

*Lilly* TuneLab™

# OUR AI/ML MODELS AT YOUR FINGERTIPS



**CDD VAULT®**  
Complexity Simplified



*Lilly* TuneLab™

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## First-of-its-kind, collaborative AI/ML drug discovery platform



Lilly provides participating companies access to powerful models trained on decades of data to accelerate their own therapeutic programs



Participants contribute training data via privacy-preserving federated learning for models to better learn their chemical space

# Lilly TuneLab™ Our Founding Year

## Participant Expansion

**135+** Companies on the platform

**Active Participants**

- 11M+ inferences made
- 675,000+ data points contributed

**Approved Regions**

USA, Canada, UK, Japan, EU, Switzerland, S. Korea, Taiwan, Singapore, India, Israel, Australia

**Small Mol. & Ab Models**

Monoclonal VHH  
Macrocycles Degraders/glues  
Beyond Rule of 5 Covalent  
Heterobifunctionals

### Examples of Early Adopters



## Partner Ecosystem Expansion

### CRO Partners



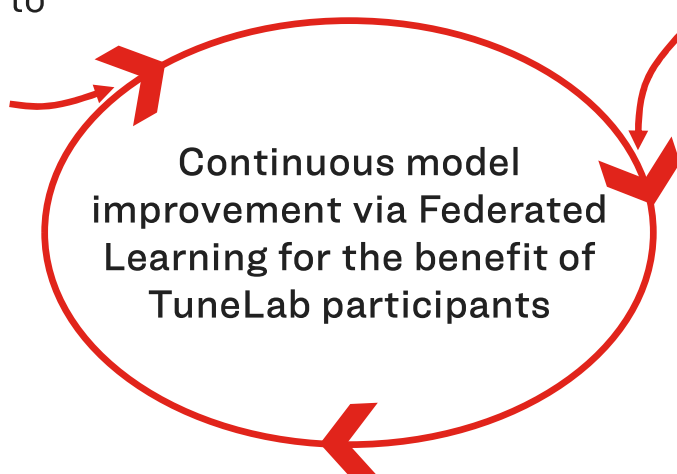
### Model Partners



# TuneLab In Action

**Contribute:** Provide wet lab data to TuneLab via Federated Learning

- Companies *with* historical data start here
- Your data is provided in a private environment, segregated from Lilly & other users



Continuous model improvement via Federated Learning for the benefit of TuneLab participants

**Inference:** Use TuneLab to predict the molecules with your desired properties

- Companies *without* historical data start here
- Save time and money by down selecting molecules in silico

**Generate:** Make selected molecules and generate wet lab data

- Your protocol or Lilly protocol

*Lilly* TuneLab™

# TuneLab Platform Partners

*Lilly*



**Rhino**  
Federated Computing

TuneLab's federated learning is managed by third party, **Rhino Federated Computing**

- Rhino meets industry information security and data privacy standards (SOC 2, ISO 27001, HIPAA, GDPR)
- Rhino Federating Computing is used by hundreds of organizations worldwide in biopharma, healthcare, energy, and finance
- Rhino's platform is powered by NVIDIA Flare (NVIDIA Federated Learning Application Runtime Environment) which is a domain-agnostic, open-source SDK for federated learning.



**Tamarind Bio**

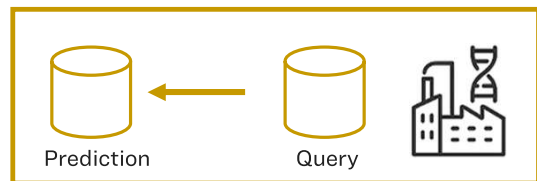
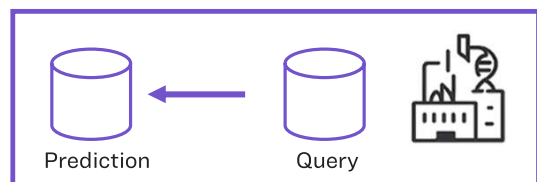
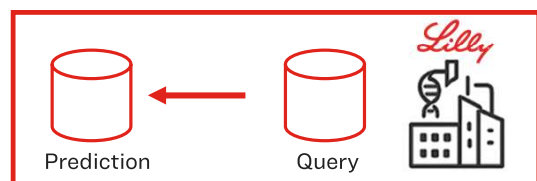
TuneLab's inferencing is managed by third party, **Tamarind Bio**

- Tamarind Bio meets industry information security and data privacy standards, including SOC2 compliance and others through AWS
- As of 2026, Tamarind is used by ~100 organizations worldwide, including top pharma companies
- Tamarind Bio provides the latest drug design infrastructure for scalable inferencing

# How TuneLab works

## Predictions

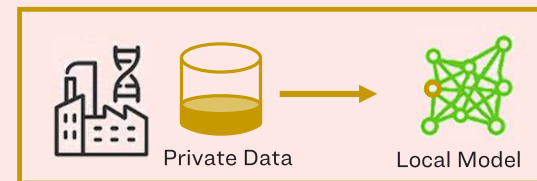
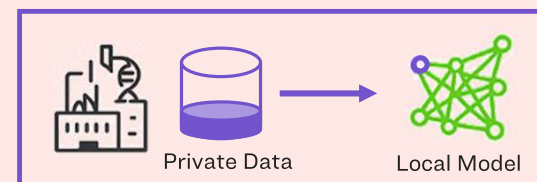
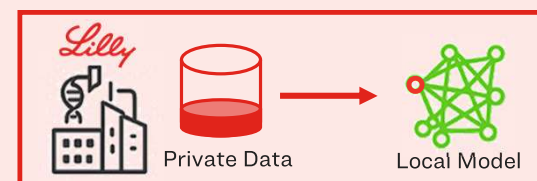
Your query and prediction use the latest global model and remain in a private environment, segregated from Lilly & other users.



Powered by  Tamarind Bio

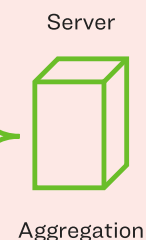
## Training

Participants contribute training data, making the models more accurate and generalizable across diverse chemical spaces. Data remains private and segregated during training.



Lilly assessment  
prior to distribution

Powered by  Rhino  
Federated Computing



*Lilly*

Restrictions: Predictions cannot be used to a) train another model or b) benefit a third party (e.g. in a collaboration)

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# Accessing TuneLab

## Direct web interface and API access

The screenshot displays the TuneLab web interface. On the left is a sidebar with navigation options: Create Job, Workflows, Job Runs, Interactive Sheets, Data, Fine-tuning, Models (highlighted), Data Contribution, SETTINGS, User Settings, Organization, Metrics, Docs (circled in red), API (circled in red), Take a Tour, What's New, TuneLab Terms Of Use, Support, support@lillytunelab.com, and Sign Out. The main area shows the 'Models' page with a search bar and filters. A table lists models:

| MODEL                                                                  | DEVELOPER | MODALITY                 | VERSION        |
|------------------------------------------------------------------------|-----------|--------------------------|----------------|
| AbLab<br>> Multitask - 22 tasks                                        | Lilly     | ANTIBODY                 | v2             |
| Antibody-Antigen Binding Affinity $\Delta\Delta G$<br>Regression       | Lilly     | ANTIBODY-ANTIGEN COMPLEX | v1             |
| ChemLab<br>> Multitask - 33 tasks                                      | Lilly     | SMALL MOLECULE           | v2 (Federated) |
| Immunogenicity (MHC-II Peptide Presentation)<br>> Multitask - 13 tasks | Lilly     | ANTIBODY                 | v1             |
| In vivo PK<br>> Multitask - 32 tasks                                   | insitro   | SMALL MOLECULE           | v1             |
| NanoLab (VHH Developability)<br>> Multitask - 5 tasks                  | Lilly     | VHH                      | v1             |

The 'ChemLab' model details are shown on the right, including a description of a message-passing neural network, an overview of the federated multi-task model, and input/output options.

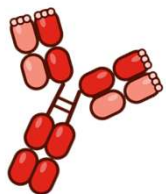
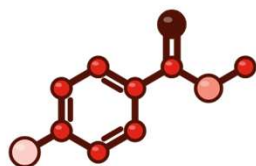
## Platform partners

- Integrations with the following platform partners will make certain TuneLab available in those environments
- Federated data contribution requirements are the same across platforms



# Small Molecule and Antibody TuneLab Models

| Model                                              | What it predicts                                                                                                                                                                                         | Trained on                                                                                                                                                                            |
|----------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ChemLab                                            | Physchem, ADME and toxicology properties like fraction unbound, permeability, Solubility, metabolic stability, microsomal clearance, CYP inhibition, hERG, phospholipidosis, lysosomotropic, and others! | Lilly proprietary physicochemical and ADMET assay data and contributed TuneLab partner data combined through federated learning, spanning hundred of thousands of unique molecules    |
| In vivo PK                                         | In vivo PK properties like Mean Residence Time, plasma clearance, volume of distribution, half-life, unbound clearance and others, across 4 species (rat, mouse, dog and monkey)                         | Model developed by insitro using Lilly proprietary <i>in vivo</i> intravenous pharmacokinetic studies, trained jointly with Lilly in vitro ADME and physicochemical assay collections |
| AbLab                                              | Antibody developability endpoints from heavy/light-chain sequences like hydrophobicity, thermal stability, solubility, aggregation, purity, non-specific binding, DC internalization and others!         | Lilly proprietary mAb discovery data combined with intentionally diversified antibody panels expressed and profiled at multiple CROs                                                  |
| NanoLab (VHH developability)                       | Developability endpoints for VHHs to predict expression, purity, integrity and aggregation                                                                                                               | Lilly proprietary purpose-built VHH developability dataset generated by a partner biologics platform                                                                                  |
| Antibody-Antigen Binding Affinity $\Delta\Delta G$ | Antibody-Antigen Binding Affinity model predicts how a specific mutation changes binding affinity between an antibody and its antigen.                                                                   | Computational binding-change values from single-mutation interface scans across a public structural antibody database                                                                 |
| Immunogenicity (MHC-II Peptide Presentation)       | MHC-II presentation likelihood per peptide across 12 HLA-DRB1 alleles, together with the predicted 9-mer binding core                                                                                    | Lilly proprietary MHC-Associated Peptide Proteomic peptides from a large panel of therapeutic antibodies, as well as public MHC-II binding and eluted-ligand data                     |



# Small Molecule Endpoints: ChemLab and *in vivo* PK

| Class        | Description                       | Species / Other          | Type |
|--------------|-----------------------------------|--------------------------|------|
| Physchem     | LogP*                             |                          | R    |
|              | LogD*                             | pH 7.4                   | R    |
| Absorption   | Kinetic solubility                | pH 2, 0.1 & 0.01mg/mL    | C    |
|              |                                   | pH 6, 0.1 & 0.01mg/mL    | C    |
|              |                                   | pH 7.4, 0.1 & 0.01mg/mL  | C    |
|              | Apparent Permeability             | MDCK                     | R    |
|              | Thermodynamic Aqueous Solubility* |                          | R    |
|              | P-gp substrate recognition*       | CNS                      | C    |
| Distribution | Fraction Unbound                  | Liver microsomes (human) | R    |
|              |                                   | Plasma (human)           | R    |
|              |                                   | Plasma (monkey)          | R    |
|              |                                   | Plasma (rat)             | R    |
|              |                                   | Brain (human)            | R    |
|              | Total Brain Concentration*        | Human                    | R    |

| Class | Description                          | Species / Other | Type |
|-------|--------------------------------------|-----------------|------|
| Tox   | Primary Hepatocyte Cytolethality     | Rat             | C    |
|       | hERG Binding                         |                 | C    |
|       | Phospholipidosis                     | HepG2           | C    |
|       | Lysosomatropic*                      | HepG2           | C    |
|       | Mutagenicity*                        | Mini Ames       | C    |
|       | Primary Hepatocyte Phospholipidosis* | Rat             | C    |

| Class            | Description                             | Species / Other | Type  |
|------------------|-----------------------------------------|-----------------|-------|
| Metabolism       | Microsomal Apparent Intrinsic Clearance | Mouse           | R     |
|                  |                                         | Rat             | R     |
|                  |                                         | Human           | R     |
|                  | Microsomal Metabolic Stability          | Mouse           | R / C |
|                  |                                         | Rat             | R / C |
|                  |                                         | Human           | R / C |
|                  |                                         | Dog             | C     |
|                  |                                         | Monkey          | C     |
|                  |                                         | Mouse           | R     |
|                  | Hepatocyte Apparent Intrinsic Clearance | Rat             | R     |
|                  |                                         | Human           | R     |
|                  |                                         | Dog             | R     |
| Metabolism (DDI) | CYP % inhibition                        | 2C9             | C     |
|                  |                                         | 2D6             | C     |
|                  |                                         | 3A4             | C     |

| Class      | Description                                    | Species / Other         | Type |
|------------|------------------------------------------------|-------------------------|------|
| In vivo PK | Mean residence time                            | Mouse, Rat, Dog, Monkey | R    |
|            | Unbound plasma clearance                       | Mouse, Rat, Dog, Monkey | R    |
|            | Plasma clearance                               | Mouse, Rat, Dog, Monkey | R    |
|            | Unbound volume of distribution at steady state | Mouse, Rat, Dog, Monkey | R    |
|            | Volume of distribution at steady state         | Mouse, Rat, Dog, Monkey | R    |
|            | Unbound intrinsic clearance                    | Mouse, Rat, Dog, Monkey | R    |
|            | Half-life                                      | Mouse, Rat, Dog, Monkey | R    |
|            | IVIVE Hepatic clearance                        | Mouse, Rat              | R    |
|            | IVIVE and Direct Prediction Clearance Ensemble | Mouse, Rat              | R    |
|            |                                                |                         |      |



R: Regression / C: Classification.  
 Not all models may be available at all times  
 \*: In development, not yet released

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# Features & Workflows

## Features



### Explainability (ChemLab)

*Understand which structural features drive a property prediction*



### Fine-Tuning (ChemLab & AbLab)

*Train TuneLab's models using your own datasets, only accessible to you*



### Uncertainty quantification (ChemLab, AbLab & NanoLab)

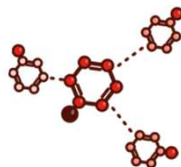
*Informs scientists when and how much to trust a prediction*

## Workflows

### Ligand-Based Virtual Screening, 2D

*Find analog molecules through the following similarity engines*

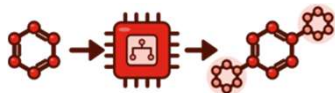
- nvMolKit (NVIDIA BioNeMo)
- Arthor (NextMove software)
- Lilly Search (Lilly proprietary)



### Generative Chemistry

*Enable the design of novel structures around the starting scaffold(s)*

- GenMol (NVIDIA BioNeMo)



- Gain property driving insights at a fragment or atom level
- Fine-tune ChemLab and AbLab on your own data without it leaving your environment
- For small molecules, go further by using our workflows: search and generate new chemistry around a known hit, then rank and explain every candidate before committing to synthesis

# Small Molecule Data Contributions

Typical biotech training contribution over the 12-month term  
**1000 total experiment readouts**

The protocol used  
determines the readouts  
required per assay

## Option 1: Partner Assay Protocol\*

At least **200 experiment readouts**  
per protocol

## Option 2: Lilly Assay Protocol

At least **100 experiment readouts**  
per protocol

## Examples of ways to reach 1000 experiment readouts

Partner protocol used exclusively

*5 Partner ADMET assays  
with 200 small molecules  
measured*

Mix of protocols

*4 Lilly ADMET assays with 100  
molecules & 3 Partner ADMET  
assays with 200 molecules*

Lilly protocol used exclusively

*10 Lilly ADMET assays  
with 100 small molecules  
measured*

- Experimental Readout: One molecule observed in a wet lab experiment to measure a property
- Training data contributions should come from the available menu (next slides) and can include historical data contributions as well
- Higher contribution levels supports additional inferences and enhanced model access



\* Sharing protocol required for contribution

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# Endpoints of Interest – Small Molecule

## Physicochemical:

| Endpoint | Data Format          |
|----------|----------------------|
| LogP     | Continuous Log units |
| LogD     | Continuous Log units |

## Absorption Endpoints (Core)

| Endpoint                              | Data Format              |
|---------------------------------------|--------------------------|
| HTSA pH2 Classifier (0.01 mg/mL)      | Binary classification    |
| HTSA pH2 Classifier (0.1 mg/mL)       | Binary classification    |
| HTSA pH6 Classifier (0.01 mg/mL)      | Binary classification    |
| HTSA pH6 Classifier (0.1 mg/mL)       | Binary classification    |
| HTSA pH7.4 Classifier (0.01 mg/mL)    | Binary classification    |
| HTSA pH7.4 Classifier (0.1 mg/mL)     | Binary classification    |
| MDCK Permeability Predictor           | Continuous (Papp values) |
| MDCK Permeability 2C Classifier       | Binary classification    |
| Thermodynamic Aqueous Solubility      | Continuous (mg/mL)       |
| Human Passive Intestinal Permeability | Continuous (Papp)        |
| Pgp Substrate Recognition             | Binary classification    |

## Absorption Endpoints (Additional)

| Endpoint                 | Data Format                  |
|--------------------------|------------------------------|
| Caco-2 Permeability      | Papp (10 <sup>-6</sup> cm/s) |
| PAMPA Permeability       | Pe (10 <sup>-6</sup> cm/s)   |
| Oral Bioavailability     | %F (in vivo or predicted)    |
| BCRP Substrate/Inhibitor | Binary or IC50               |
| OATP1B1/1B3 Substrate    | Binary or uptake rate        |
| OCT2 Substrate/Inhibitor | Binary or IC50               |

## Distribution Endpoints (Core)

| Endpoint                   | Data Format               |
|----------------------------|---------------------------|
| Fraction Unbound Microsome | Continuous (fu)           |
| Fraction Unbound Plasma    | Continuous (fu)           |
| Fraction Unbound Brain     | Continuous (fu,brain)     |
| Total Brain Concentration  | Continuous (brain/plasma) |
| Kp Brain                   | Continuous ratio          |

## Distribution Endpoints (Additional)

| Endpoint                        | Data Format                 |
|---------------------------------|-----------------------------|
| Volume of Distribution (Vdss)   | L/kg (in vivo or predicted) |
| Blood-to-Plasma Ratio           | Ratio                       |
| HSA Binding                     | %bound or Kd                |
| AGP Binding                     | %bound or Kd                |
| Tissue Distribution (Kp values) | Tissue/plasma ratios        |

## Excretion Endpoints (Additional)

| Endpoint             | Data Format    |
|----------------------|----------------|
| Renal Clearance      | mL/min/kg      |
| Biliary Excretion    | % dose in bile |
| Total Body Clearance | mL/min/kg      |
| Terminal Half-life   | Hours          |
| Mean Residence Time  | Hours          |

## Metabolism Endpoints (Core)

| Endpoint                       | Data Format                               |
|--------------------------------|-------------------------------------------|
| Mouse Microsomal Clearance     | Continuous (μL/min/mg)                    |
| Rat Microsomal Clearance       | Continuous (μL/min/mg)                    |
| Human Microsomal Clearance     | Continuous (μL/min/mg)                    |
| Mouse Metabolic Stability      | Continuous (t½)                           |
| Rat Metabolic Stability        | Continuous (t½)                           |
| Human Metabolic Stability      | Continuous (t½)                           |
| Dog Metabolic Stability 2C     | Binary classification                     |
| Mouse Metabolic Stability 2C   | Binary classification                     |
| Human Metabolic Stability 2C   | Binary classification                     |
| Rat Metabolic Stability 2C     | Binary classification                     |
| Monkey Metabolic Stability 2C  | Binary classification                     |
| Mouse Hepatocyte Clearance     | Continuous (μL/min/10 <sup>6</sup> cells) |
| Rat Hepatocyte Clearance       | Continuous (μL/min/10 <sup>6</sup> cells) |
| Human Hepatocyte Clearance     | Continuous (μL/min/10 <sup>6</sup> cells) |
| Dog Hepatocyte Clearance       | Continuous (μL/min/10 <sup>6</sup> cells) |
| Rat IV Clearance               | Continuous (mL/min/kg)                    |
| Rat IV Vd Area Classifier      | Binary classification                     |
| Rat IV CL Class (50 mL/min/kg) | Binary classification                     |

## Metabolism Endpoints (Additional)

| Endpoint                    | Data Format               |
|-----------------------------|---------------------------|
| UGT Inhibition Panel        | IC50 values               |
| Metabolite Identification   | Major metabolites list    |
| Species Comparison (Met ID) | Cross-species metabolites |
| Aldehyde Oxidase Substrate  | Binary or % metabolism    |
| FMO Substrate               | Binary or % metabolism    |

# Endpoints of Interest – Small Molecule

## Toxicity Endpoints (Core)

| Endpoint                                | Data Format           |
|-----------------------------------------|-----------------------|
| Rat Primary Hepatocyte Cytotoxicity     | Continuous (IC50)     |
| hERG Binding Classifier                 | Binary classification |
| HepG2 Phospholipidosis                  | Binary classification |
| HepG2 Lysotracker                       | Continuous or binary  |
| Mutagenicity (Mini Ames) Class          | Binary classification |
| Rat Primary Hepatocyte Phospholipidosis | Binary classification |

## Toxicity Endpoints (Additional)

| Endpoint                      | Data Format                 |
|-------------------------------|-----------------------------|
| Mitochondrial Toxicity        | Glu/Gal IC50 ratio          |
| Bile Salt Export Pump (BSEP)  | IC50 or % inhibition        |
| Reactive Metabolite Formation | GSH adduct levels           |
| Genotoxicity (Micronucleus)   | Binary or fold increase     |
| Chromosome Aberration         | Binary classification       |
| Carcinogenicity Alerts        | Structural alerts count     |
| Skin Sensitization            | LLNA EC3 or in vitro        |
| Phototoxicity                 | PIF or MPE values           |
| Eye Irritation                | Score or classification     |
| Developmental Toxicity        | Binary or severity score    |
| Cardiotoxicity (beyond hERG)  | Multi-ion channel panel     |
| Neurotoxicity Panel           | Multiple endpoints          |
| Immunotoxicity Markers        | Cytokine levels or ratios   |
| Nephrotoxicity Biomarkers     | KIM-1, NGAL levels          |
| Endocrine Disruption Panel    | Nuclear receptor activation |

## Pharmacology Panel Endpoints (Core)

| Endpoint                           | Data Format               |
|------------------------------------|---------------------------|
| 5HT2B Agonist (Ca Mobilization)    | IC50/EC50 or % inhibition |
| 5HT2B Antagonist (Ca Mobilization) | IC50 or % inhibition      |
| ADORA2A Agonist/Antagonist         | IC50/EC50 or % inhibition |
| ADRA1A Agonist/Antagonist          | IC50/EC50 or % inhibition |
| ADRB2 Agonist (cAMP)               | EC50 or % activation      |
| ADRB2 Antagonist (Arrestin)        | IC50 or % inhibition      |
| Cav1.2 (Ca Channel)                | IC50 or % inhibition      |
| D2L Agonist/Antagonist             | IC50/EC50 or % modulation |
| hERG Channel Binding               | IC50 or Ki                |
| GABAA Ion Channel                  | IC50 or % modulation      |
| Glucocorticoid Receptor Binding    | IC50 or Ki                |
| H1R/HRH1 Agonist/Antagonist        | IC50/EC50 or % modulation |
| Kainate Receptor                   | IC50 or % modulation      |
| LXRα Binding                       | IC50 or Ki                |
| M2 Muscarinic Agonist/Antagonist   | IC50/EC50 or % modulation |
| Nav1.5 Sodium Channel              | IC50 or % inhibition      |
| PDE10A Binding                     | IC50 or Ki                |
| PDE3A Binding                      | IC50 or Ki                |
| PDE4D Binding                      | IC50 or Ki                |
| PPARγ Binding                      | IC50 or Ki                |
| RARα Binding                       | IC50 or Ki                |
| RXRα Binding                       | IC50 or Ki                |
| rAMPA Receptor                     | IC50 or % modulation      |

## Drug-Drug Interaction Endpoints (Core)

| Endpoint                         | Data Format           |
|----------------------------------|-----------------------|
| CYP2C9 SP 2 Class                | Binary classification |
| CYP2D6 SP 2 Class                | Binary classification |
| CYP3A4 SP 2 Class                | Binary classification |
| CYP3A4 Time Dependent Inhibition | Binary classification |

## Drug-Drug Interaction Endpoints (Additional)

| Endpoint                       | Data Format            |
|--------------------------------|------------------------|
| CYP1A2 Inhibition              | IC50 or Ki             |
| CYP2C19 Inhibition             | IC50 or Ki             |
| CYP2C8 Inhibition              | IC50 or Ki             |
| CYP2B6 Inhibition              | IC50 or Ki             |
| CYP Induction (PXR activation) | Fold induction or EC50 |
| CYP Induction (CAR activation) | Fold induction or EC50 |
| CYP Induction (AhR activation) | Fold induction or EC50 |

## Emerging/Specialized Endpoints (Additional)

| Endpoint                             | Data Format             |
|--------------------------------------|-------------------------|
| PROTAC Ternary Complex Formation     | Binary or Kd            |
| PROTAC Hook Effect                   | Dose-response profile   |
| PROTAC Degradation Kinetics          | t½ degradation          |
| Molecular Glue Activity              | Binary or EC50          |
| Targeted Covalent Inhibitor Kinetics | kinact/Ki               |
| Lysosomal Accumulation               | Fold accumulation       |
| Autophagy Modulation                 | LC3B ratio or flux      |
| Ferroptosis Induction                | Lipid ROS levels        |
| Environmental Toxicity               | EC50 aquatic species    |
| Bioaccumulation Factor               | BCF or LogP-based       |
| Gut Microbiome Impact                | Growth inhibition panel |

# Developability Models for Large Molecules

## AbLab

Trained on Lilly proprietary monoclonal antibody discovery data combined with intentionally diversified antibody panels (~10,000 mAbs) expressed and profiled at multiple CROs. All task types = Regression

| Class                | Tasks (units)                                                   |
|----------------------|-----------------------------------------------------------------|
| Hydrophobicity       | HIC retention time Lilly (min)                                  |
|                      | HIC Fluorescence time CRO1 (RFU)                                |
|                      | HIC Fluorescence time CRO2 (RFU)                                |
| Thermal Stability    | Primary Melting Temperature Tm1 (CRO1, DSF, °C)                 |
|                      | Primary Melting Temperature Tm1 (CRO2, nanoDSF, °C)             |
|                      | Primary Melting Temperature Tm1 (Lilly, nanoDSF, °C)            |
|                      | Onset Temperature (CRO1, DSF, °C)                               |
|                      | Onset Temperature (CRO2, nanoDSF, °C)                           |
|                      | Radius Unfolding Temperature (CRO2, DLS, °C)                    |
|                      | Secondary Melting Temperature Tm2 (CRO2, nanoDSF, °C)           |
| Self-Interaction     | AC-SINS $\Delta\lambda_{max}$ (CRO1, nm)                        |
| Solubility           | Apparent Solubility (Lilly, H6 buffer PEG precipitation, % PEG) |
|                      | Apparent Solubility (Lilly, PBS PEG precipitation, % PEG)       |
| Aggregation          | Polydispersity Index (CRO2, DLS, unitless)                      |
|                      | SEC Main Peak Retention Time (CRO2, min)                        |
| Purity               | SEC Total Main Peak Area (CRO2, mAU)                            |
|                      | SEC Main Peak (CRO2, % of total)                                |
| Polyreactivity       | OVA Polyreactivity (CRO1, normalized score)                     |
|                      | BVP Polyreactivity (CRO2, ELISA, OD)                            |
| Non-Specific Binding | Nonspecific Binding (Lilly, MSD, unitless)                      |
| Surface Charge       | Heparin Retention Time (Lilly, min)                             |
| Immunogenicity       | DC Internalization Index (Lilly, unitless)                      |

## NanoLab

Trained on a purpose-built VHH developability dataset (2500 sequences) generated by a partner biologics platform. All task types = Regression

| Class              | Tasks (units)                               |
|--------------------|---------------------------------------------|
| Expression         | Protein Concentration (ng/uL)               |
|                    | Total Protein Yield (ng)                    |
| Purity & Integrity | A260/A280 ratio (n/a)                       |
|                    | CE-SDS Main Peak Apparent Mol. Weight (kDa) |
| Aggregation        | SEC Main Peak (% main peak)                 |

Not all models may be available at all times

# Immunogenicity & Antibody-Antigen Binding Affinity ( $\Delta\Delta G$ )

## Immunogenicity MHC-II Peptide Presentation:

TuneLab's Immunogenicity model predicts which peptides from an antibody sequence are likely to be presented on MHC class II (DRB1)

| Tasks                |                |                | Output Units                                                 | Type |
|----------------------|----------------|----------------|--------------------------------------------------------------|------|
| HLA-DRB1*01:01       | HLA-DRB1*04:05 | HLA-DRB1*13:01 | Number of peptides that reach a preselected binder threshold | C    |
| HLA-DRB1*03:01       | HLA-DRB1*07:01 | HLA-DRB1*13:02 |                                                              |      |
| HLA-DRB1*04:01       | HLA-DRB1*09:01 | HLA-DRB1*15:01 | Max binding probability: (0 to 1)                            |      |
| HLA-DRB1*04:04       | HLA-DRB1*11:01 | HLA-DRB1*15:02 |                                                              |      |
| Cross-allele summary |                |                | As above, for all HLA-DRB1 alleles                           |      |

## Antibody-Antigen Binding Affinity ( $\Delta\Delta G$ ):

Predicts how a mutation changes binding affinity between an antibody and its antigen, with an uncertainty estimate

| Task                       | Output Units | Type |
|----------------------------|--------------|------|
| Binding free energy change | kcal/mol     | R    |



R: Regression / C: Classification.  
Not all models may be available at all times  
\*: In development, not yet released

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# Antibody Data Contributions

Typical biotech training contribution over the  
12-month term

**At least 1 property measured/endpoint with  
125 sequences**

- Diversity of Ab data accepted as contributions (monoclonal, VHH)
- Sharing protocol and associated meta data required for contribution

- Training data contributions should come from the available menu of endpoints (next slide) and can include historical data contributions as well
- Higher contribution levels supports additional inferences and enhanced model access

# Endpoints of Interest – Antibody

Endpoint  
Antibody–Antigen Binding Affinity ( $\Delta\Delta G$ )

Data Format  
kcal/mol

## Core Developability Endpoints

| Endpoint                              | Data Format                                  |
|---------------------------------------|----------------------------------------------|
| Hydrophobicity/Aggregation (HIC)      | Binary classification or retention time      |
| Thermostability (DSF T <sub>m</sub> ) | Binary classification or T <sub>m</sub> (°C) |
| Non-specific Binding (MSD-NSB)        | Binary classification or binding score       |
| Solubility (PEG Precipitation)        | Binary classification or mg/mL               |
| Immunogenicity Risk Score             | Ensemble score (0-1) or risk category        |
| Deamidation Liability (LC-MS)         | Binary classification or site identification |
| Viscosity at High Concentration       | Binary classification or cP at 150 mg/mL     |

## Stability & Formulation Endpoints (Additional)

| Endpoint                 | Data Format                |
|--------------------------|----------------------------|
| Aggregation by SEC       | % monomer over time        |
| Freeze-Thaw Stability    | Aggregate % after 5 cycles |
| Shear Stress Stability   | Aggregate % post-stress    |
| pH Stability Range       | pH range for <5% aggregate |
| Oxidation Susceptibility | % oxidized Met/Trp         |
| Isomerization Risk       | % Asp isomerization        |
| Fragmentation Propensity | % fragments by CE-SDS      |
| Charge Heterogeneity     | Main peak % by IEX         |

## Binding & Specificity Endpoints (Additional)

| Endpoint                      | Data Format           |
|-------------------------------|-----------------------|
| Species Cross-reactivity      | Binary or EC50 ratio  |
| Epitope Binning               | Competition matrix    |
| Target Specificity Panel      | Off-target hits count |
| Cell Binding (Flow Cytometry) | EC50 or MFI           |
| Tissue Cross-reactivity       | IHC score panel       |
| pH-dependent Binding          | KD at pH 6.0 vs 7.4   |

## Manufacturing Endpoints (Additional)

| Endpoint                       | Data Format                     |
|--------------------------------|---------------------------------|
| Expression Yield (Transient)   | mg/L in HEK/CHO                 |
| Expression Yield (Stable Pool) | g/L in CHO fed-batch            |
| Protein A Elution pH           | pH for 90% recovery             |
| Host Cell Protein Clearance    | Log reduction value             |
| DNA Clearance                  | Log reduction value             |
| Endotoxin Levels               | EU/mg                           |
| Glycosylation Pattern          | % fucosylation, galactosylation |
| Sialylation Level              | % sialylated                    |
| C-terminal Lysine              | % K0/K1/K2                      |
| N-terminal Pyroglutamate       | % pyroGlu                       |

## Specialized Format Endpoints

| Endpoint                           | Data Format                                        |
|------------------------------------|----------------------------------------------------|
| Bispecific T-cell Engagement       | EC50 cytotoxicity                                  |
| B Cell Killing (TCE)               | EC50 B cell depletion                              |
| Cytokine Release (TCE)             | pg/mL (IL-2, IL-6, TNF- $\alpha$ , IFN- $\gamma$ ) |
| Bispecific Dual Binding            | KD for both targets                                |
| ADC Drug-Antibody Ratio            | Average DAR                                        |
| ADC Linker Stability               | % intact over time                                 |
| ADC Bystander Activity             | Killing of antigen-neg cells                       |
| Fragment (Fab/scFv) Stability      | T <sub>m</sub> and aggregation                     |
| Nanobody Stability                 | T <sub>m</sub> and aggregation                     |
| Fc Fusion Properties               | Expression and stability                           |
| Antibody-Oligonucleotide Conjugate | Conjugation efficiency                             |

## Functional Activity Endpoints (Non-core)

| Endpoint                    | Data Format                         |
|-----------------------------|-------------------------------------|
| ADCC Activity               | EC50 or % max lysis                 |
| CDC Activity                | EC50 or % max lysis                 |
| ADCP Activity               | % phagocytosis                      |
| Fc $\gamma$ R Binding Panel | KD for all Fc $\gamma$ Rs           |
| Clq Binding                 | KD or relative binding              |
| FcRn Binding (pH 6.0/7.4)   | KD ratio                            |
| Neutralization Potency      | IC50 or IC90                        |
| Agonist/Antagonist Activity | EC50/IC50                           |
| Internalization Rate        | t <sub>1/2</sub> or % at timepoints |
| Target Shedding Impact      | Activity with shed target           |

## Clinical Translation Endpoints

| Endpoint                     | Data Format                           |
|------------------------------|---------------------------------------|
| PK Profile (Mouse)           | t <sub>1/2</sub> , CL, V <sub>d</sub> |
| PK Profile (Rat)             | t <sub>1/2</sub> , CL, V <sub>d</sub> |
| PK Profile (Monkey)          | t <sub>1/2</sub> , CL, V <sub>d</sub> |
| Tissue Distribution          | Tissue/blood ratios                   |
| Tumor Penetration            | Tumor/blood ratio                     |
| Anti-Drug Antibody Incidence | % positive (preclinical)              |
| In Vivo Efficacy             | Tumor growth inhibition               |
| Safety/Tox Findings          | NOAEL or findings                     |
| Clearance (CL)               | mL/hr/kg                              |
| Bioavailability (F)          | % (SC/IM routes)                      |
| Biodistribution              | Tissue concentration profiles         |

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