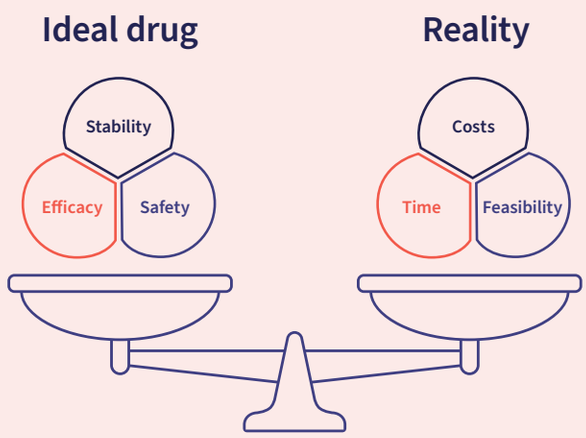
ABZENA
Moving medicine forward.

Drug Developability: the Derisker

Starting smart, finishing fast, with Abzena

Drug development is a balancing act

Designing a drug means balancing everything we'd want in a perfect candidate with everything we face in reality.

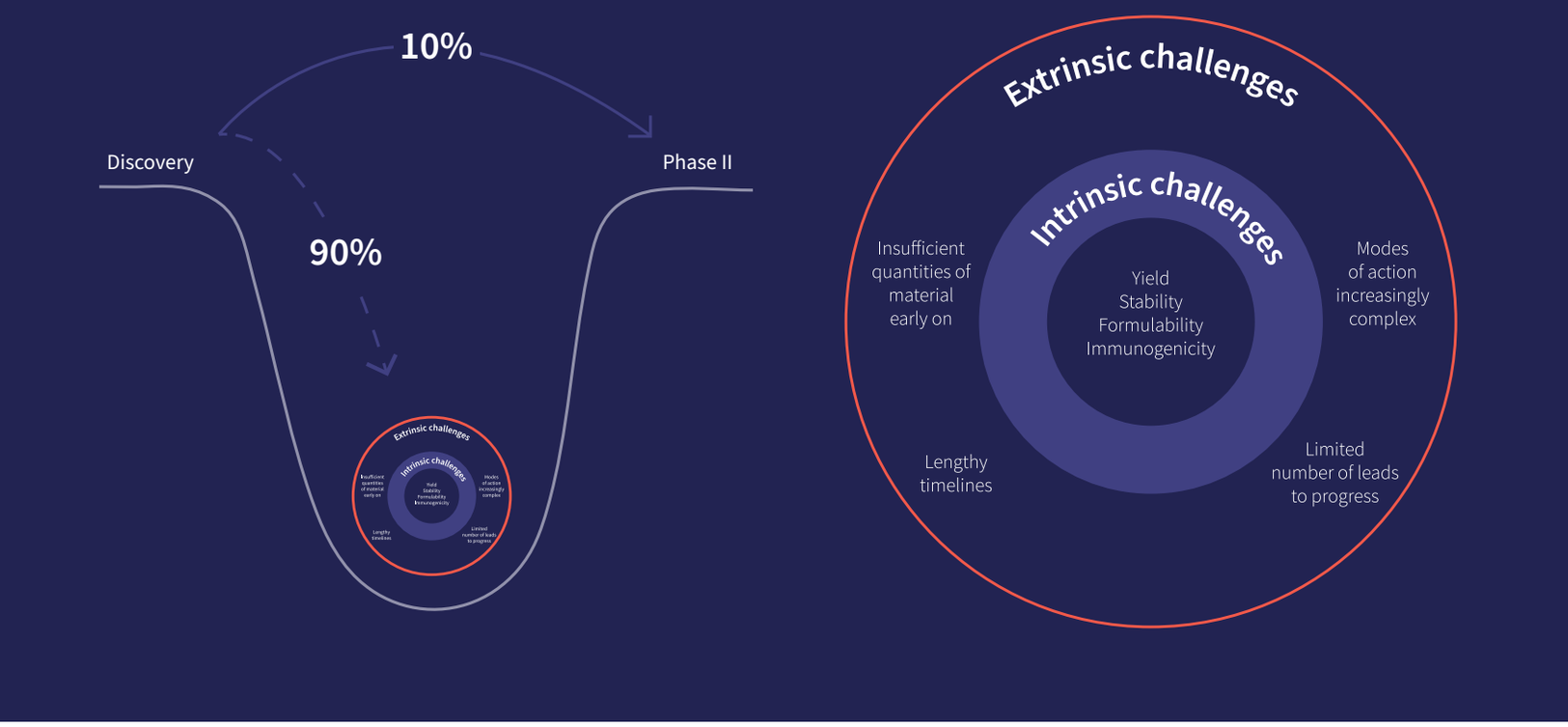


Drug development

$1-2 billion	10-15 years	90%
Average cost	Average time	Rate of failure

(Sun D et al. (2022) Acta Pharm Sin B. Jul;12(7):3049-3062)

To work towards that ideal drug we have to overcome a host of challenges and avoid falling into the "valley of death," where drugs fail between discovery and an effective proof of concept.



Balancing the scales

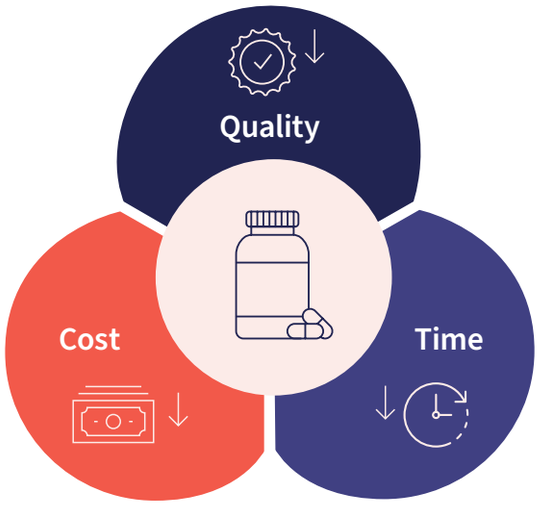
To mitigate some of the biggest risks in drug development, it's essential to gather as much information about a candidate early on to make better, more informed decisions further down the line. This is where the idea "developability" comes in.

Developability helps balance the scales of an ideal drug candidate vs the challenges of reality. To do that, we ask two simple questions:

Can we make it?

Can we make the drug as a stable compound in the required form and **quality** to treat patients?

Can we make the drug at scale, with an acceptable **cost**, within acceptable **timeframe**, with enough doses to treat the patient population?



Does it work?

Does the drug do what we expected it to do - is there a predictable **mechanism of action**?

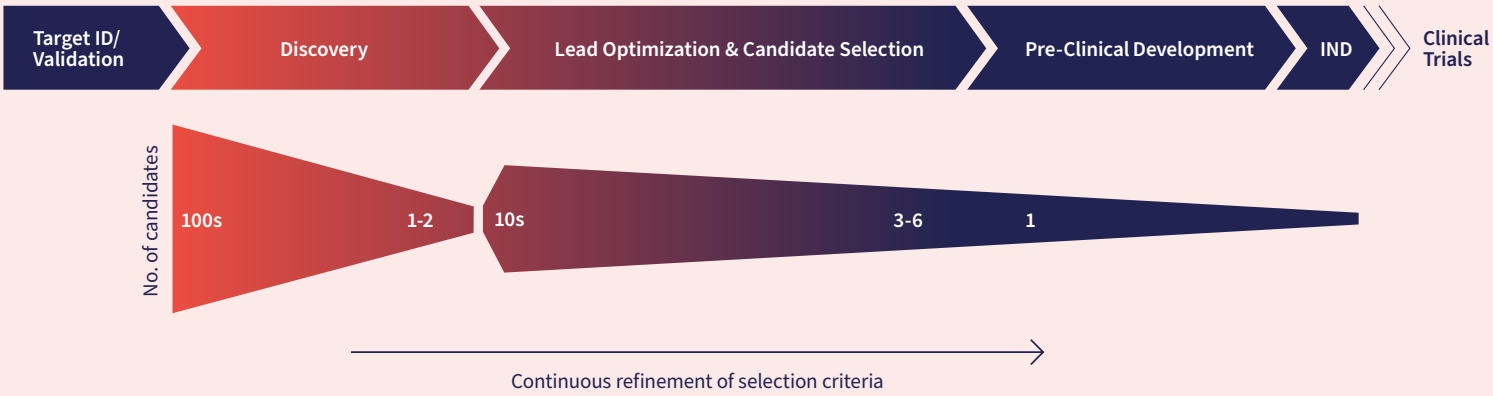
Does the drug have the desired **efficacy**?

Is the drug **safe** for the target patient population?

Developability is therefore identifying and managing risk early in development to reduce major cost, quality and time issues at later stages of manufacture and clinical evaluation.

Derisking through developability

By asking those simple questions, “Can we make it?” and “Does it work?” right from the start, we can start to whittle down candidates from hundreds to a handful. From there, we can keep refining the selection criteria, continually derisking a project and moving closer to that ideal drug.



Discovery

Hit generation followed by high throughput in silico and in vitro screening to screen out candidates with undesirable properties.

Lead Design & Selection

Candidates are designed and engineered to remove undesirable properties and introduce desirable properties.

Lead Characterization

Detailed biological and biophysical characterization of a small panel of molecules in order to select a lead candidate for progression.

Full Development & Manufacture

Comprehensive understanding of a single candidate and capability to develop, manufacture and deliver your drug for both clinical and commercial scale.

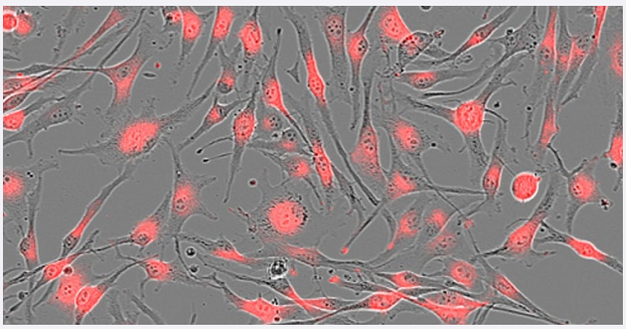
The steps to success

The more you understand about your molecule earlier, **the better.**

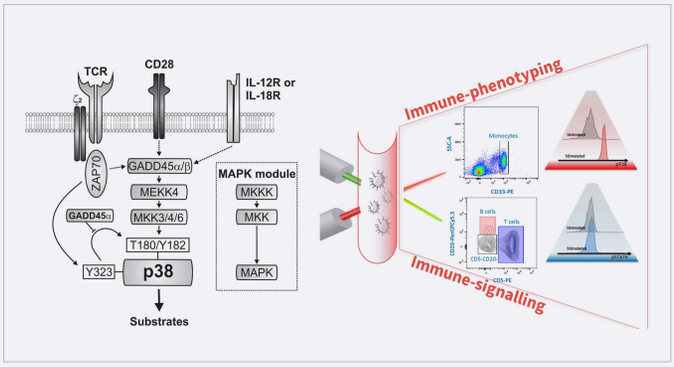
1

Binding and function

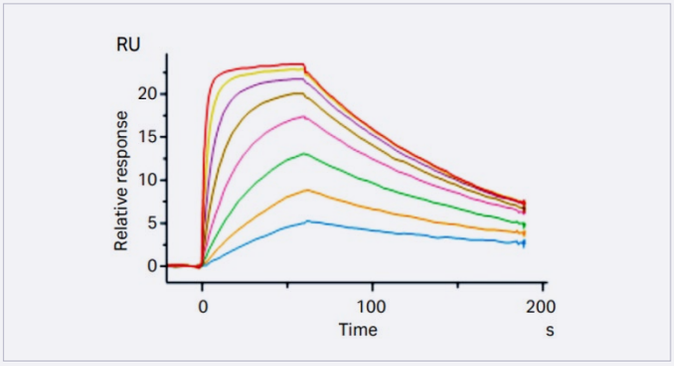
Early on we look to answer that “Does it Work?” question by understanding the functional activity and mechanism of action. This means using cell-based and biochemical assays, Fc-binding and affection function assays, along with other immunological and oncological assays.



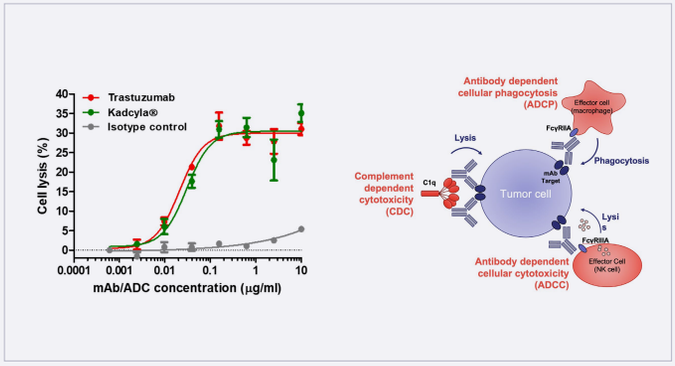
Internalization
e.g. using Incucyte®



Signaling
e.g. Phosphoflow



Binding
e.g. by Biacore™



Fc-mediated Effector Function
e.g. ADCC assay

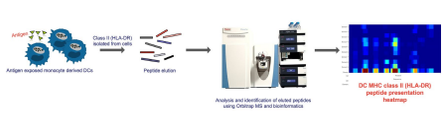
2 Immunogenicity and safety

One of the most important parts in the process is assessing how safe a candidate is and whether it interacts with the immune system in ways that could be dangerous to patient health.

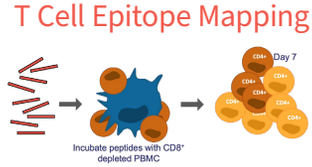
Our EpiScreen™ platform is vital here, allowing us to better select candidates, identify potential T cell epitopes and ultimately reduce MHC class II binding.

"Hot spot" identification

MAPPs (Class II)



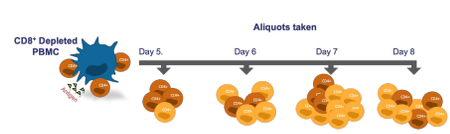
T Cell Epitope Mapping



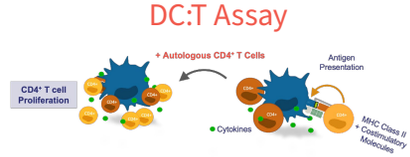
Immunogenicity assessment

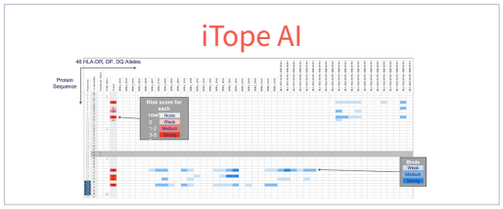
Whole molecule assessment

Time Course

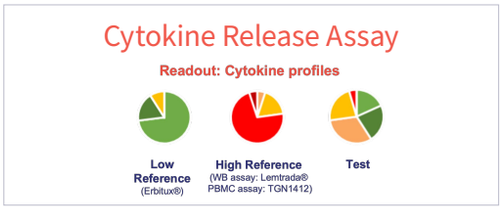


DC:T Assay





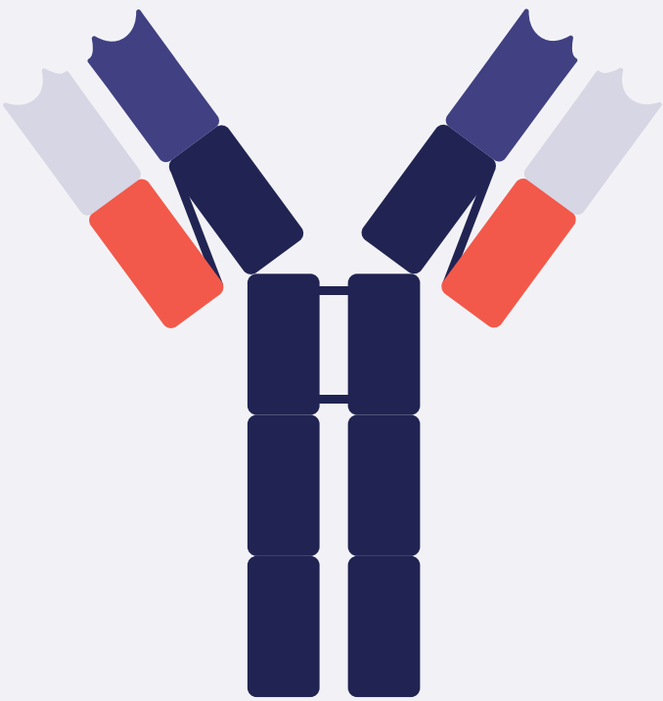
Precise regions identified for modification



Selection of lead variant(s) for development

3 Analytics and stability

A candidate is only as good as it is stable – that's why we put so much weight on in-depth analytics. Let's take a look at something like an antibody-drug conjugate (ADC) to demonstrate:



In silico analysis

- Identify potential sequence liabilities so we can engineer and de-risk the molecule

Variant selection and biophysical analysis

- Aggregation and thermal stability
- Pharmacokinetics
- Chemical stability
- Impact of PTMs and charge

Conjugate characterization and linker-payload analysis

- Serum stability analysis
- Pharmacokinetics sample analysis

Choosing your developability package

Now you know more about what goes into the developability process at Abzena, what exactly can you get? Well, we offer both pre-defined and tailored work packages so you can get exactly what your project needs.

Details	Variants	Material required	Estimated length of work
Early stage micro-developability assessment			
• In silico developability and immunogenicity assessment • 3-Buffer Pre-screen (Tm, Tagg) • Stability (freeze-thaw, heat, and low pH stress) • Polyspecificity and self-association propensity	5–10+	<5 mg	4 weeks
Later stage developability assessment			
• Pre-formulation and aggregation study • Freeze-thaw and thermal stability studies • Forced degradation studies	3–5	~50 mg	6–8 weeks Assumes a typical study concentration of ~5 mg/ml. Higher study concentrations will require more sample
Biological and functional assessment			
• Target-mediated binding and function – off-the-shelf or developed to suit novel mode of action • Fc-mediated binding and function • ADC function – cytotoxic or novel mode of action	3–5	2–5 mg	6–8 weeks Depending on mode of action and assays chosen
Immunogenicity and safety risk assessment			
• In silico immunogenicity assessment • Assessment of immunogenicity risk (EpiScreen™) • Assessment of cytokine release-mediated toxicity (Cytokine Screen™)	3–5	5–10 mg	8 weeks Depending on assays chosen and number of donors selected

Ready to derisk and develop your next biologic with us?

Get in touch and let's work together to move medicine forward faster.

ABZENA

Moving medicine forward.