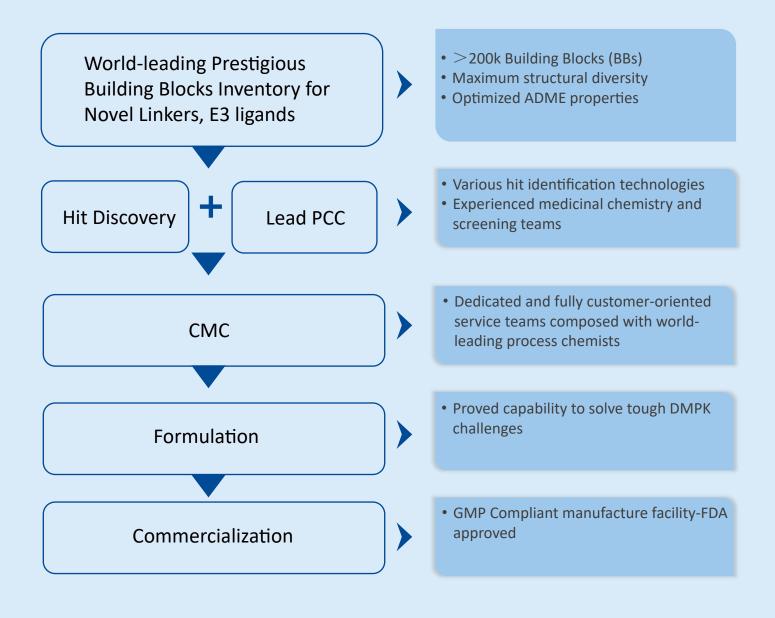
TPD Capability at PharmaBlock

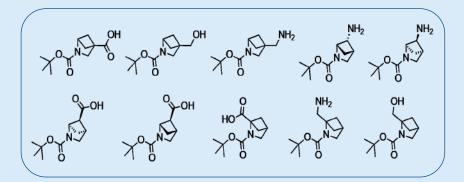
From hits to clinical candidates to commercial products



Building Blocks to Inspire and Accelerate TPD Discovery

- Efficient linker for optimal degradation, selectivity, ADME properties
- PB's prestigious BB collections significantly enhance efficiency and success rate

Unique Spiro, Bridge ring BB collections for accurate confirmation control and ADME optimization



BocNNH	O HN NH	MeO-NH	ON NH
F_NH	F NH	F	BocN
HN NH	o NH	BocN_NH	BocN

Exit Vector	Availability	
-СООН	> 200	
-ОН	> 200	
-NH2	> 200	
Alkyl	> 200	
Azide	> 100	
-X	> 100	

Pharma Block

Wide Selection of CRBN and VHL Ligands

- 2500+ / 700+ of CRBN/VHL ligands designed, respectively
- One of the largest collections for novel TPD design and screening
- Grams to hundreds of kg scale in stock for most commonly used ligands

Enabling prompt material supply for early discovery and development

Early Discovery to PCC Identification

New Ligand PROTAC Identification

Hit to Lead



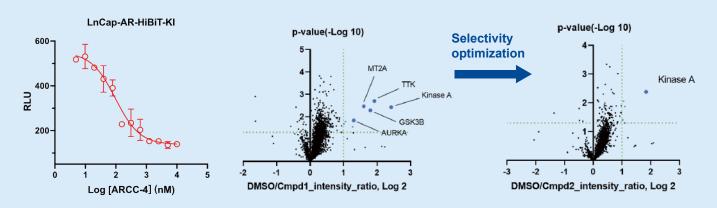
Lead Optimization

- DELT
- FBDD
- Rational Design

Discovery Chemistry

- Medicinal Chemistry Expertise
- CADD/Al Support

Supported by cascade of crucial screening and characterization assays



- Multiple-interface biophysical assays for binary and ternary binding elucidation
- High efficient cell based HiBiT-Nanoluciferase—96/384 well plate screening system supporting SAR studies
- Proteomics based degradation selectivity evaluation platform, critical to de-risk potential off-target degradation and toxicity

Formulation Solutions Overcoming DMPK Challenges

Physiochemical Characteristics
Beyond Rule of 5

Major
Challenges
for TPD APIs

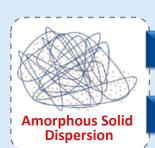
2 Transport and Absorption Limitations
Poor DMPK Properties

3 Poor Oral Exposure and Bioavailability

Formulation strategies







Hot Melt Extrusion

Spray Drying





- Polymers and additives
- Maximize the drug loading in ASDs
- Dry Granulation and Direct Compaction
- Excipients optimization

One-stop Solutions for TPD

Proved CMC Capability Supported by Dedicated Team

Problem solving capability for challenging TPD API: Injection

- 7 chiral centers, M.W. > 1000
- Solid state study showed no crystalline
- API produced as HCl salt in amorphous form
- Solvent residue issue
- High hygroscopicity, packing and storage difficulty
- Purification difficulty
- 50 g demo batch (5 months)
- 120 g GLP toxic batch (1 month)
- 500 g non-GMP batch (3 months)
- 700 g GMP batch (3 months)
- IND application approved by FDA, 2022.10
- 1.5 kg GMP batch (2023.02 started)

Challenges

Accomplishments