Tas Braithwaite
& Lynn Hassman

On behalf of Pirro Hysi, Felyx Wong, Manik Sharma, Alastair Denniston, Andrew Dick, Becca Edward, Simon Epps, Ed Hughes, Jen Jung, Sharon Kerr, Jess Kraker, Phil Murray, Alan Palestine, Michael Paley, Mina Pantcheva, Amit Reddy, Miles Stanford, Will Tucker, Graham Wallace, Wayne Yokoyama, and the i3eye Genomic Consortium

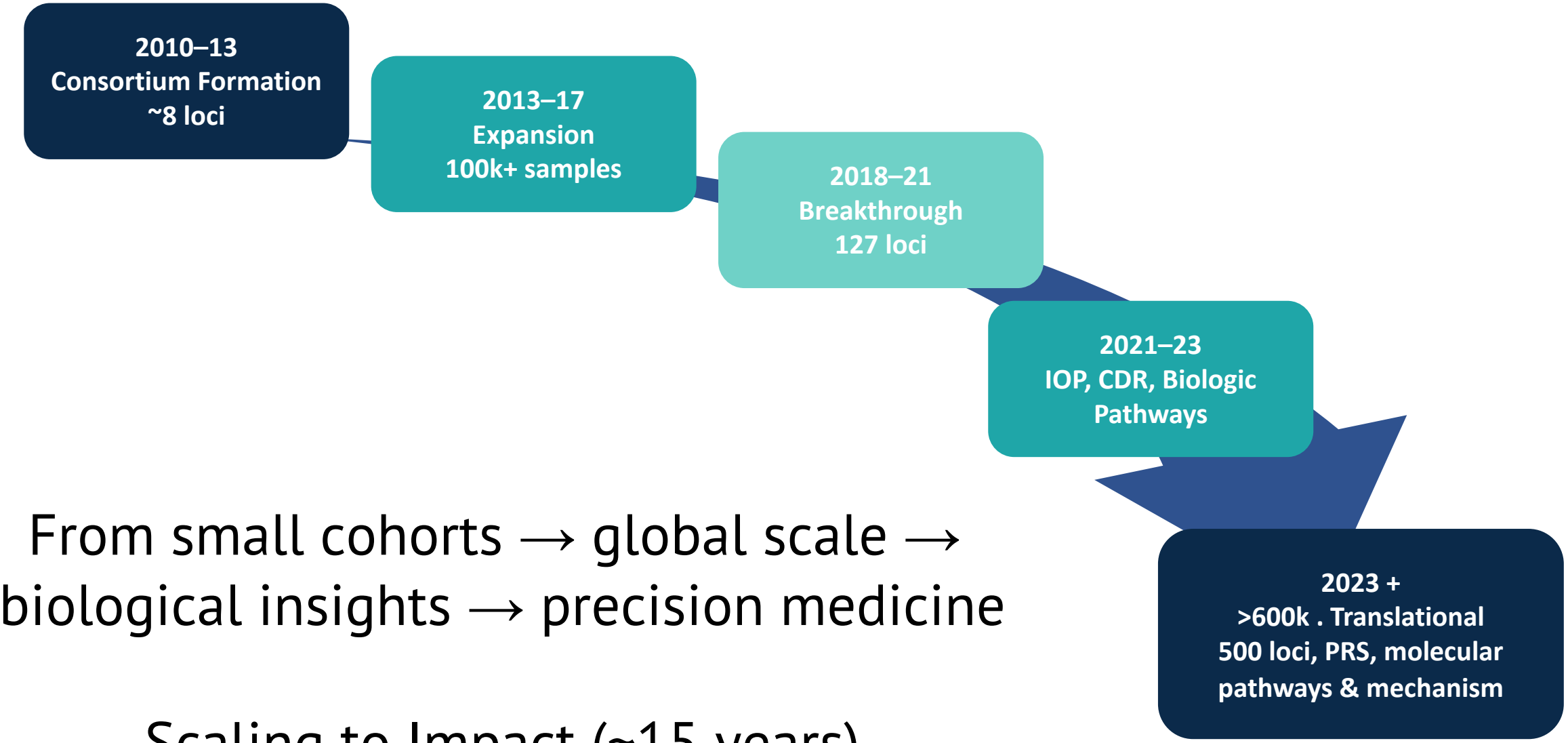
What do we know about uveitis genomics?

- **Kuiper JJ, et al. 2014.** GWAS identifies a functional ERAP2 haplotype associated with birdshot chorioretinopathy.
- **Robinson PC, et al. 2015**. Acute anterior uveitis and ankylosing spondylitis. Similarities and differences.
- **Huang XF, et al. 2020**. GWAS in AAU – new loci.
- **de Groot EL, et al. 2023**. Association of Risk Variants in the CFH Gene With Elevated Levels of Coagulation and Complement Factors in Idiopathic Multifocal Choroiditis.
- **Gelfman S, et al. 2023**. GWAS meta-analysis in anterior uveitis.
- **Koskimaki F, et al. 2025** GWAS in anterior uveitis.

I3eye rationale

- Inflammatory eye diseases are **rare, heterogeneous, and underpowered for genetics**
- Single-centre cohorts → **miss modest-effect variants**
- Biobanks
  - ICD codes lack phenotypic precision
  - Intermediate and posterior uveitis infrequent
- Need **global scale + diversity** to:
  - Detect genetic risk
  - Understand shared immune pathways (e.g. MS, sarcoidosis)
  - Enable **precision medicine and trial stratification**

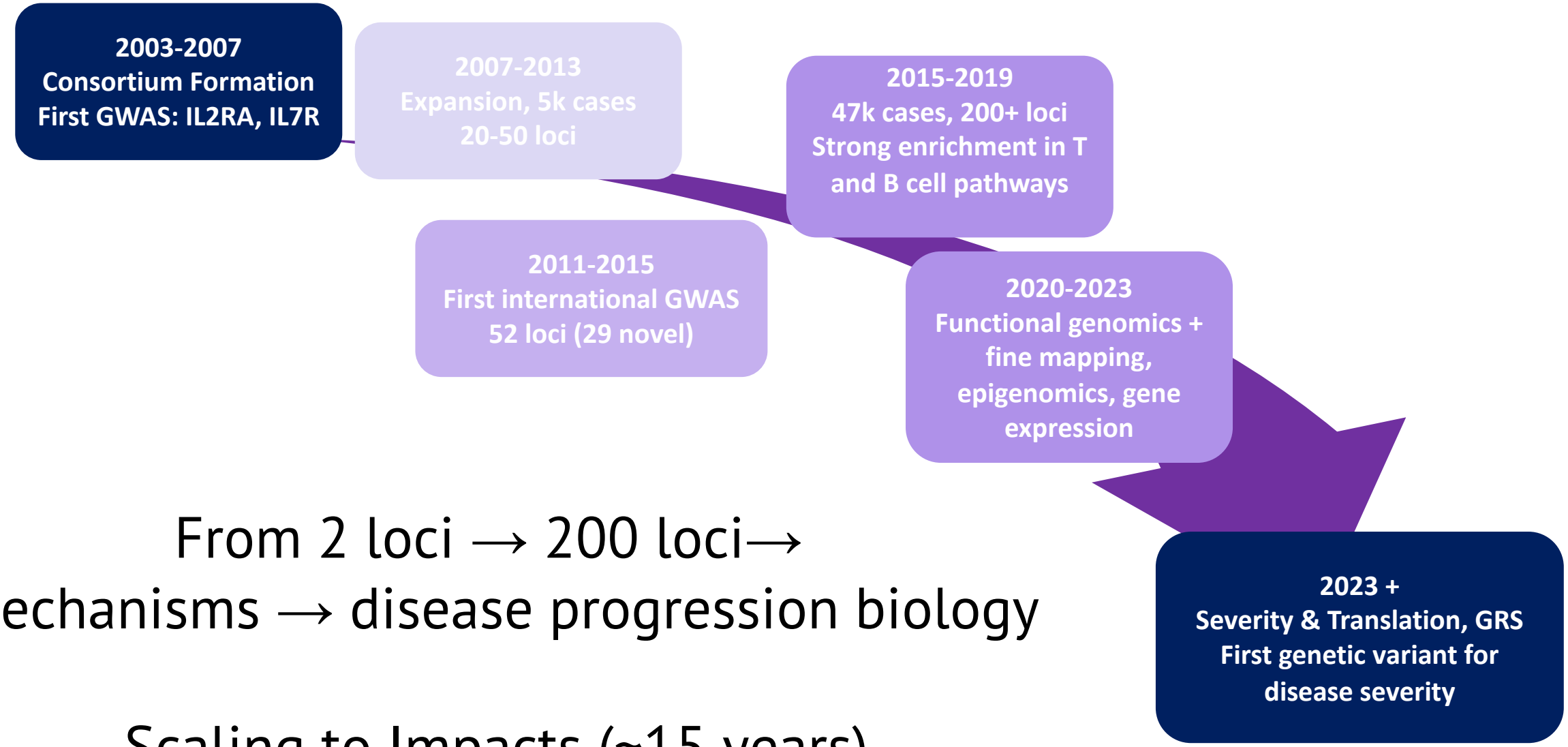
International Glaucoma Genetics Consortium



From small cohorts → global scale → biological insights → precision medicine

Scaling to Impact (~15 years)

International MS Genetics Consortium



From 2 loci → 200 loci→
mechanisms → disease progression biology

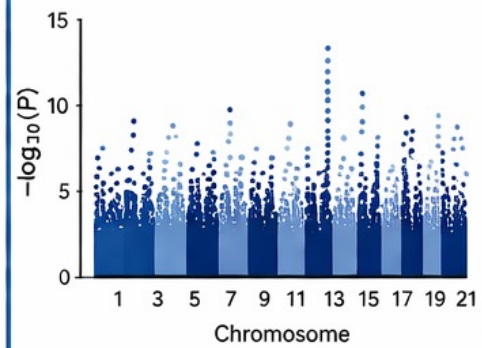
Scaling to Impacts (~15 years)

THE 4 PILLARS OF SUCCESS

Lessons from Global Genomics Consortia

1. SCALE

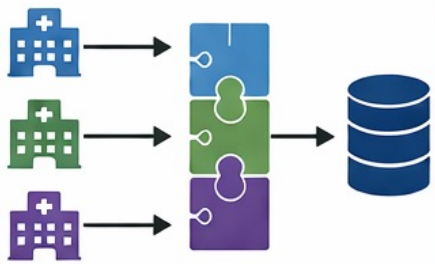
Large sample sizes are essential for discovery and replication.



More data → More power → More discoveries

2. HARMONISATION

Consistent phenotyping, data standards and analytical approaches enable meaningful meta-analysis.



Different sites, one standard, shared data, stronger results

3. DIVERSITY

Including diverse ancestries and populations improves generalizability and reveals novel biology.

Representation matters – for discovery, equity and impact

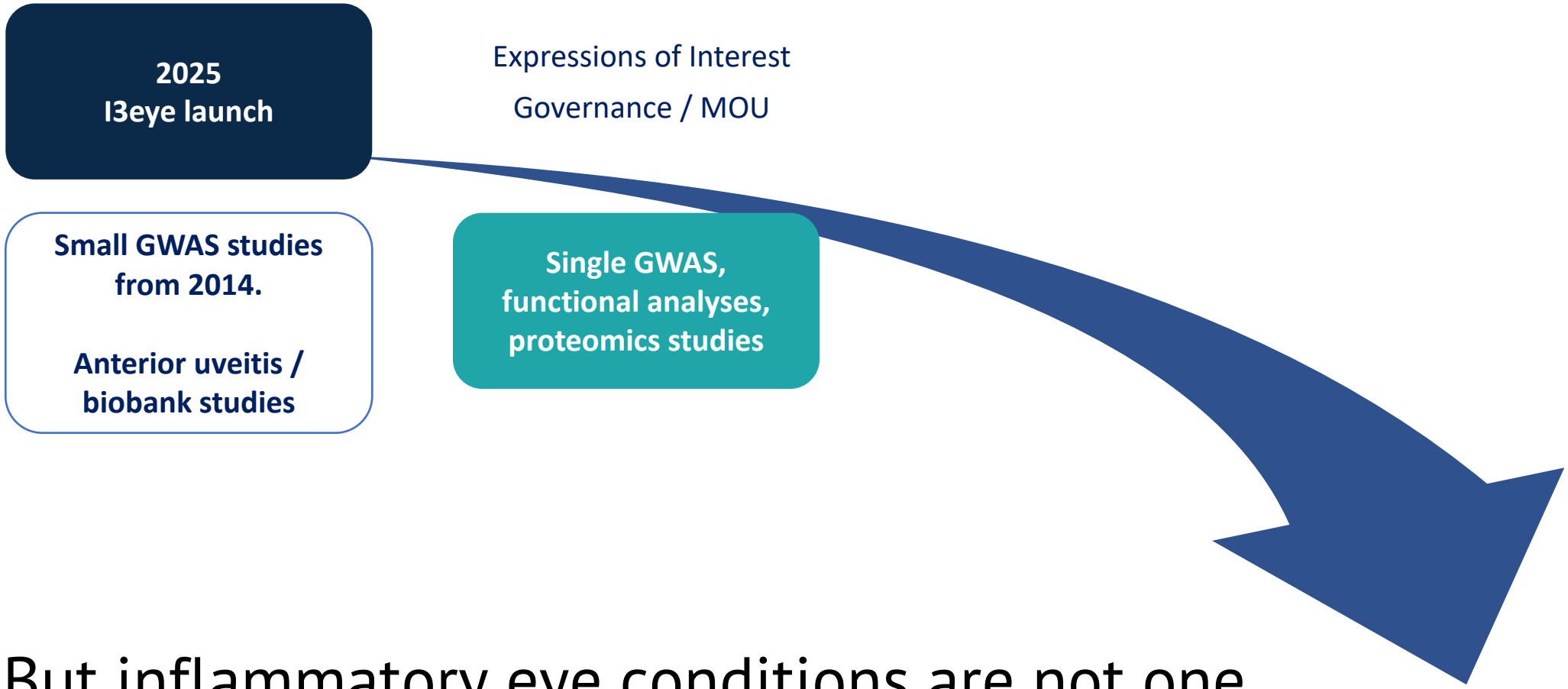
4. TRUST & GOVERNANCE

Transparent governance, data sharing and mutual respect build trust and sustain collaboration.

Ethics, data security, fair access and shared credit drive long-term success

Together, these pillars turn collaboration into discovery

i3eye Genomics Consortium: where are we?



But inflammatory eye conditions are not one disease

i3eye Genomics Consortium: Strategic Vision

2025
I3eye launch

Many centres, contributing small and well phenotyped ‘n’, with multiomincs, over a long period of time -> Stratified meta-analyses

Expressions of Interest from both academic biobanks (Unavailable to Industry) and smaller case/control studies, and also potential new clinical academic collaborators, not yet collecting samples

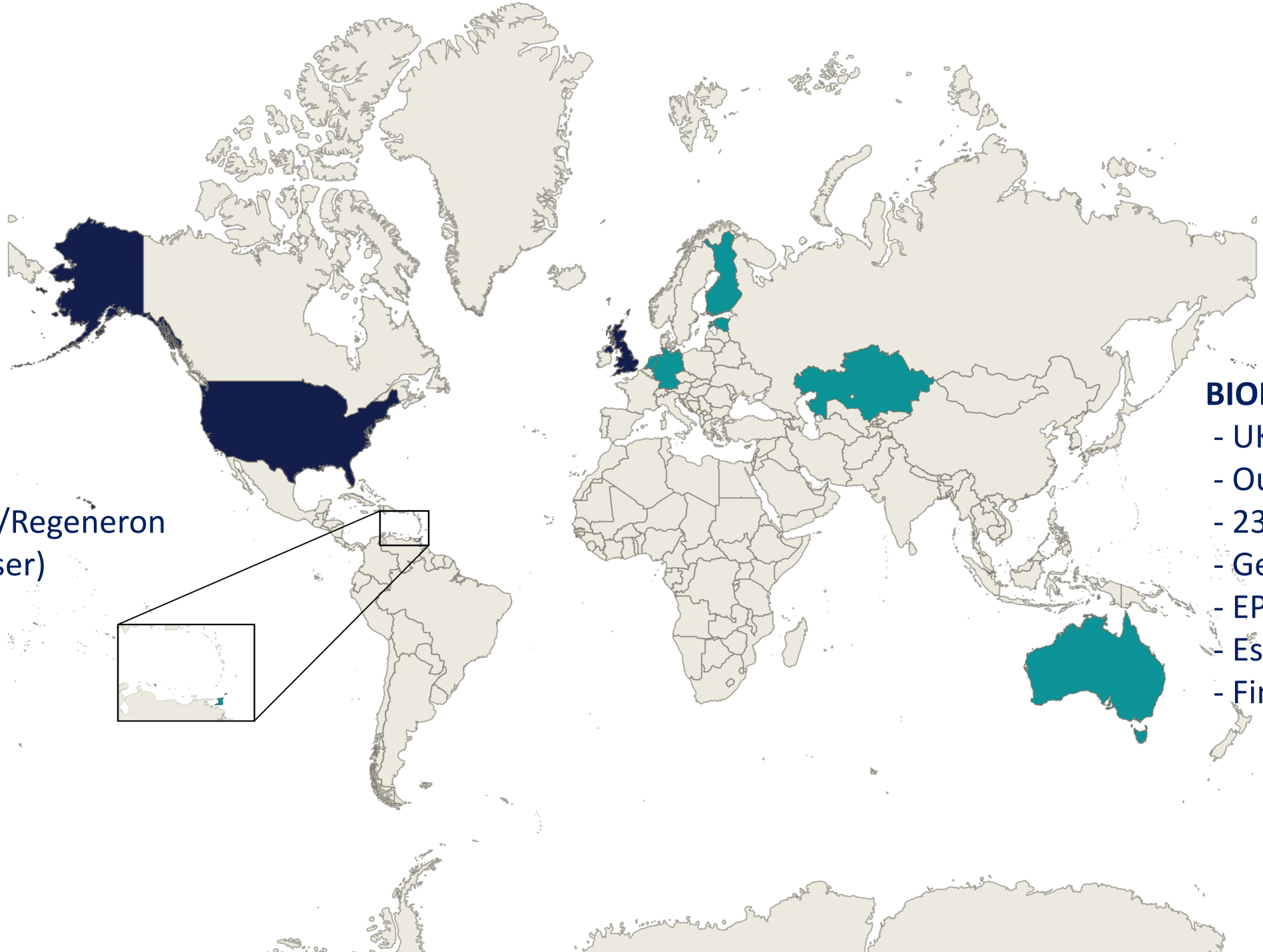
Governance / MOU

Harmonise data collection fields

Not only drug discovery, but deep phenotyping to yield clinically actional risk stratification for clinical care management

i3eye

BIOBANKS
- MVP
- All of Us
- Geisinger/Regeneron
- JERA (Kaiser)



BIOBANKS
- UKBB
- OurFutureHealth
- 23andMe
- Genes&Health
- EPICNorfolk
- Estonian BB
- Finngen

The history of genomics consortia tells us that rare, heterogeneous, immune-mediated eye diseases will not yield their biology to isolated studies or biobank meta-analyses alone. They require what i3Eye is building: phenotypic enrichment at scale, diversity, harmonisation and trust, for stratified meta-analyses.

Joining i3Eye: What You Give. What You Gain.

A global genomics collaboration to transform understanding and outcomes in inflammatory eye diseases

WHAT YOU CONTRIBUTE

SAMPLES & DATA
Phenotyped cohorts (uveitis, optic neuritis, scleritis)

STANDARDISATION
Shared definitions and protocols (SUN criteria for uveitis, ICON criteria for optic neuritis)

COLLABORATION
Input into study design, data curation and analyses

YOUR DATA STAYS YOURS —

but together, we achieve global scale.

WHAT YOU GAIN

SCALE
Access to large, international datasets and diverse ancestries

DISCOVERY POWER
Well-powered genetics to detect meaningful risk variants

AUTHORSHIP & LEADERSHIP
Lead analyses, first-author opportunities and pre-publication access to results

IMPACT
Advance precision medicine, clinical trials and novel therapeutics

INDEPENDENT ANALYSES
Permitted with transparency; avoid competing with consortium analyses

FAIR AUTHORSHIP
Based on ICMJE criteria; contribution-based, not site-based

SECURE & ETHICAL DATA SHARING
GDPR-compliant and consent-respecting

TRUST & COLLABORATION
Built on openness, respect, confidentiality and timely engagement

LOW BARRIER TO ENTRY
No mandatory financial commitment

i3Eye is an academic, not-for-profit consortium. Open to academic centres worldwide.

What i3Eye offers is simple: you keep ownership of your data, but gain the power of global scale through a long-term **academic** collaboration—within a framework that ensures fairness, credit, and scientific impact

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