Generate : Biomedicines

A Flagship Pioneering Company

# AI for drug development & potential applications to dermatology

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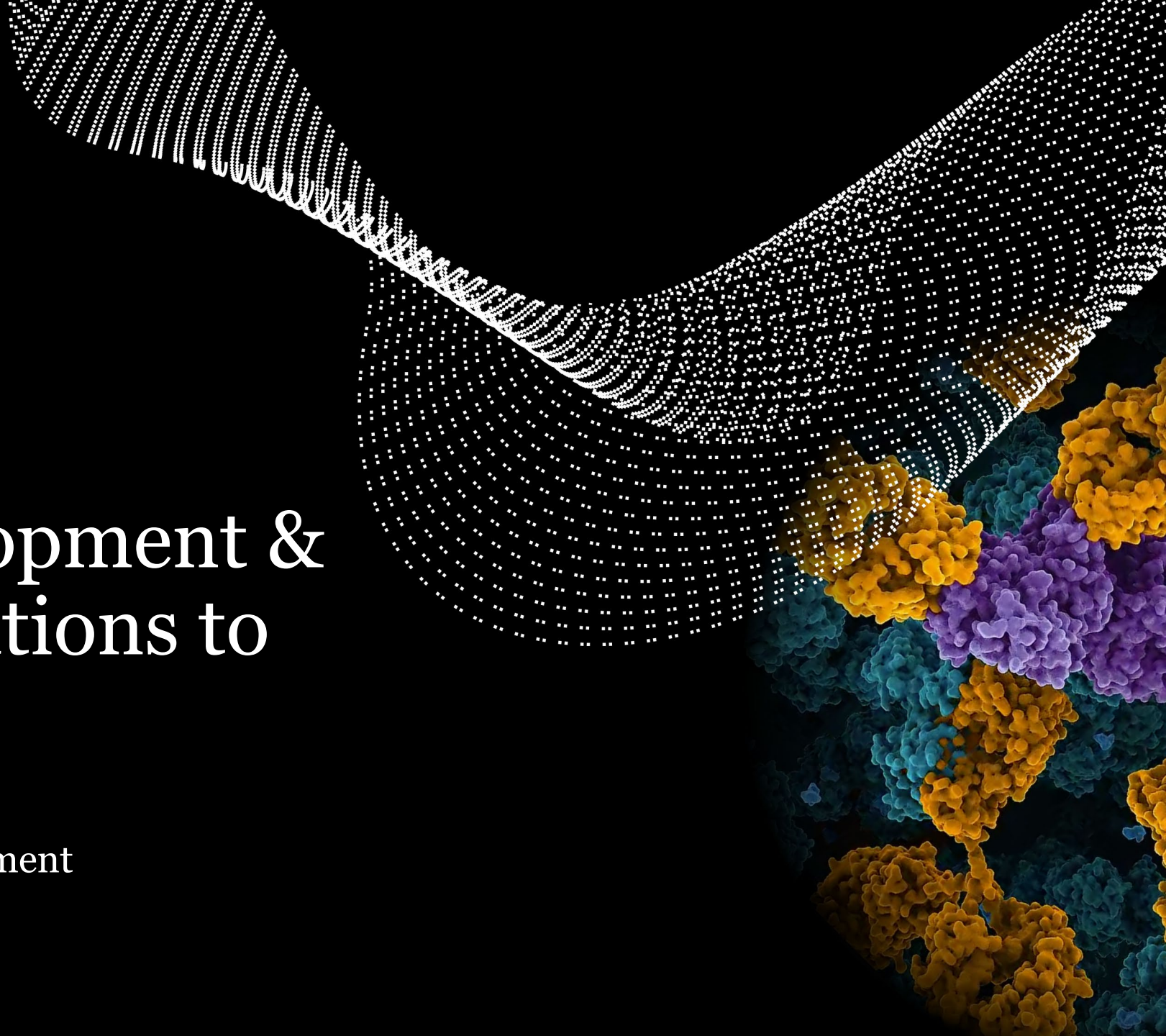
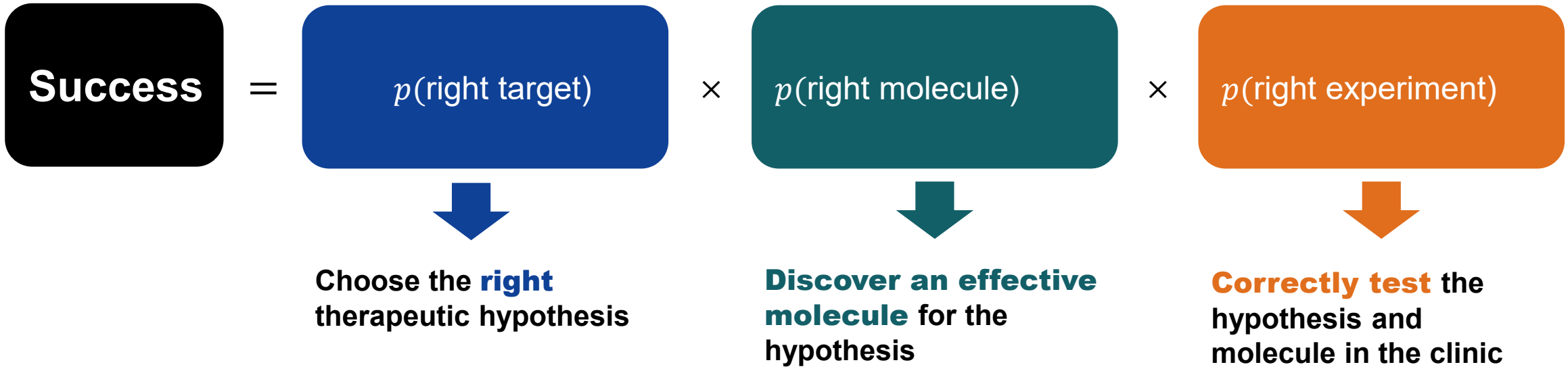


# Topics for Discussion

- What are the roles for AI in drug development?
- Generate's applications of AI to immunology targets
- Potential implications for drug development in Dermatology

# *AI is being applied to each stage of drug development*



# Goal: Address some of the fundamental challenges of drug discovery

**Traditional drug discovery**

From a **laborious, high-cost exploration** that in very rare cases leads to success…

**Generate's drug *generation***

…To a **programmatic, at-scale prosecution** of a therapeutic hypothesis with the right tools

- Ability to bind to anything, generating **molecules that answer a specific molecular question**
- **Modality-agnostic**
- Prosecuting **simultaneous hypotheses**
- **At-scale** with high efficiency
- Ultimately to achieve the **desired therapeutic outcome every time**

# **Lab in the Loop:** end-to-end AI integration of wet- and dry lab data

## CryoEM microscopy

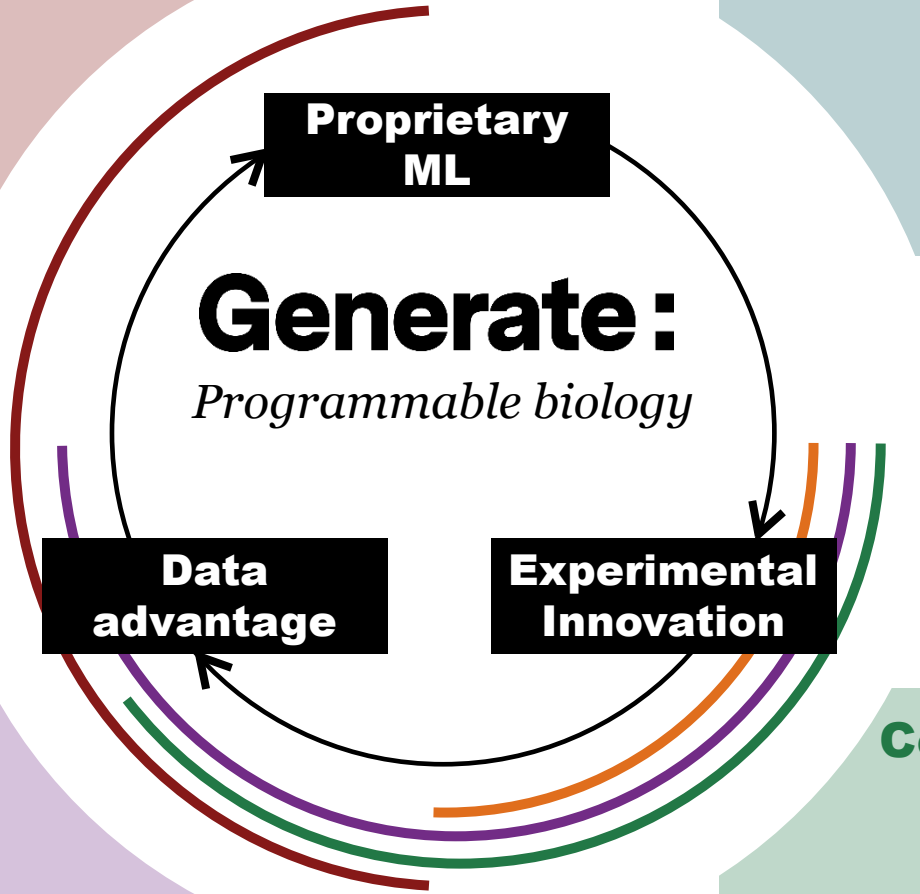
*~20 structures/month, with a goal of increasing significantly*

## Microfluidics screens

*Functional screening and analysis up to 1M mol/min*

## Display screens

*Screening of biophysical properties and analysis up to 300k mol/min*




## Protein design

*Protein design models, including Chroma, developability models*

## Mega-set DNA libraries

*Synthesizing up to 350k therapeutically-relevant complex molecules*

## Cell-free protein expression

*Expressing and purifying up to 200k proteins in 2 days*

# Technology applies the starting point appropriate for the biological and medical challenge under study

## Structure

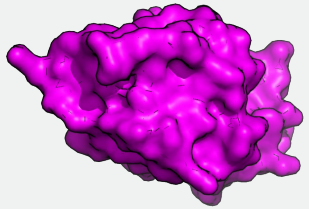
E.g., Known antibody-antigen structure

## Partial Structure

E.g., Known antibody-homolog structure

## *No Structure (de novo)*

E.g., Known antigen structure



New compositions, optimization

Generated biologics to any target

# We have *leveraged our Platform* to create a **robust, clinical stage pipeline**

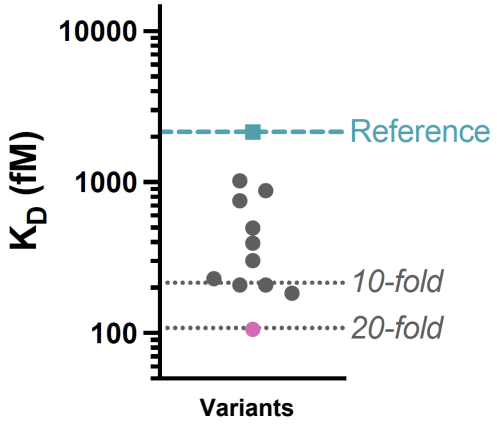
| Program | Lead Indication | Target | Generating | IND-enabling | Phase I | Collaborations |
|---|---|---|---|---|---|---|
| **IMMUNOLOGY** | | | | | | |
| **GB-0895** | Severe Asthma | TSLP | | | | |
| **GB-7624** | Atopic Dermatitis | IL-13 | | | | |
| Coform and bispecific | Severe Asthma | TSLP x IL-13 | | | | |
| mAb | Ulcerative Colitis | TL1A | | | | |
| mAb | Atopic Dermatitis | OX40L | | | | |
| Bispecific | Ulcerative Colitis | TL1A x IL-23 | | | | |
| Mono & combo incl. bsAb | | Various | | | | |
| **IMMUNO-ONCOLOGY** | | | | | | |
| Armored CAR-T | Advanced Solid Tumors | Undisclosed | | | | ROSWELL PARK 50:50 |
| Bispecific | NSCLC | Undisclosed | | | | MD Anderson Cancer Center 50:50 |
| **ADCs** | | | | | | |
| Protein binder | ADC Toxin Neutralizer | Free MMAE | | | | |
| ADC | Advanced Solid Tumors | Undisclosed | | | | |
| **INFECTIOUS DISEASE** | | | | | | |
| **GB-0669** | Covid-19 | SARS-CoV-2 S2 | | | | |
| mAb | Covid-19 | SARS-CoV-2 RBD cl.IV | | | | |
| **UNDISCLOSED** | | | | | | |
| Amgen | 6 undisclosed programs | | | | | AMGEN |
| Novartis | Multiple undisclosed programs | | | | | NOVARTIS |

# For known targets, antibody optimization is used

**20–40x improvement** in affinity over other molecules while **retaining specificity and drug-like properties**

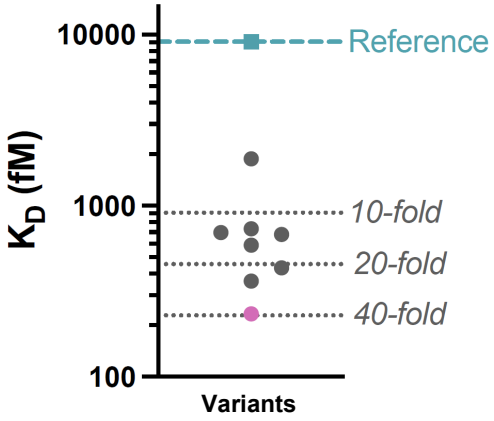
● Select top hits ● Development candidate

## anti-TSLP *mAb*



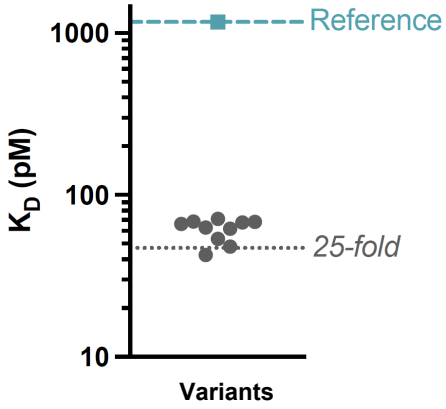

**106 fM**

## anti-IL-13 *mAb*



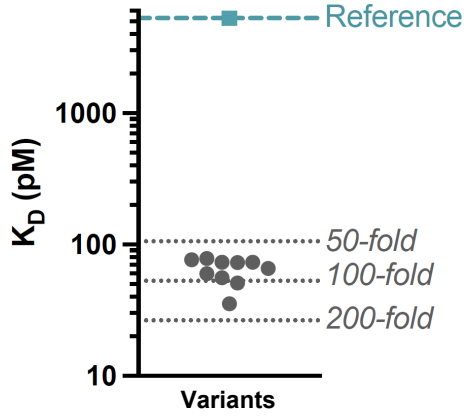

**233 fM**

## anti-OX40L *mAb*




**21.8 pM**

## anti-TL1A *mAb*




**35.3 pM**

- Preliminary ranking based on screening data, measured at 37C.

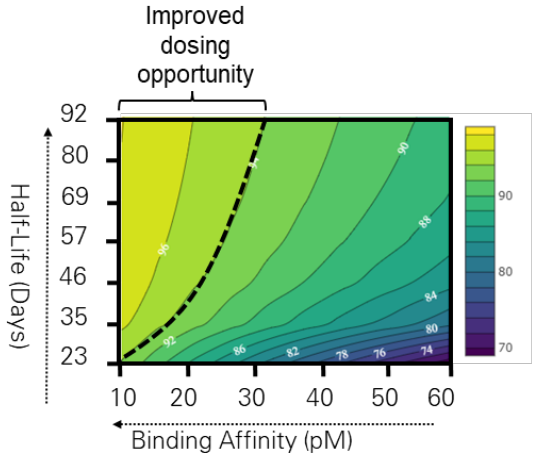
# **GB-0895,** a Phase 1 anti-TSLP mAb for the treatment of **inflammatory diseases**

**High affinity and potency anti-TSLP antibody,** potential to significantly extend dosing regimen

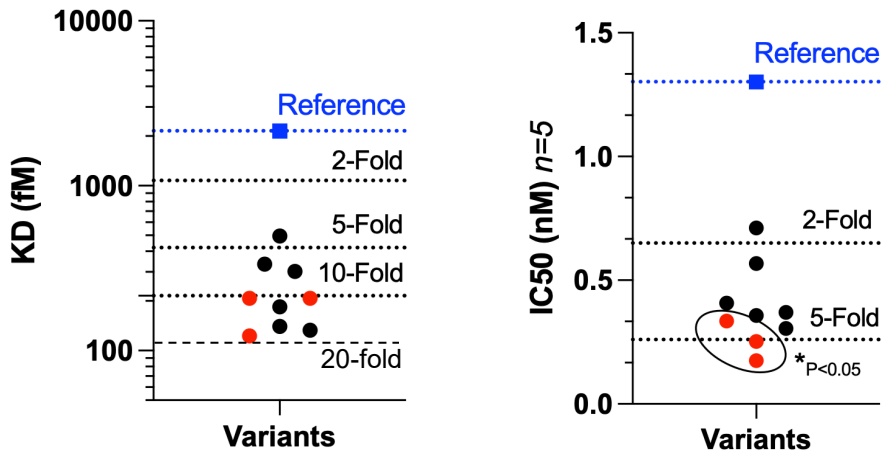
Potential for development in Severe Asthma, Chronic Obstructive Pulmonary Disease, Chronic Rhinosinusitis with Nasal Polyps, Chronic Urticaria, and more

**First patient dosed in December 2023**

## We identified an opportunity for long-acting highly optimized mAbs




## … and generated mAbs with >20-fold improved binding to TSLP and >5-fold improved potency




## Phase 1 Part A

- Single-ascending dose (SAD)
- Patients with Mild to Moderate Asthma
- Subcutaneous administration
- N=60

**Cohort 1** *Accrued*

**Cohort 2** *Accrued*

**Cohort 3** *Accrued*

**Cohort 4** *Accrued*

**Cohorts 5/6** *Accrued*

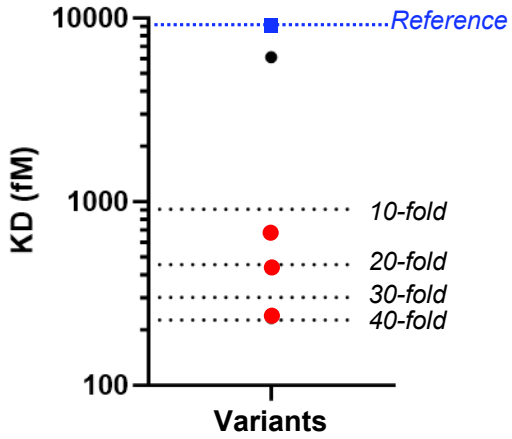
# **GB-7624** is an anti-IL-13 mAb combining **extended half-life with affinity optimization for a best-in-class profile**

**High affinity IL-13 antibody**, potential to significantly extend dosing regimen

Potential for development in Atoptic Dermatitis, and as a combination with TSLP, in severe Asthma and COPD

**Expected to initiate Ph 1 in 1H 2025**

**Generated mAbs with >35-fold improved binding to IL-13, delivering sub-pM affinity**




## Phase 1 Part A

- Single-ascending dose (SAD)
- Healthy volunteers
- Subcutaneous administration
- N=30

**Cohort 1** — *On track for 1H25*

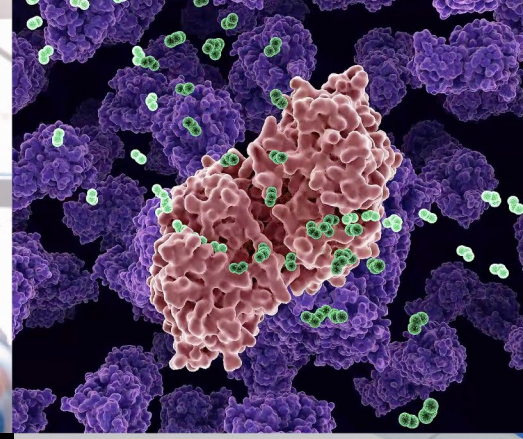
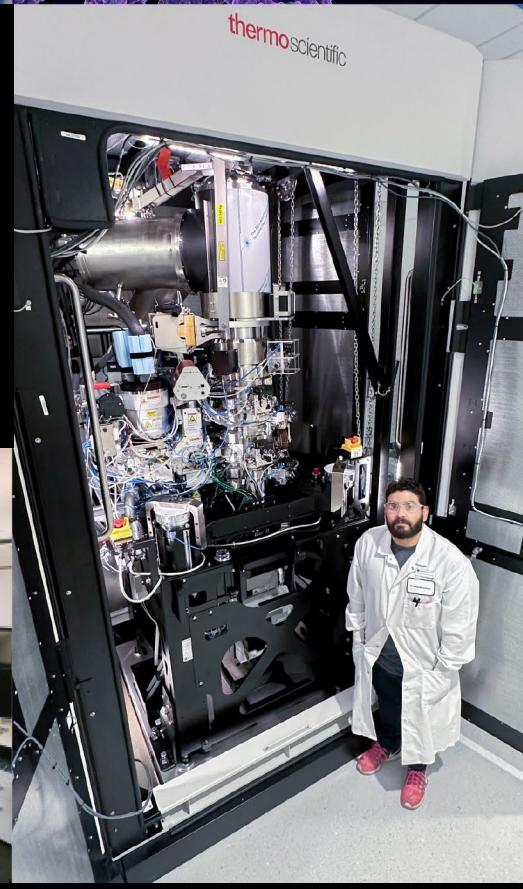
**Cohort 2** — *On track for 1H25*

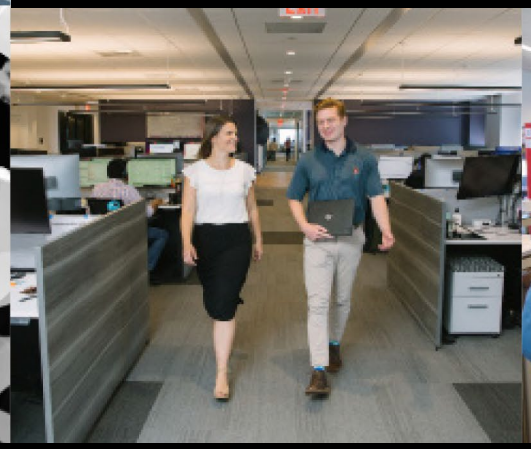
**Cohort 3** — *On track for 2H25*

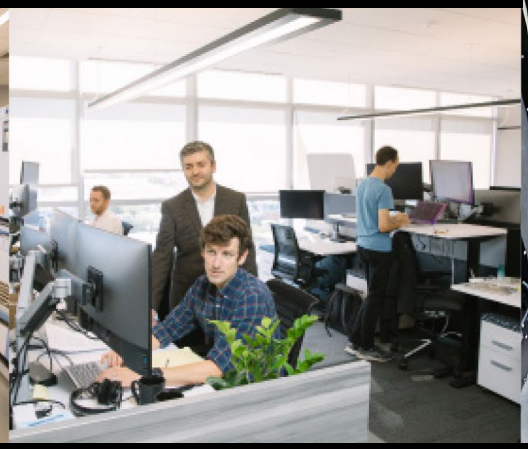
# Potential implications for Dermatology

- Improve patient quality-of-life by developing long-acting agents for targets with an excellent safety profile
- Improve efficacy through combinations and/or bispecifics for patients with difficult-to-treat disease
- Pursue targets that have posed challenges to the field, e.g. those with low immunogenicity or epitopes necessitating exquisite specificity
- Remaining challenges:
  - translatability of preclinical models
  - identification of targets from translational studies
  - patient selection (particularly for monos/combos) and heterogeneity





# Generate: *New Science*