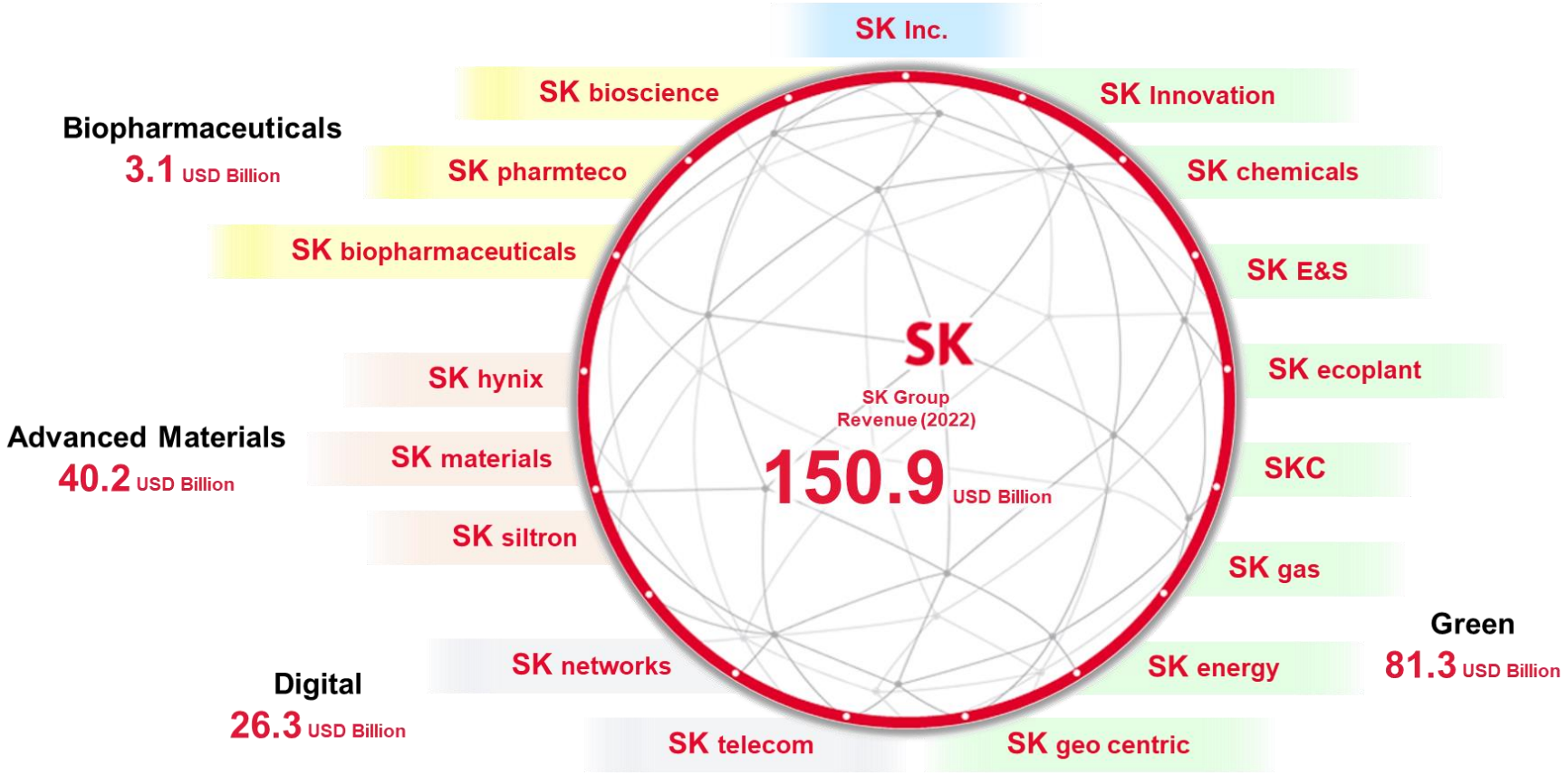
SK life science labs

a subsidiary of SK biopharmaceuticals

Discovering Better Medicines through Target-Centric TPD Powered by MOPED™ Glue Platform

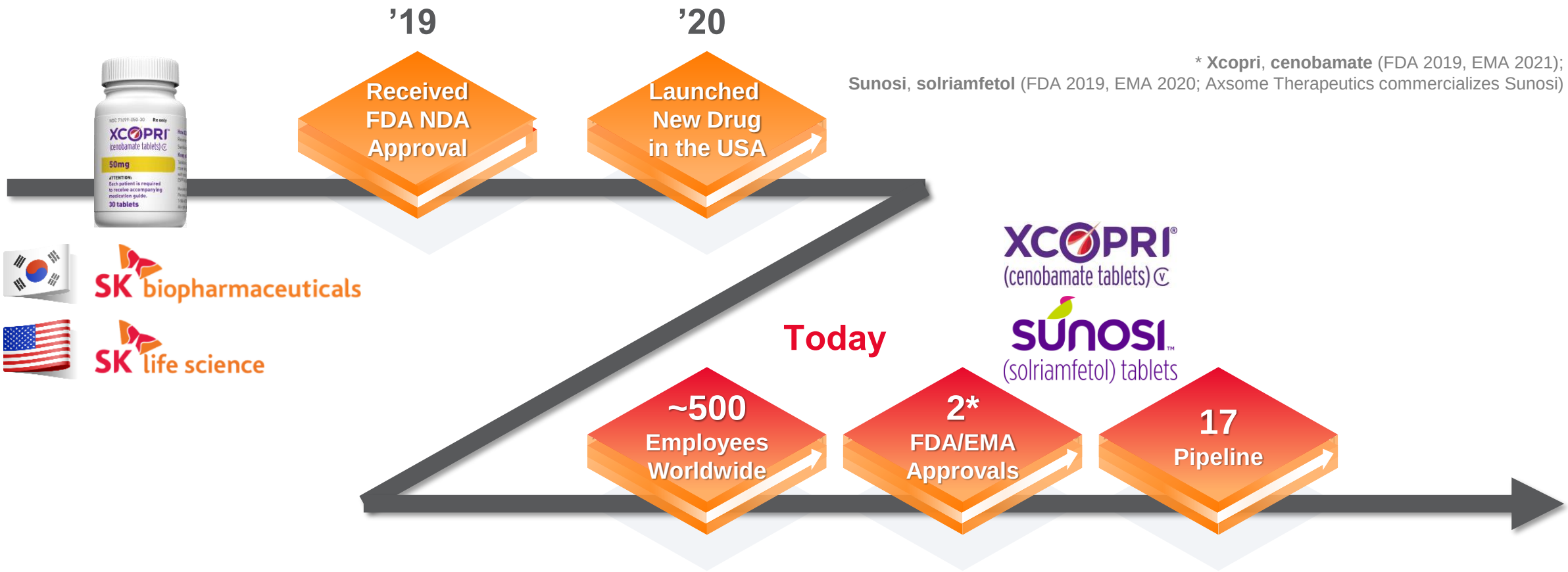
SK Group at Glance

SK Group invest in game-changing business and nurture them for long-term success



SK Biopharmaceuticals (SKBP)

The first & only Korean company to independently develop & commercialize a new drug in the USA



* **Xcopri**, **cenobamate** (FDA 2019, EMA 2021);
Sunosi, **solriamfetol** (FDA 2019, EMA 2020; Axsome Therapeutics commercializes Sunosi)

SK Biopharmaceuticals (SKBP) & Subsidiaries

From bench (Korea) to market (the USA)

Headquarters

SK biopharmaceuticals

Executes company-wide strategies, develops businesses and identifies new drug candidates

- Drug Research Center
- Cancer Research Center
- Global Business Development
- R&D Innovation Department
- Corporate Strategy

Subsidiaries

SK bio-pharm tech

Explore new business opportunities and obtains relevant licenses in China

- Business Development
- Discovery Support
- Regulatory Activity

SK life science labs

Performs global R&D of TPDs for oncology and immunology

SK life science

Performs global clinical development and marketing directly

- Clinical Development
- Operation Office
- Project Management
- Quality Assurance
- Regulatory Affairs

SK Life Science Labs (SKLSL) & Leadership

120 years of R&D leadership in drug discovery & development

2 Integrated Platforms

2 Development Candidates

5+ Discovery Programs

40 Scientists

Zhihua Sui, Ph.D.
Chief Scientific Officer

30+ years in drug discovery and advancement of >20 compounds to the clinic in multiple therapeutic areas. Previously VP of Chemistry and Strategic Outsourcing at Agios, and Senior Scientific Director/Senior Janssen Fellow at Johnson & Johnson. Studied and practiced medicine in China before becoming a chemist

Corey Strickland, Ph.D.
VP, Molecular Technology

25+ years in building structural biology drug discovery platforms across multiple disease areas. Previously Senior Principal Scientist at Merck

Helai Mohammad, Ph.D.
VP, Head of Biology

12+ years of experience in cancer biology and leading oncology drug discovery teams. Previously Senior Scientific Director at GlaxoSmithKline

Larry Jolivette, Ph.D.
VP, Head of DMPK/Safety

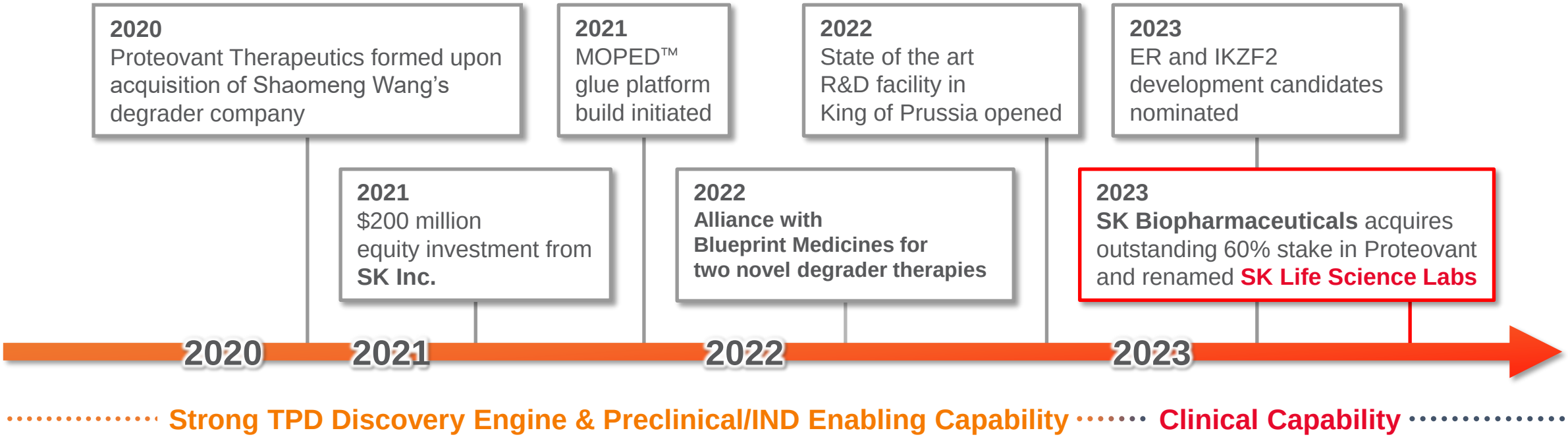
20+ years in DMPK teams across modalities and therapeutic areas at GSK, supporting preclinical and translational DMPK strategies

Winston Wu, Ph.D.
VP, CMC

30 years in process development and manufacturing. Previously VP of Chemical Research, Development & manufacturing at Lexicon

History of SKLSL

Discovering & developing medicines to improve the lives of patients with life-altering diseases



Why targeted protein degradation?

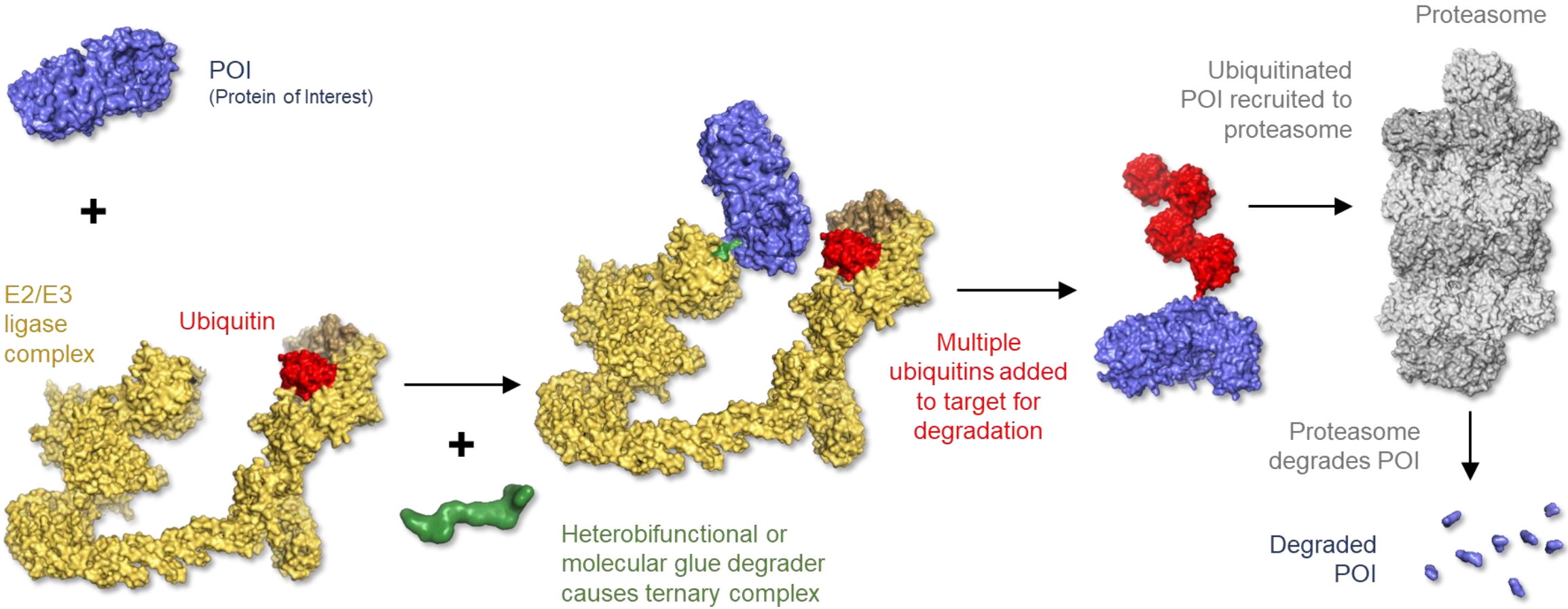
Protein degradation offers advantages to improve clinical outcomes

TPD
(Targeted Protein Degradation)

1	**Impact all protein's functions**	Target enzymatic and non-enzymatic roles
2	**High selectivity potential**	Opportunity to target less conserved regions of the protein of interest vs related family members
3	**Expand target space**	Target historically "undruggable" proteins
4	**Event-driven pharmacology**	Catalytic mechanism reduces the drug concentration required at site of action

Targeted protein degradation

Unlocking a vast opportunity to expand the druggable proteome

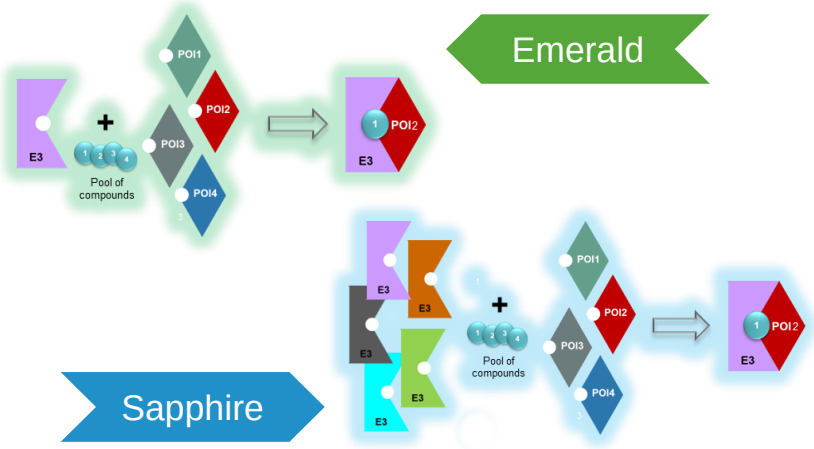


SKLSL TPD capabilities powered by innovative platform

Proprietary drug discovery & preclinical development engine

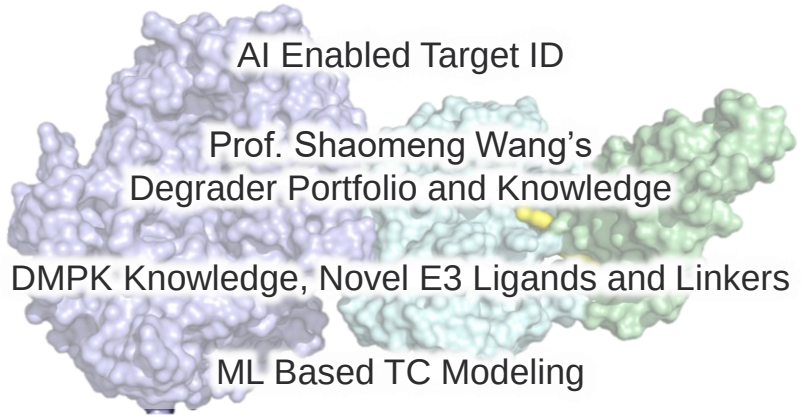
MOPED™ Glue Platform

Drug discovery platform
to find molecular glue degraders
to increase access to difficult targets



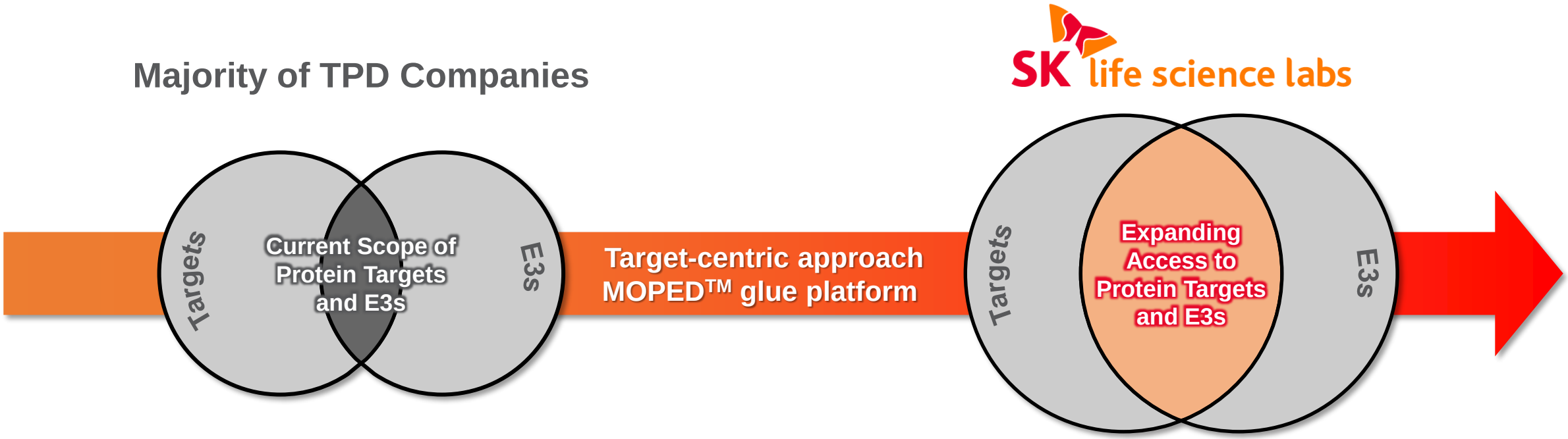
Core TPD Platform

Fully integrated cross-functional expertise
from target identification
through preclinical development



SKLSL differentiated approach breaks through limits of TPD

MOPED™ expands SKLSL core TPD capabilities to include E3 & target agnostic glues

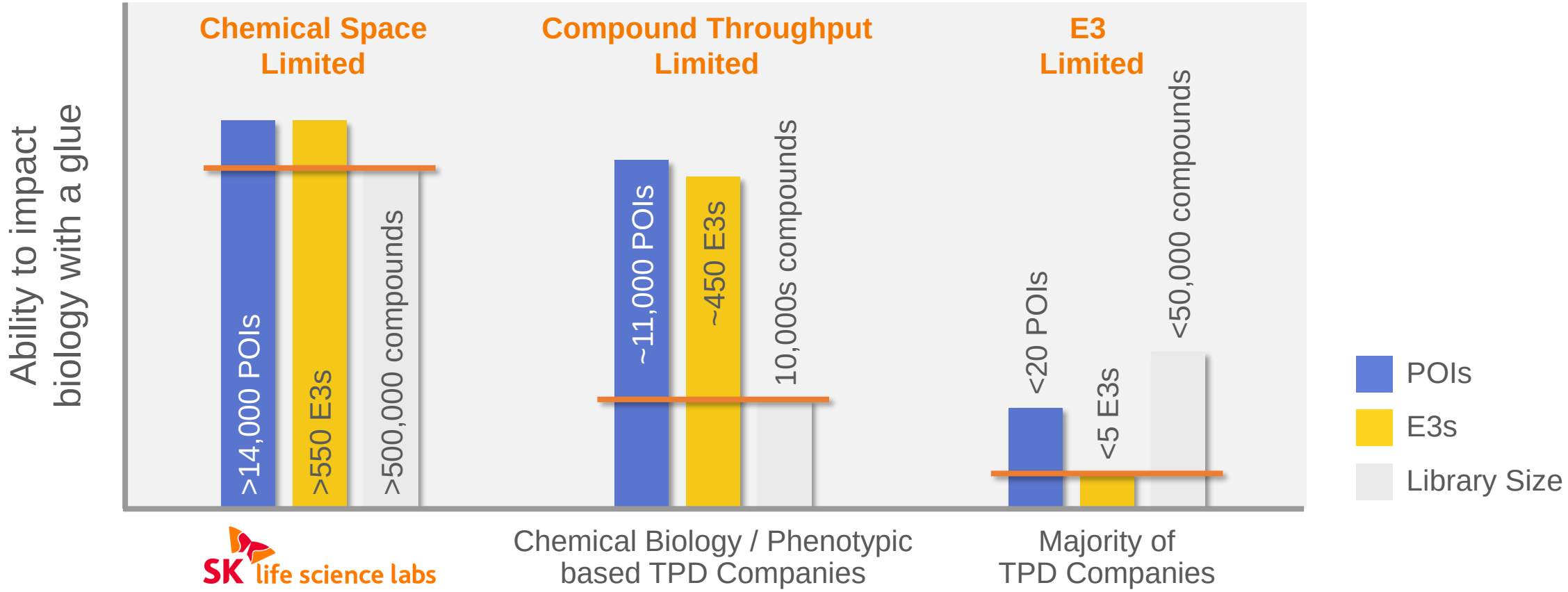


*Heterobifunctional TPD companies primarily use **CRBN** and **VHL**, Molecular glue TPD companies predominantly exploit **CRBN** or **phenotypic discovery***

SKLSL target-centric approach and MOPED™ platform expands access to a wider range of targets and E3s

SKLSL expands access to targeted biology accessible by TPD

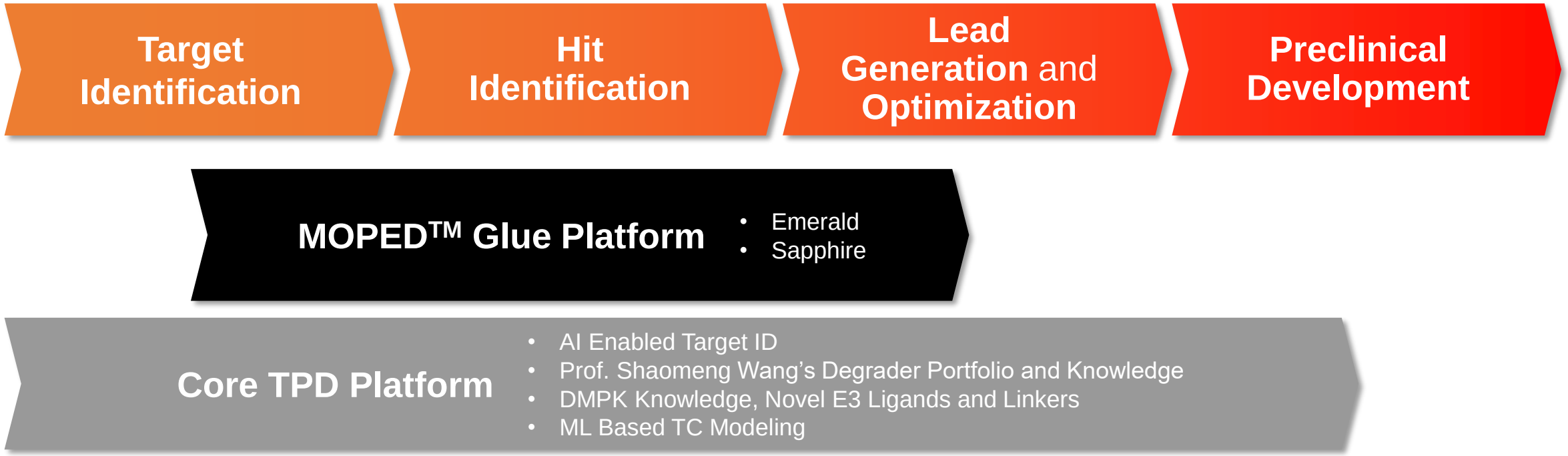
MOPED™ enables target & E3 agnostic glue discovery at scale



MOPED™ Glue Platform

Differentiated platforms & capabilities enable each phase of discovery

MOPED™ enables molecular glue target identification through lead optimization



MOPED™ is an innovative platform for glue discovery

MOlecular **P**roximity **E**nabled **D**etection (MOPED™)

Emerald

A highly sensitive biochemical workflow to discover glues from defined drug target and pre-selected E3s

Sapphire

An E3 agnostic mass spectroscopy workflow to discover glues against defined drug targets

Molecular Glue Discovery

INCREASE ACCESS TO TARGETS

Targeting structured and unstructured regions

INCREASE NUMBER OF LEADS

Multiplexing compounds, targets, and/or E3s

BROADEN BIOLOGICAL IMPACT

Exploring potential biological functions beyond TPD

EXPAND E3 OPPORTUNITIES

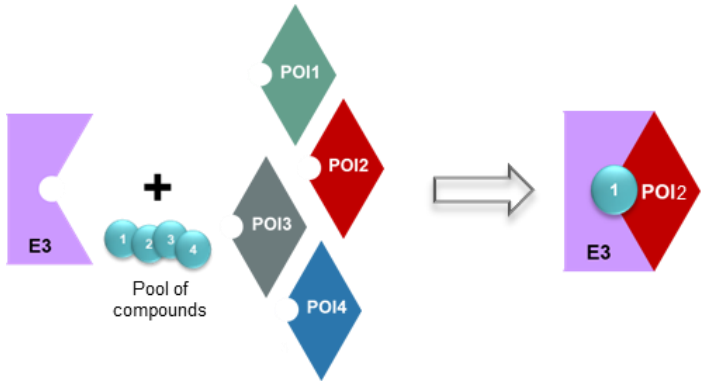
Known E3s, target matched E3s, and/or E3 agnostic

Emerald: Biochemistry designed for molecular glue discovery

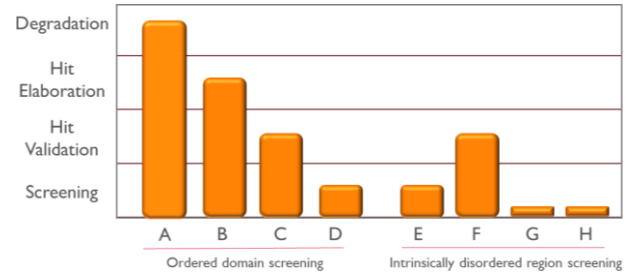
Highly Sensitive design to find leads for chemical optimization

- **Glue screen to measure ternary complex formation**
  - Biochemical assay format with sensitivity to detect <2 nM of ternary complex
  - 10-20 E3s are tested individually and include widely used E3s and target matched E3s
  - Library of E3s expanding throughout 2024
  - Pools of compounds and POIs are tested for efficient 1536-well screening of a >500,000 compound library
- **8 targets in screening through hit follow-up**
- **Oncology target A was screened, yielding molecular glues that demonstrate degradation**
  - Screening start to validated hits in 2 months
  - Validated hits to degradation in 1 month

MOPED™ Emerald



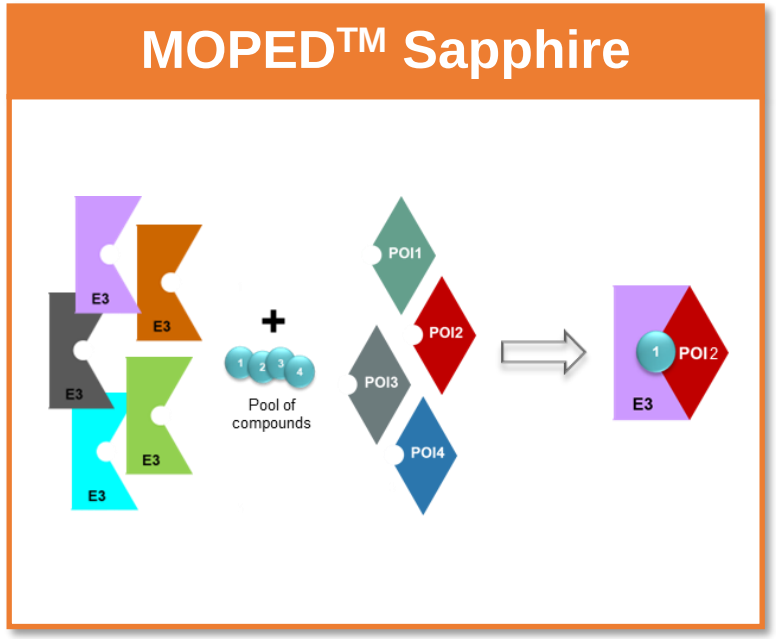
Progressing Hits from Targets



Sapphire: Molecular glue screening in a cellular context

Expanding target & E3 opportunities

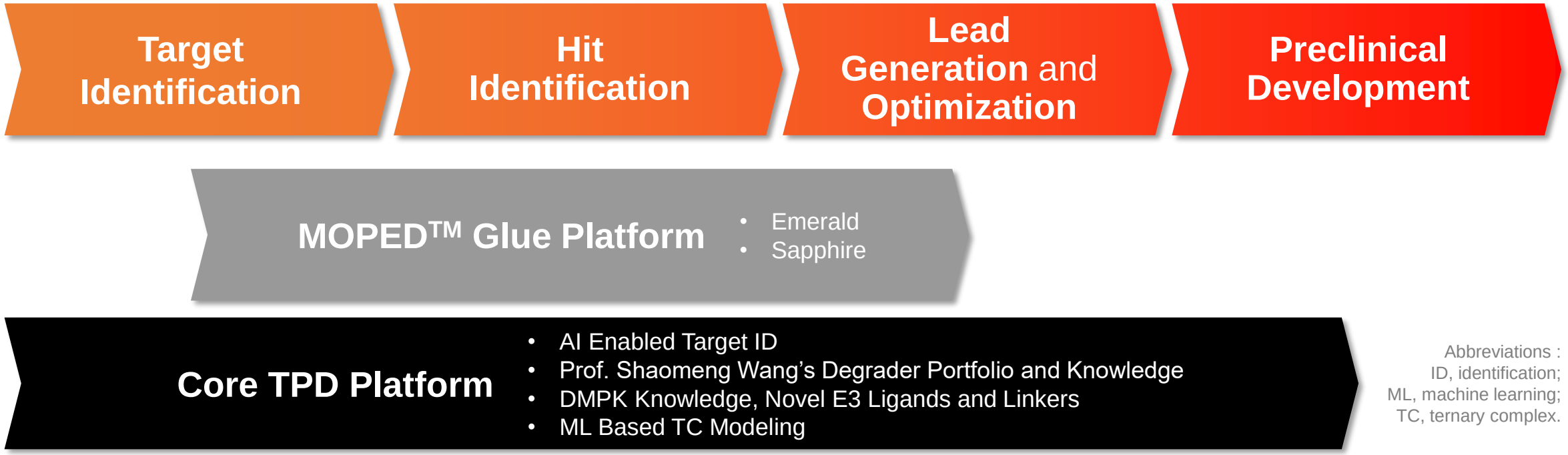
- **Mass spectrometry assay to detect ternary complex formation**
  - Assay format identifies ternary complexes in a cellular context
  - Mixtures of E3s and POIs are tested for efficient screening of >500,000 compound libraries
  - Sensitivity to detect 10 μM EC50 ternary complexes
  - High-throughput 384 well assay
- **Leverages proprietary high-throughput proteomics**
- **Ternary complexes identified using Emerald confirmed in cellular context by Sapphire**



Core TPD Platform

Differentiated platforms & capabilities enable each phase of discovery

Core TPD capabilities are leveraged from target identification through preclinical development



Abbreviations :
ID, identification;
ML, machine learning;
TC, ternary complex.

AI enabled approach provides continuous flow of target opportunities

Target identification & prioritization

Data Aggregation

More than 40 sources of data are accessed containing >60 million data points

depmap | Cancer Dependency Map
ClinVar
UniProt
TCGA
CCLE Cancer Cell Line Encyclopedia
intOgen
OncoKB MSK's Precision Oncology Knowledge Base
STRING
HGNC HUGO Gene Nomenclature Committee

Data Structuring

Millions of data points aggregated into ~2TB and structured into 5 different databases

AI Optimization of Target Features

Proprietary AI trained on well validated targets using **~250 numeric and categorical features**

Gene	Feature1	Feature2	Feature3
A			
B			
C			

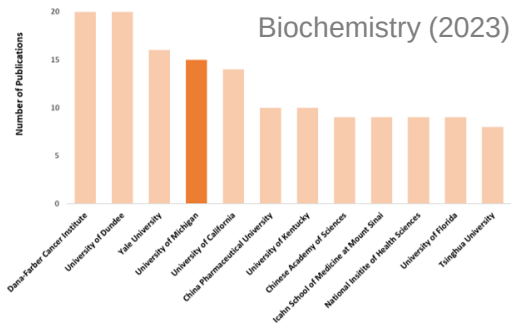
Filtering to Select Candidates

The AI model ranked **>20,000 proteins** and identified **>150 potential first-in-class targets**

In-licensing Prof. Shaomeng Wang's degrader portfolio & knowledge

- Greater than 20 degrader patents licensed to SKLSL

Research



UNIVERSITY OF MICHIGAN

Top 5 Ranking
among all degrader publications

Shaomeng Wang

Professor of Medicine, Pharmacology and Medicinal Chemistry, University of Michigan

Business

proteovant THERAPEUTICS

亞盛醫藥 Ascentage Pharma

ASCENTA THERAPEUTICS

ONCOFUSION THERAPEUTICS

Medsyn Biopharma

Renowned Entrepreneur
co-founded 5 companies

Professor Shaomeng Wang founded Oncopia Therapeutics, which was acquired by Proteovant and now renamed SKLSL

The combination of DMPK database, novel E3 ligands & linker libraries

Lead generation & optimization

Novel E3 Ligand and Linker Libraries

>5000 heterobifunctional degraders

Type of compound	Number of unique compounds (chemotypes)
Linker	>1400 (~450)
VHL ligand	>100 (~15)
CRBN ligand	>900 (~110)
Other E3 ligand	>15 (~15)

Diverse DMPK Database

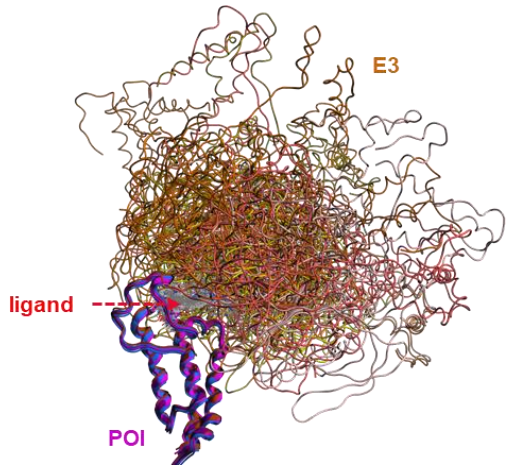
DMPK data for >900 unique heterobifunctional or molecular glue degraders from 6+ programs

Screening assay	Number of unique compounds
Plasma protein binding	>300
Metabolic stability	>600
Mouse PK	>300
Rat PK	>250

Proprietary machine learning based ternary complex modeling

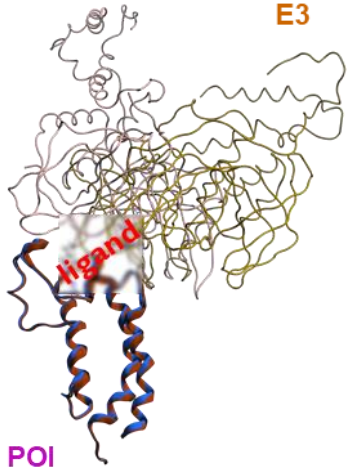
Lead optimization

Possible Ternary Complexes



Protein-protein docking + ligand constraints
Ternary complex modeling packages suggest 100s of candidate poses

Probable Productive Complexes



Accuracy	Project 1	Project 2
Predicting TC formation	75%	80%
Predicting Degradation	76%	83%

Identify unique poses of active compounds
Machine learning model was validated with retrospective analysis of two independent projects

Pipeline

SKLSL Current Focus: Oncology & Immunology

SKLSL programs and platforms are well positioned for partnering

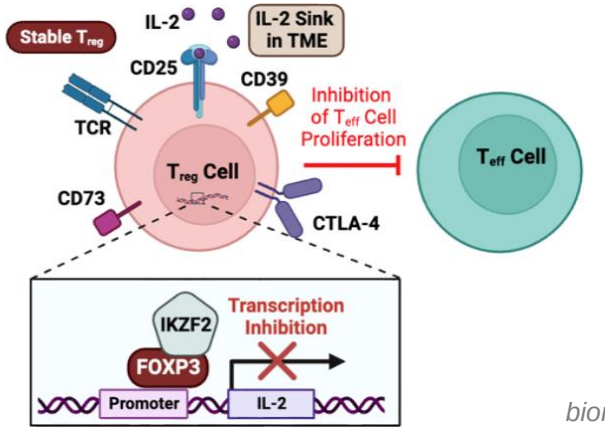
Program	Disease Area	Discovery	Preclinical
IKZF2	Solid Tumors	PVTX-405	
ER	HR+ Breast Cancer	PVTX-321	
p300	Oncology		
STAT3	Immunology, Oncology		
SMARCA2	Oncology		
Heterobifunctional Target	Oncology		
Molecular Glue Target	Oncology		

PVTX-405 : Best-in-Class IKZF2 Degrader

GLP-Tox Scale-Up Ready Orally Available IKZF2 Molecular Glue Degrader for Solid Tumors

IKZF2 (Helios)

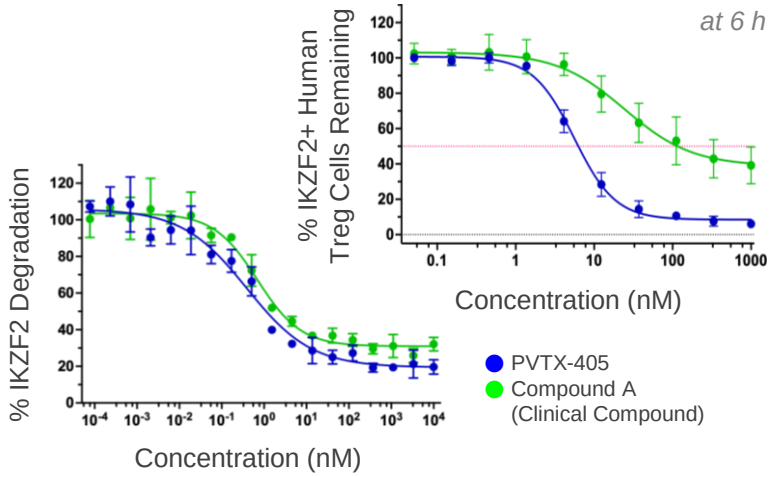
- Stable immunosuppressive activity of Tregs in TME requires IKZF2 expression
- IKZF2 degradation destabilizes Tregs and activates Teffs
- ~450,000 patients with solid tumors (US) with up to 100,000 predicted to respond to IKZF2 MoA



biorender.com

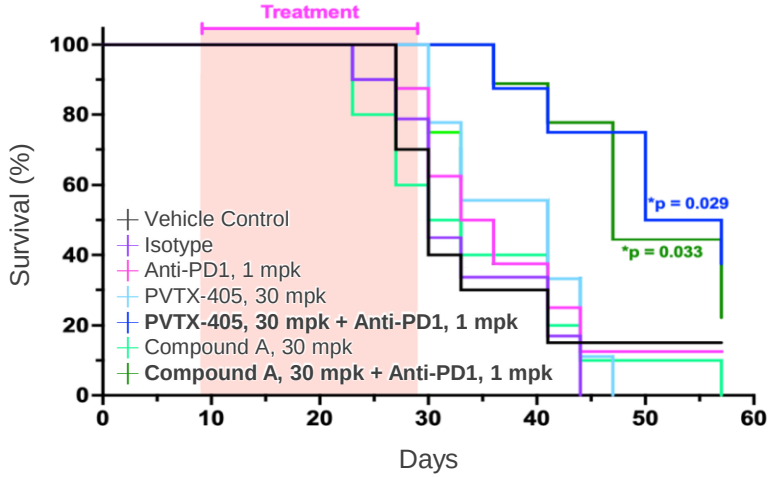
IKZF2 Molecular Glue Degrader

- Rapid, potent, and selective IKZF2 degrader for immuno-oncology with **improved off-target activity against SALL4 (10X)** and **improved hERG IC50 (5X)** (vs Compound A)
- **Orally bioavailable** and **low clearance** across species (mouse, rat, and monkey)



In Vivo PoC & Non-GLP Tox Completed

- **Significant increase in CRs** (4/10) in the combo with anti-PD1 in syngeneic mouse model compared to Compound A + anti-PD1 (1/10)
- **Favorable** (non-GLP) **safety margin** in rat and monkey DRF studies

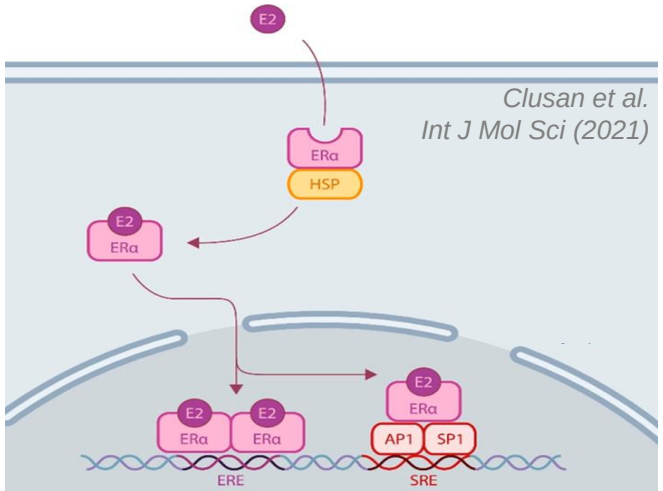


PVTX-321 : Best-in-Class Estrogen Receptor Degrader

GLP-Tox Scale-Up Ready Orally Available ER Heterobifunctional Degrader for Breast Cancer

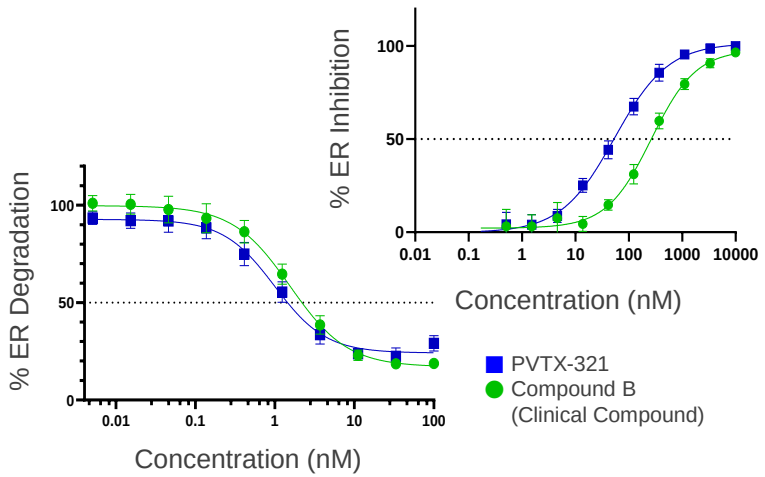
Estrogen Receptor (ER)

- Validated oncogenic target in breast cancer
- ER pathway suppression leads to inhibition of cancer cell growth
- 70-80% of breast cancers are ER+ with incidence of >180,000 cases per year (US)



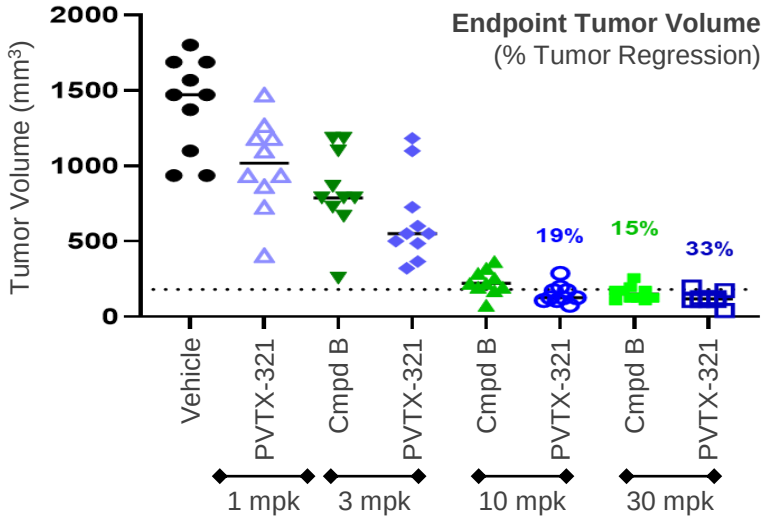
ER Heterobifunctional Degrader

- Potent and selective degrader of wild-type ER and clinically relevant mutations with **enhanced antagonistic activity** (vs compound B)
- **Orally bioavailable** and **low clearance** across species (mouse, rat, dog, and monkey)



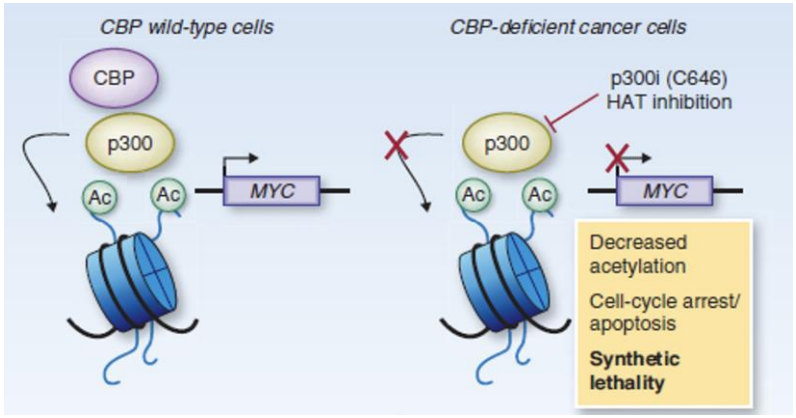
In Vivo PoC & Non-GLP Tox Completed

- **Enhanced tumor regression** in CDX model of breast cancer (vs compound B)
- **Favorable** (non-GLP) **safety margin** in rat and dog DRF studies

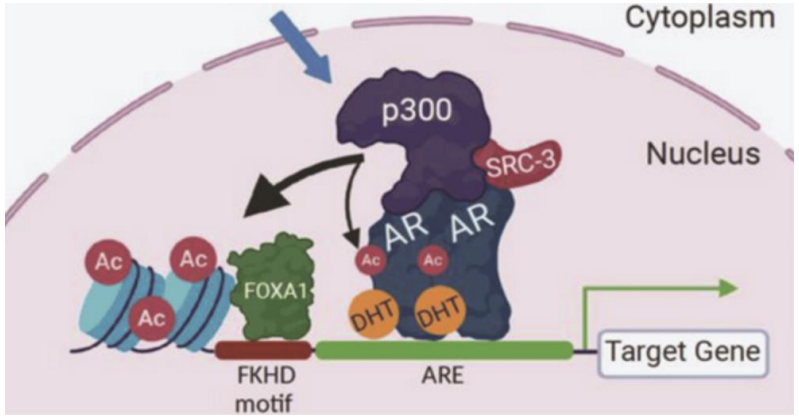


Discovery: First-in-Class p300 Degrader

Orally Available p300 Selective Heterobifunctional Degrader for CBP Mutant Cancer and mCRPC



C Kadoch et al., Cancer Discovery (2016), AR Waddell et al., Cancers (2021)



p300/CBP Regulate Histone Acetylation & Gene Expression

Selective Growth Inhibition of CBP mutant Cancer Cells

Tumor Regression in Prostate Cancer CDX Model

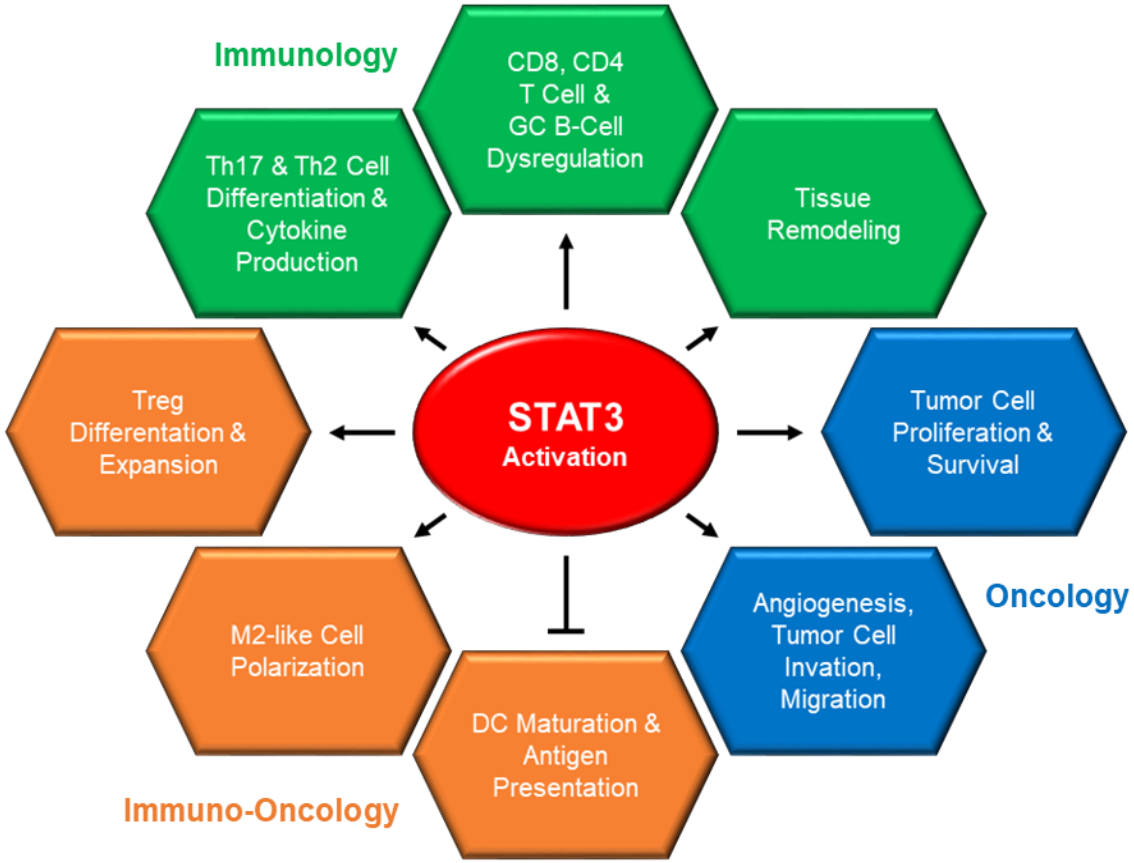
Orally Bioavailable & Low Clearance

Over 100X Improved Margin in HemeTox Assay (vs Clinical Compound)

Potential to treat >20,000 AR+ mCRPC as well as >20,000 CBP mutant liquid and solid tumors (US incidence per year)

Potential Best-in-Class STAT3 Degrader

STAT3 Heterobifunctional Degrader for Immunology & Oncology



STAT3 is Validated Target for Immunology & Oncology

Potent & Selective STAT3 Heterobifunctional Degrader

5X Enhanced Potency (vs KT-333)

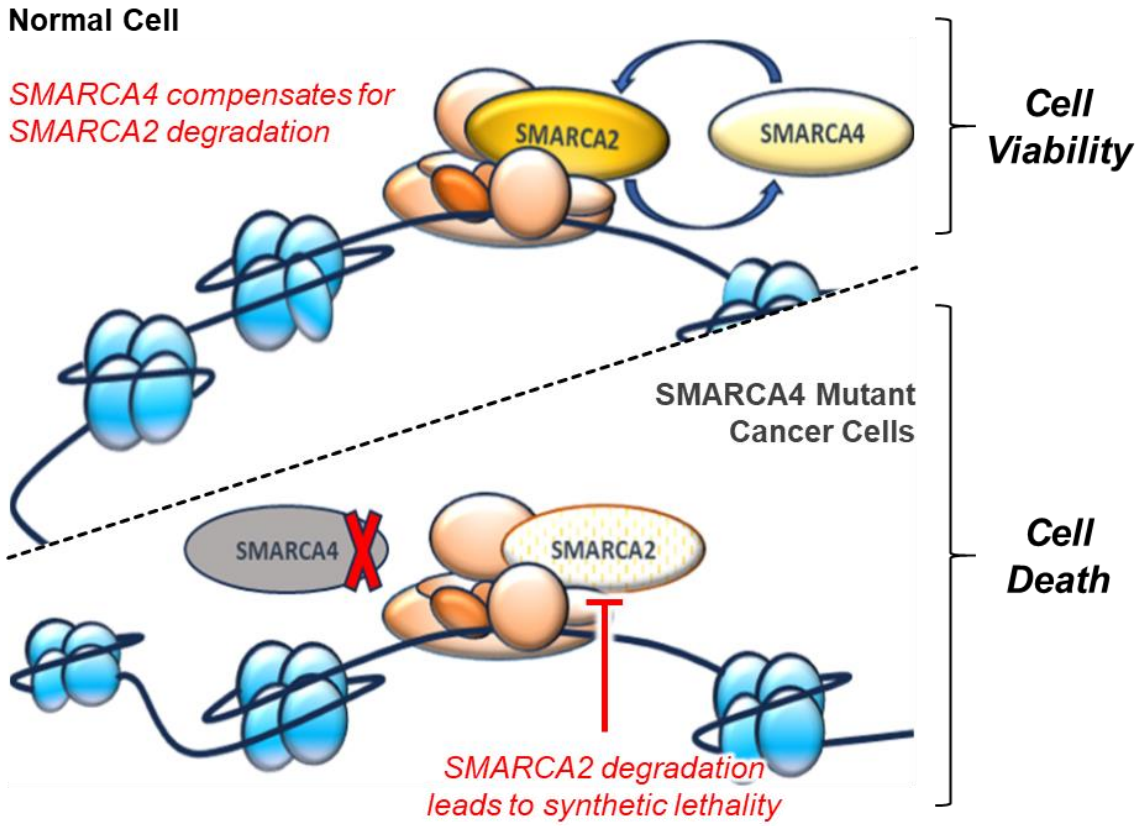
Lower Plasma Clearance (vs KT-333)

Durable STAT3 Degradation in Mice and Tumor Regression in CDX Model

Potential to treat >250,000 patients (US) across immunology and oncology

Discovery : Best-in-Class SMARCA2 Degrader

Orally Available SMARCA2 Selective Heterobifunctional Degrader for SMARCA4 Mutant Cancer



SMARCA2/4 Regulate Chromatin Accessibility & Gene Expression

Rapid, Potent & Selective SMARCA2 Heterobifunctional Degrader

Selective Growth Inhibition of SMARCA4 Mutant Tumors Representing up to 65,000 cases per year (US)

Orally Bioavailable & Low Clearance

Over 90% SMARCA2 Selective Degradation in Mice (P.O.)

Three Structurally Diverse Series of Heterobifunctional Degraders

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jchung1218@sk.com

Thank You