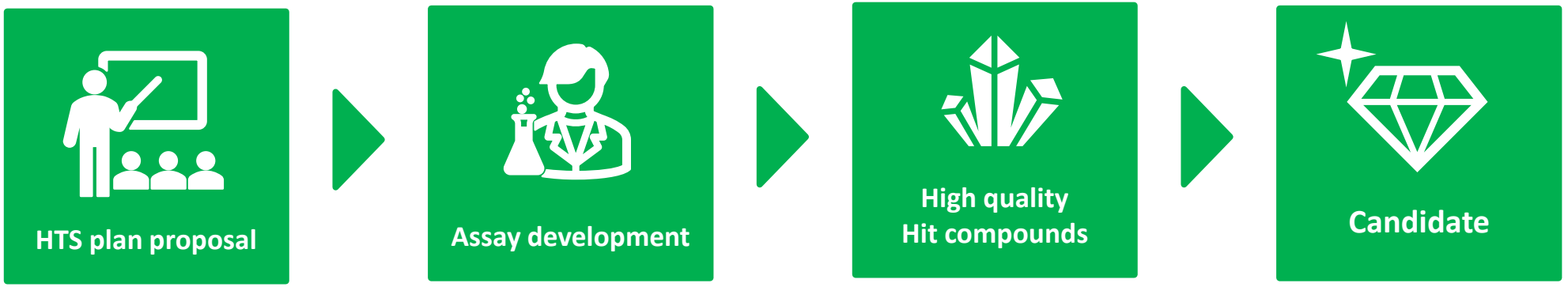
Screening Capabilities

Driving innovative drug discovery through integrated data-driven HTS platform

Axcelead Drug Discovery Partners, Inc.

May 2024

Integrated data-driven HTS platform under one-roof



Pharma origin high-quality library

1.5M
Axcelead compound library

60%
In-house compounds

Proven track record

>700
Screening Experience

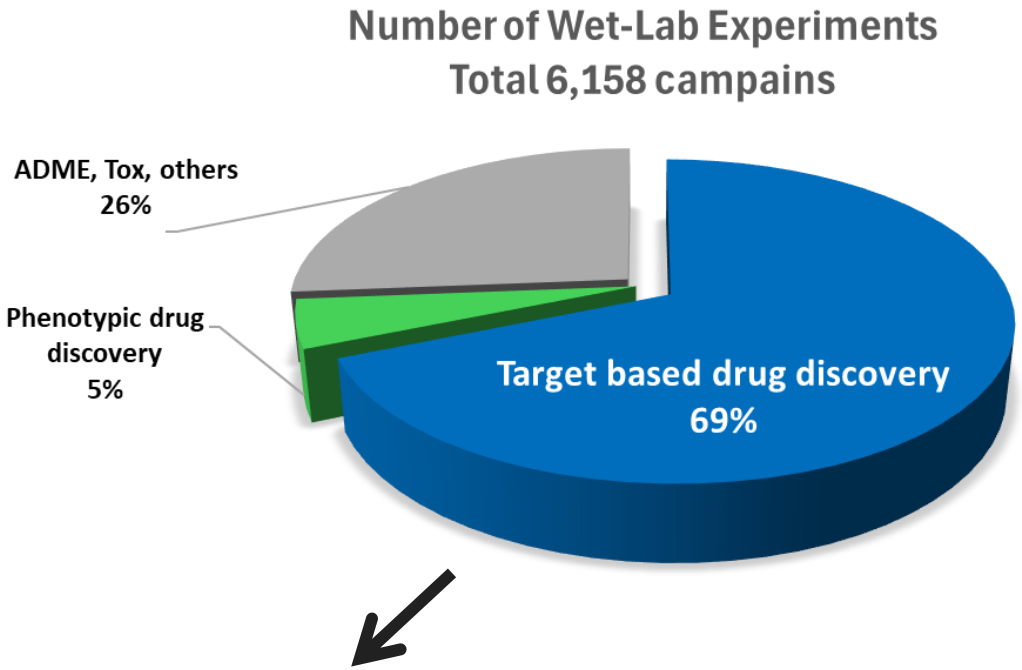
>90%
Successful Hit finding

Pharma standard science

Medicinal chemistry & Comp. Chem

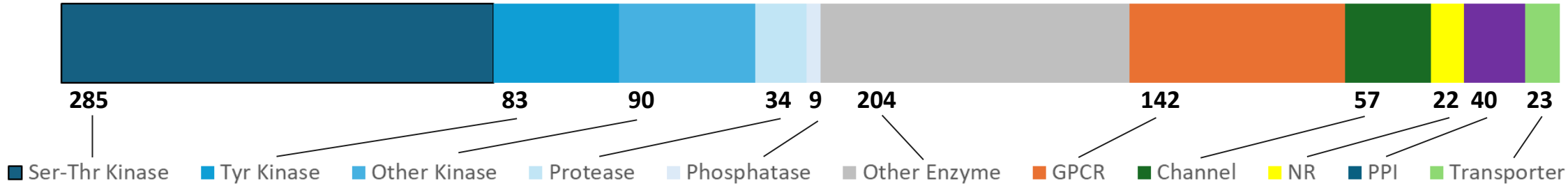
Utilization of exclusive data sets

Unique and high-quality dataset exclusive to Axcelead group



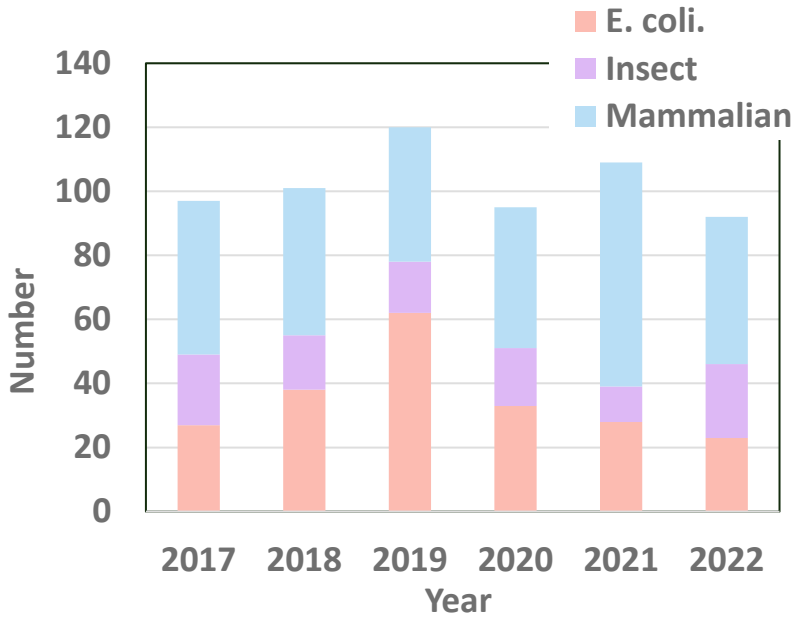
- Axcelead has a unique and high-quality dataset anchored by over 25 years of drug discovery data from a global pharmaceutical company, covering 989 individual targets.
- Data-driven screening platform;
  - Focused library design
  - Annotation information or ADME profiling data to HTS hit compounds if available
  - Utilization for Molecular Prediction Model or computational chemistry platform

989 targets



Robust protein purification capacity & wide range of assay development experience

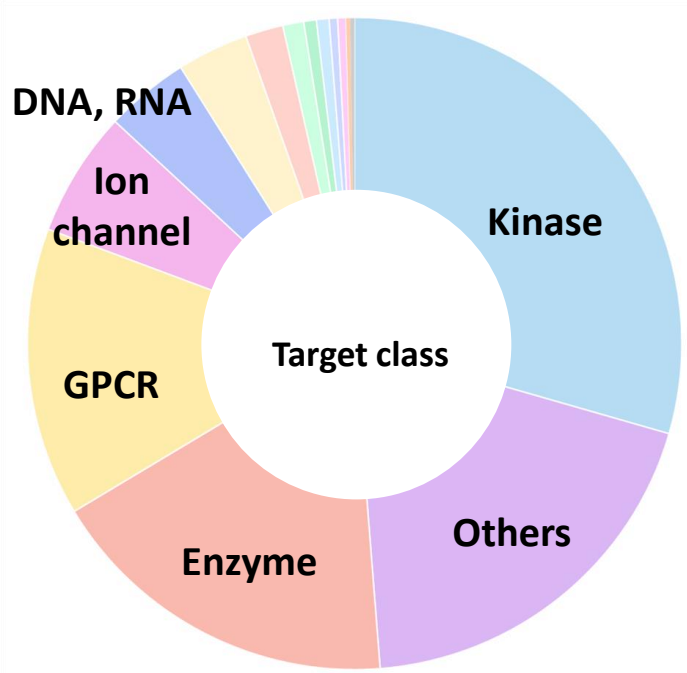
Protein preparation



>610
Protein purification in 6 years

- E. coli. 3-10 weeks
- Insect or mammalian; 4-12 weeks
- Membrane protein purification using Virus-Like Particle (VLP)

Assay development



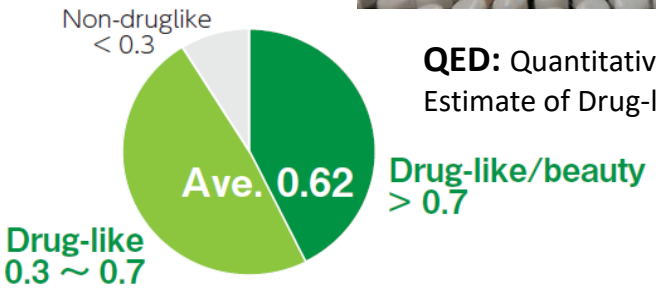
>480
Assay developments in 6 years

>80%
Developed at Axcelead

High-quality pharma-origin HTS libraries and curated Focused Libraries using exclusive data sets

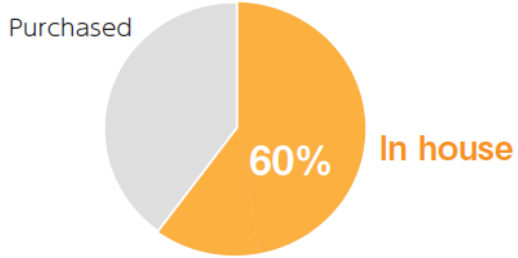
1.5M
Axcelead compound library

Lead likeness



QED: Quantitative Estimate of Drug-likeness

In-house compounds



60%
In-house compounds

Library sets for HTS

- **Diversity libraries**
  - Single library 317,000 cpds
  - Pooled library 500,000 cpds (Standard set 320,000 cpds)
- **Focused libraries** (48,000 cpds in total)
  - Target oriented (Kinase, GPCR, PPI, RNA, molecular glue etc.)
  - CNS
  - Extended rule of 5
  - PPI, Macrocycle
  - Natural product
  - Covalent
  - Biological annotation

500K
Pooled diversity library

317K
Single diversity library

✓ Axcelead offers Virtual Screening against 1.5M library for efficient hit identification

Comprehensive Assay Menu

Enzyme

- Luminescence, Absorbance, Coupling, Fluorescence, TR-FRET, AlphaScreen
- Label-free assay (Rapidfire-MS)
- ELISA
- Radiometric assay

GPCR

- cAMP assay
- Ca^{2+} flux assay (FLIPR, FDSS)
- Reporter gene assay
- Arrestin/Internalization assays
- Binding assay

Phenotype

- High content imaging assay
- Reporter gene assay, qRT-PCR
- Cell growth etc.

Protein/Protein Interaction

- TR-FRET, AlphaScreen
- ELISA
- NanoBit, NanoBRET
- Two-hybrid assay
- Biophysical assay

Ion channel / Transporter

- Ion influx assay
- Membrane potential
- Electrophysiology
- Substrate uptake
- Binding

Biophysics

- SPR
- ASMS
- ITC
- Thermal Shift
- Crystal structure

Nucleic Acids

- Biophysical assay (e.g. ASMS)
- Fluorescence probe binding
- FRET
- Cell-based assay (Reporter gene, RT-qPCR)

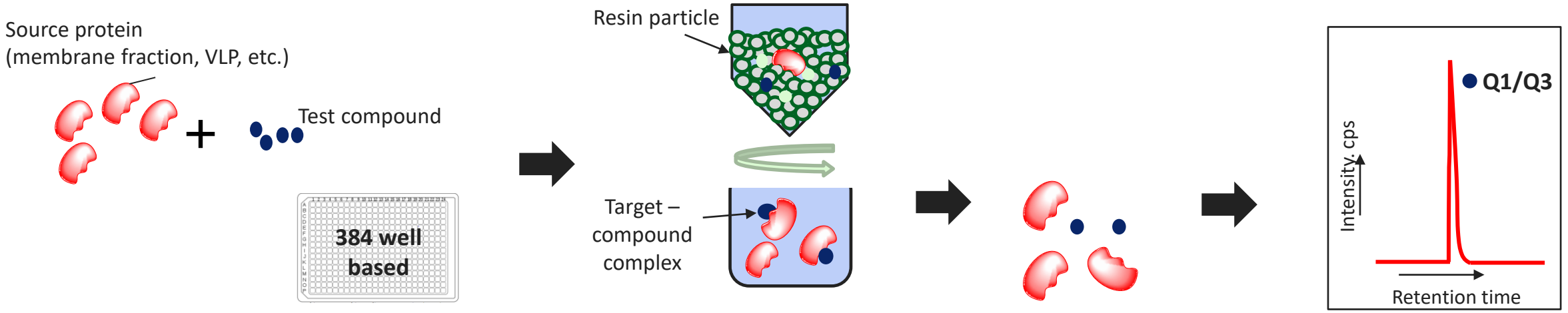
Nuclear Receptor

- Binding assay
- Cofactor recruitment assay
- Reporter gene assay
- Nuclear translocation assay

We have comprehensive assay development capability and experience. Please inquire if your assay menu of interest is not covered in this list.

AS-MS screening track records with membrane proteins

Affinity Selection Mass Spectrometry (AS-MS)



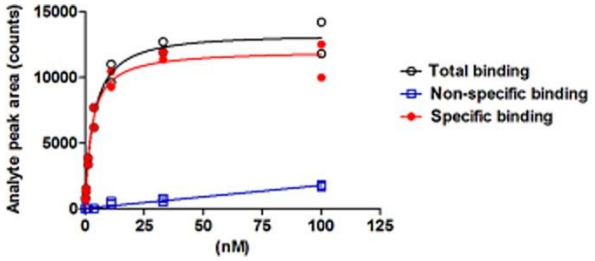
Incubation
Incubate test compound and VLP

Size exclusion chromatography
Remove unbound compounds

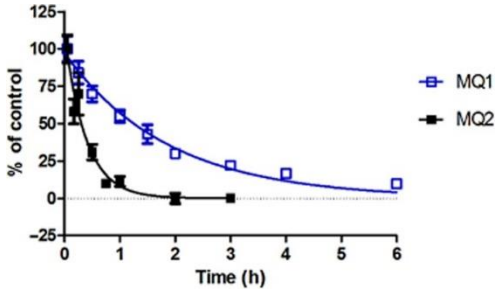
Dissociation
Separate compounds from VLP by denaturation

Detection
Identify by Mass Spectrometry

Kd determination (GPCR VLP)



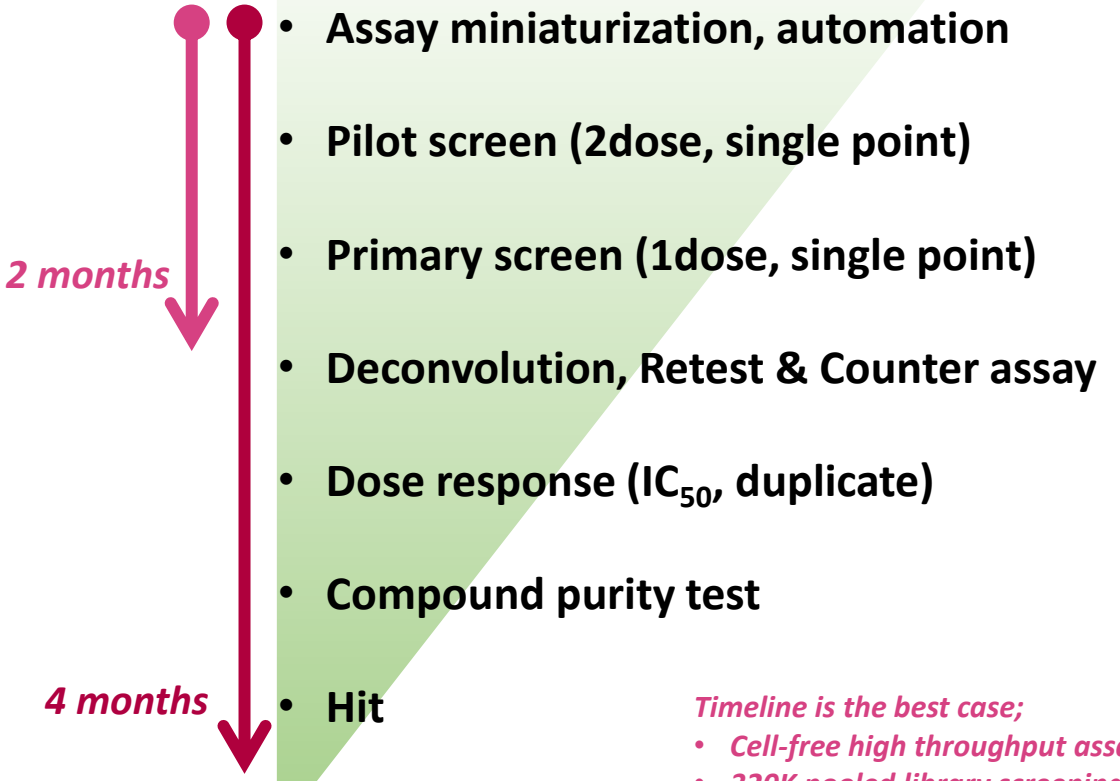
Dissociation analysis (GPCR VLP)



- We have successful AS-MS screening results using; recombinant protein, membrane fraction, VLP (Virus-Like Particle), etc.

HTS package and optional profiling items

HTS minimum package



- **Assay transfer or development**
- **Assay miniaturization, automation**
- **Pilot screen (2dose, single point)**
- **Primary screen (1dose, single point)**
- **Deconvolution, Retest & Counter assay**
- **Dose response (IC_{50}, duplicate)**
- **Compound purity test**
- **Hit**

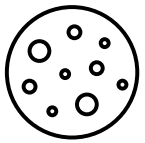
Timeline is the best case;
- *Cell-free high throughput assay*
- *320K pooled library screening*
- *No time loss for next step decision*

Optional profiling

- Virtual screening from 1.5M library
- Hit profiling and validation
  - MOA analysis, selectivity
  - Biophysics, structure analysis
  - High-throughput ADMET profiling
  - Re-synthesis
  - In vitro / in vivo follow-up assay
- Hit expansion
  - Quick similar compounds search from 1.5M library
  - High-throughput parallel synthesis
  - Medicinal chemistry

Full chemistry & evaluation capabilities to support Lead Generation

Hit / Lead compound



Design

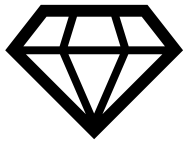
- Medicinal Chemistry
- eADME
- Hopping
- AutoDesign
- FARMING

Synthesis

- Parallel synthesis
- Late-stage functionalization
- Chiral synthesis, flow chemistry, photo chemistry
- Route and scale-up synthesis
- Purification, analysis, structure determination

Evaluation

- Compound management
- Routine assay
- Xtal, biophysics
- High-throughput ADME



Candidate compound

In-silico

- Virtual screening
- A-CODE
- AI drug discovery

A-code

A-Intelligence

Inherited assets

- Compound library
- Legacy data

1.5 million compounds

Platforms to support quick transition from Hit to Lead

Step 1 : Obtain Structure Activity Relationship (SAR)

- Related compounds search from 1.5 M compounds library
- Compounds search by both mechanical method and chemists' aspect
- Manual and parallel synthesis for SAR study (optional)

Step 2 : Determine Priority Hit Compounds

- Data acquisition of Physicochemical property by high-throughput system
- Data acquisition of ADME-Tox by high-throughput system
- Clarification of Pros and Cons of each hit compound (chemotype)

Step 3 : Expand Hit Compounds to Lead

- Core structure hopping by in-silico system (**Hopping**)#
- Jump-up SAR exploration by ultra-fast search for proprietary SAR database **(SARfer)#**
- Removal of ADME issue using accumulation of SAR data for ADME (**eADME, OptADMET**)#
- Evaluation of Ultra-large virtual library (>2.0 B) space with building blocks (**FARMING**)#

 # Axcelead original system

Proprietary in silico drug discovery tool; A-code Link here

Contact Us for Details
E-mail address / Contact form

AXCELEAD
Drug Discovery Partners

Please contact us for any questions!

E-mail
intl_contact@axcelead.com

Contact Form
https://axcelead-us.com/contact-us/

Scan to open
our contact form

We value your concerns and questions!