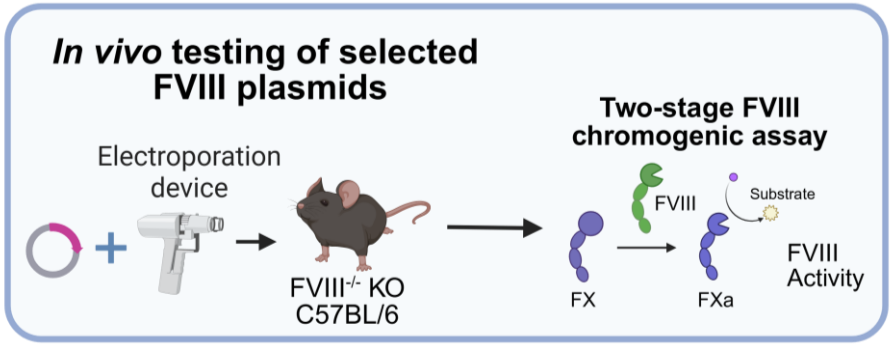
- **Well-tolerated: most common side effects were mild, temporary injection site reactions; no SAEs related to study drug**
- **Long-lasting in vivo antibody production**: DMAb levels remained stable for 72 weeks in all participants reaching that timepoint
- **No anti-drug antibodies (ADA):** no immune rejection of the DMAbs detected across ~1,000 blood samples
- **Effective target binding**: expressed DMAbs successfully bound to SARS-CoV-2 Spike protein receptor-binding domain, 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



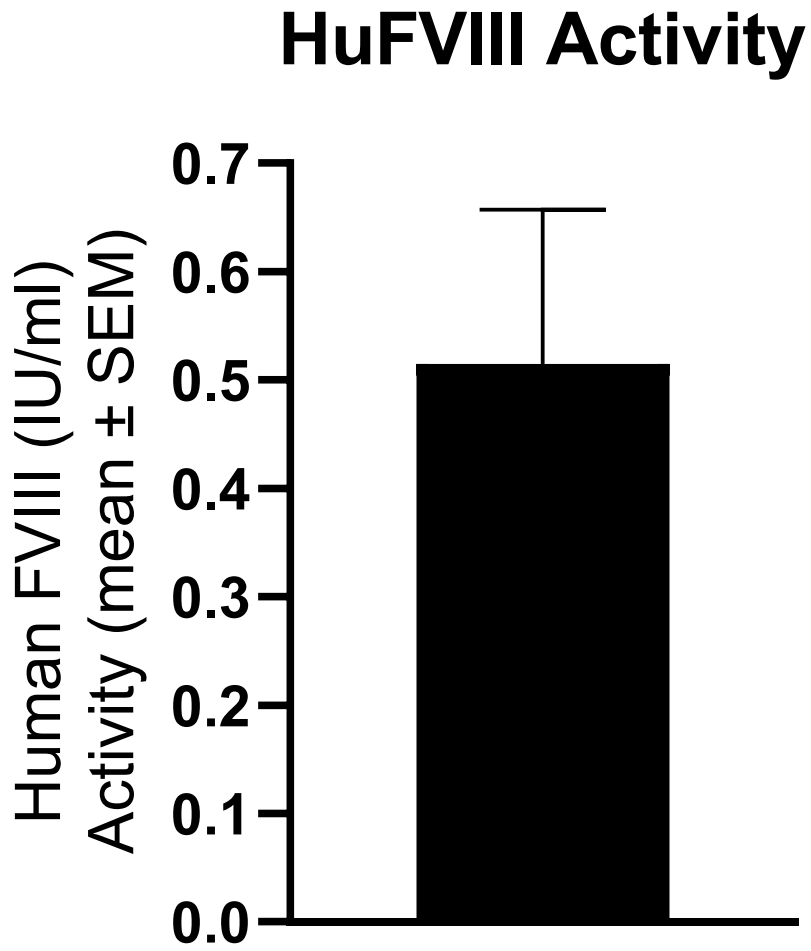
Quantifiable DMAb expression at all dose levels in all subjects tested

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.

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

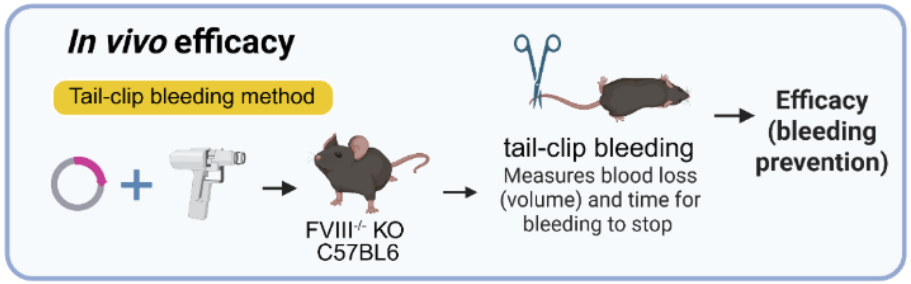


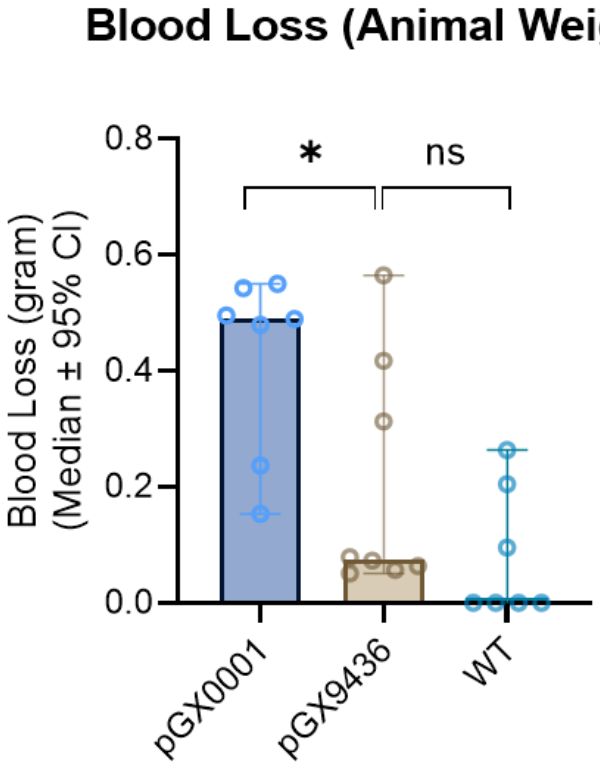
- Demonstrates ectopic expression of huFVIII can be achieved in skeletal muscle cells: activity reaching 50% over baseline
- Confirms complex proteins as huFVIII can be effectively produced and assembled in myocytes

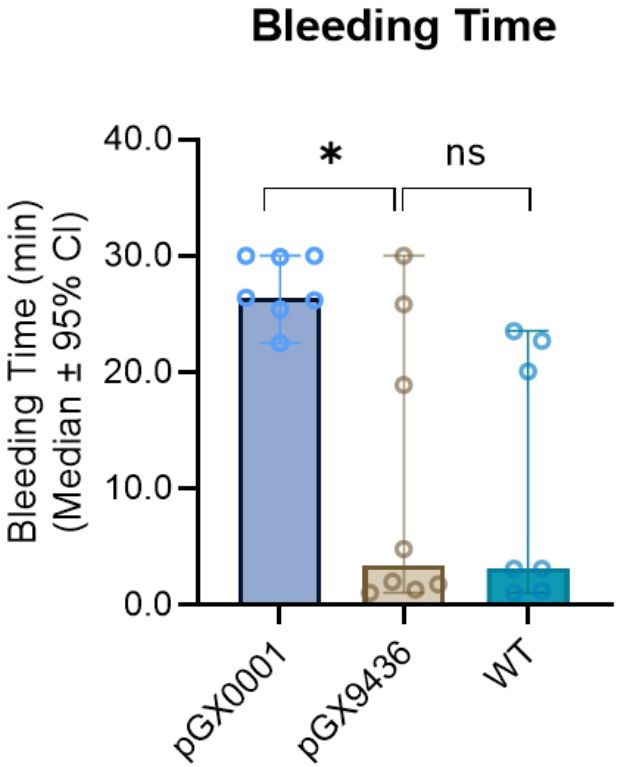


Inovio DPROT Approach for Hemophilia A: Phenotypic Correction of Bleeding in FVIII KO Mice

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 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
- Preparing for Pre-IND meeting with the FDA for the Hemophilia A program
- 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 program development

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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