

CDD **WEBINAR**

Targeted Protein Degradation: New Modalities and Techniques

LIVE

Thursday, June 20 2024

8:00 AM (PDT) | 11:00 AM Eastern (EDT) | 4:00 PM (BST)



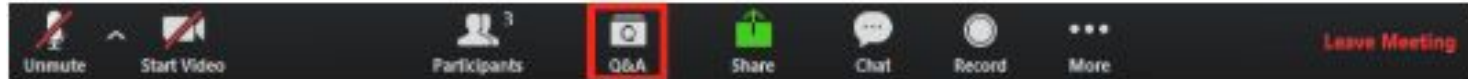
BERNHARD FASCHING, PHD
VP Chemistry, Monte Rosa Therapeutics



BENEDICT CROSS, PHD
CTO, PhoreMost Therapeutics

Do you have a question to ask our panel?

Open the **ZOOM Q&A**
type in your question during the webinar



We will reserve time and answer as many questions as we can at the end

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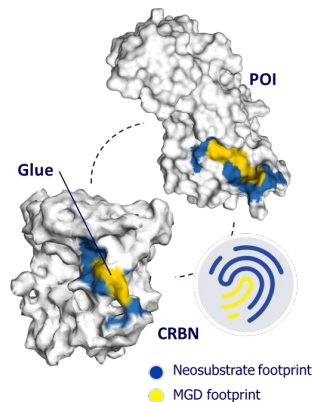
Bernhard Fasching, PhD

VP Chemistry @ Monterosa Therapeutics

- PhD in Total Synthesis @ MPI KoFo Mülheim
- PostDoc in Glycoprotein research @ Memorial Sloan Kettering in New York
- Drug discovery scientist and project leader at Hoffmann-La Roche Basel in Neuroscience, Infectious Diseases and Oncology
- Biotech startup enthusiast for novel modalities and modes of action
- Successful multiple platform builder, author and inventor of over 30 papers and patents.



From Serendipity to Rational Design



QuEEN Platform

purpose-built to support the discovery and development of molecular glue degraders

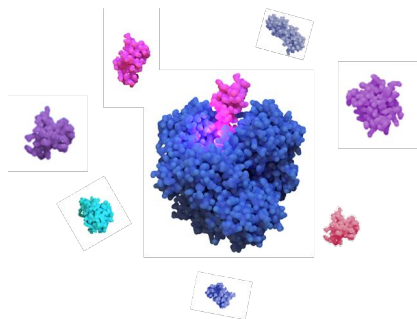
Proprietary Pipeline

for oncology and immunology with a focus on so far undruggable targets

Target	Compound	Indication(s)	Discovery	IND-Enabling	Clinical
GSPT1	MRT-2359	NSCLC, SCLC and other MYC-driven malignancies	[Progress bar]		
VAV1	MRT-6160	Autoimmune Disease – Systemic and CNS	[Progress bar]		
NEK7	MRT-8102	IL-18/NLRP3 driven Inflammatory Diseases	[Progress bar]		
LO (2nd generation)			[Progress bar]		
CDK2	LO	Breast Cancer	[Progress bar]		
CCNE1 (Cyclin E1)	LO	CCNE1 amplified tumors	[Progress bar]		
Discovery Targets	-	Multiple	[Progress bar]		

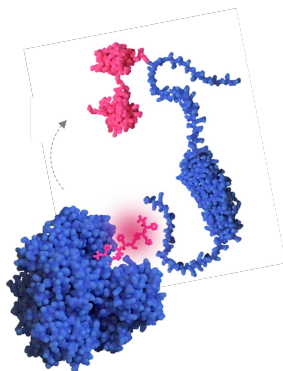
PHOREMOST

Drugging the Undruggable®



Technology

Phenotypic screening with engineered mini-proteins to enable and rationalise small molecule drug discovery



Pipeline and focus

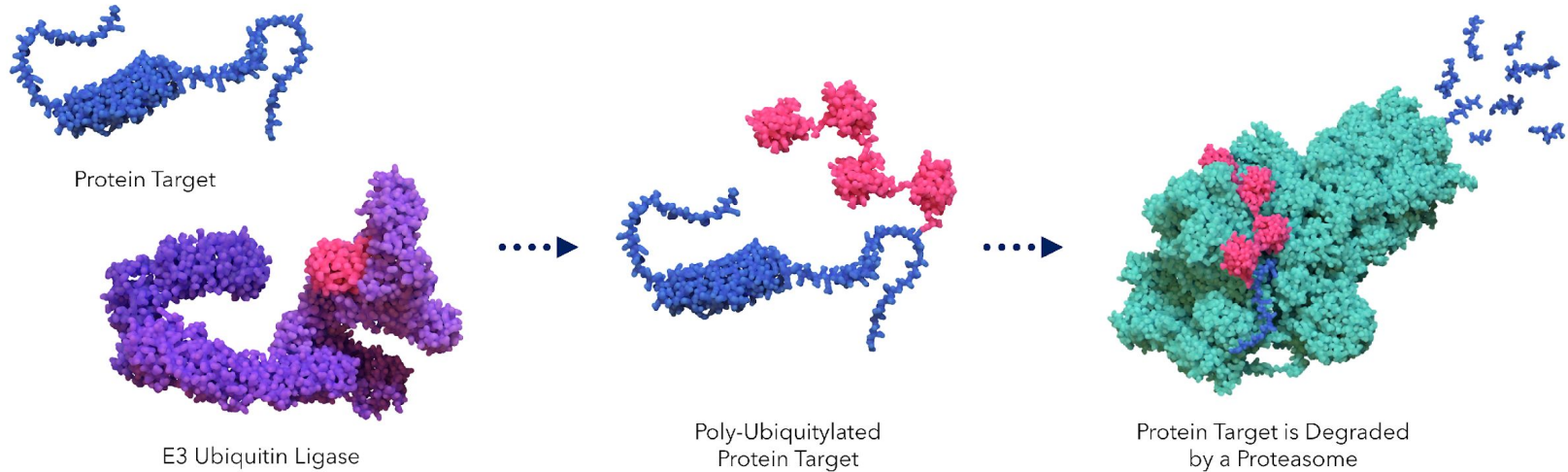
Degrader drug asset pipeline
Unlocking unprecedented E3s
Systematic molecular glue design
Target discovery alliances

Benedict Cross, PhD

*Chief Technology Officer and Head of Platform
PhoreMost Ltd*

- PhD and postdoctoral training in biochemistry at University of Manchester and Cambridge UK
- Discovered first class of inhibitors of proteostasis master regulator IRE1 with covalent mechanism
- Established first CRISPR-based functional genomics screening technology and published first dual perturbation approach for drug MOA
- Pioneered use of mini-proteins as new class of enabling perturbagen at PhoreMost UK
- Biotech platform builder & author of more than 30 peer-reviewed publications and patents

The Ubiquitin Proteasome System (UPS)



Hijacking the UPS for new drug discovery: Why we need Targeted Protein Degradation (TPD)

85%

85% of proteins are deemed unligandable or undruggable with conventional small molecule inhibitors

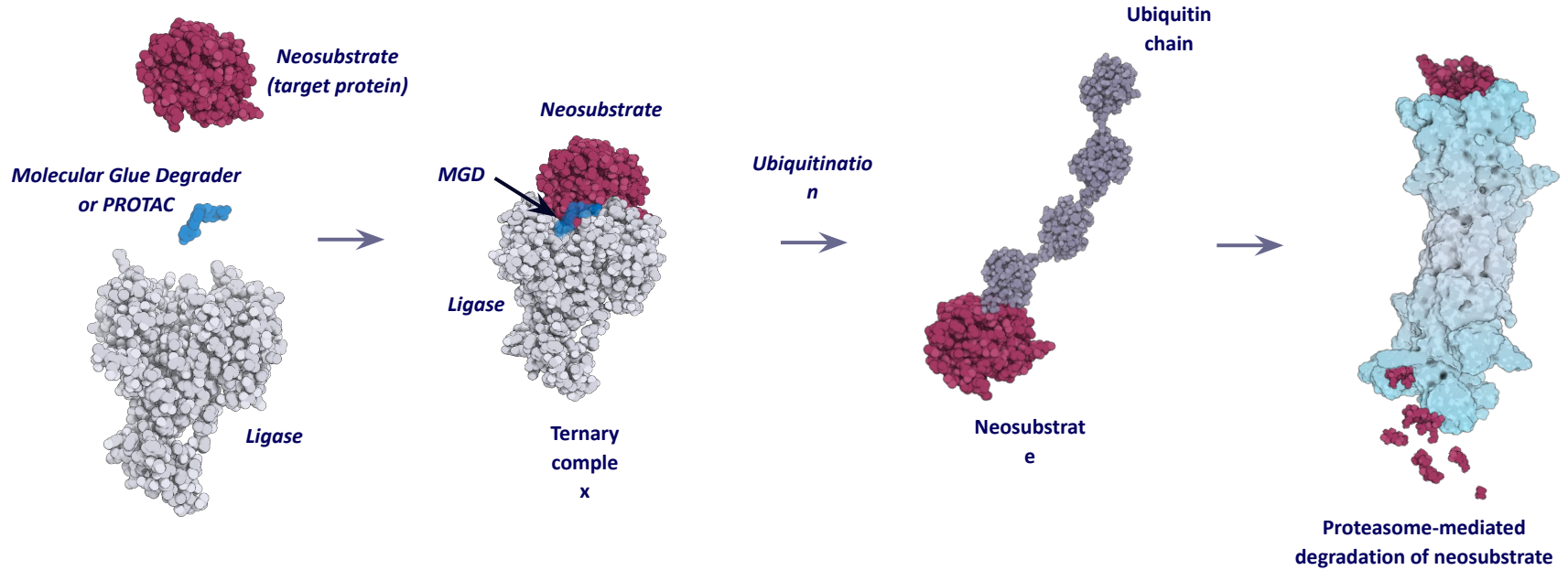


Many challenging targets with multiple functions are unassailable by single inactivating drugs



Emerging resistance mechanisms can limit the long-term effectiveness of treatments

Targeted Protein Degradation (TPD) Editor of the Proteome



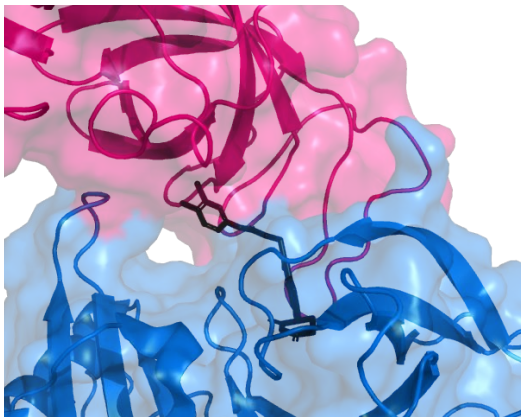
Molecular Glue Degraders: Features and Origins

- Remodelling ligase surfaces with small molecules can mimic the side-chain interactions found in native PPIs
- MGDs predominantly discovered serendipitously and with richness of examples from CRBN and imide chemistry
- Functionally permissive glues can be found that work by stabilising existing PPIs or through *de novo* interactions

IMiD diversification MGD

CRBN:CC885:GSPT1 (5HXB)

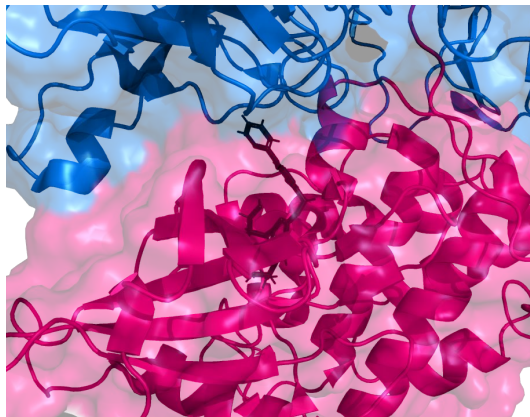
Discovered by SBDD library screening



Prospectively discovered MGD

DDB1:CR-8:CDK12/CycK (6TD3)

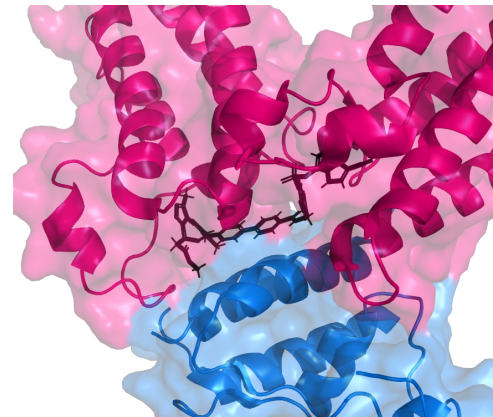
Discovered by phenotypic screening



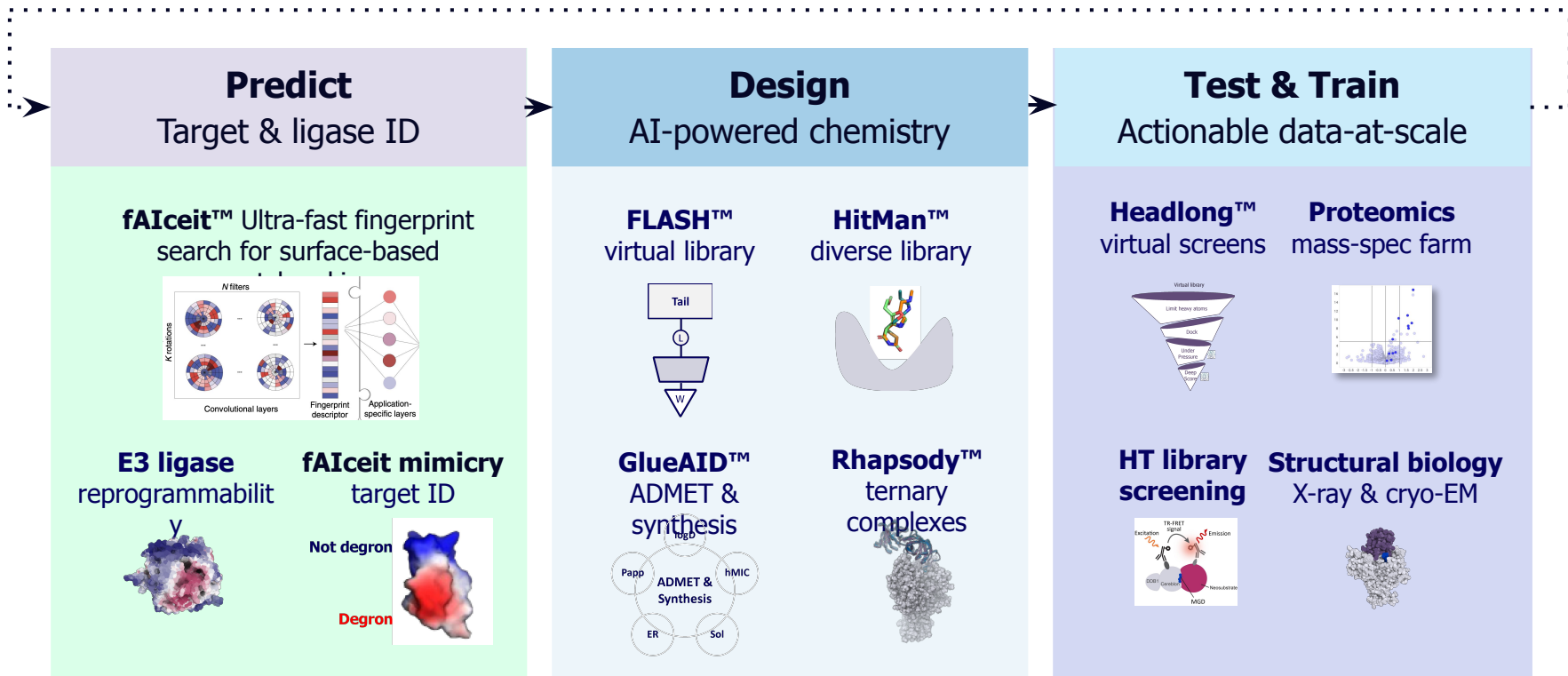
Redefined MGD

DCAF16:IBG1:BRD4 (8OV6)

MOA from functional genomics

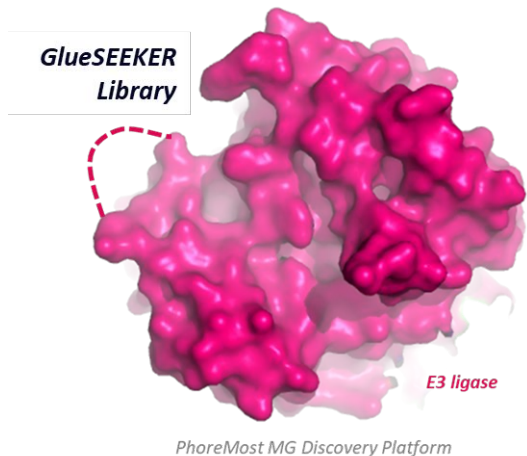
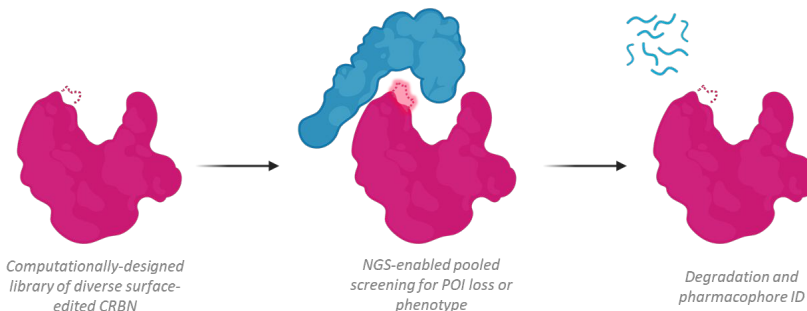


Monte Rosas QuEEN™ Toolbox for Rapid Discovery of Oral MGDs

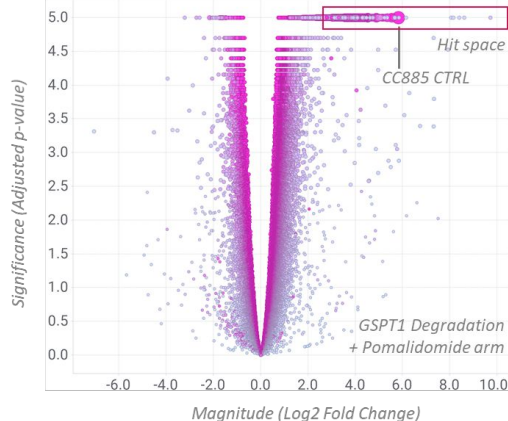


GlueSEEKER™: editing the substrate repertoire of E3 ligases

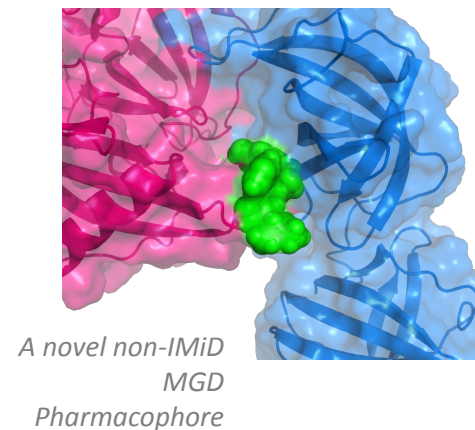
Enabling the systematic discovery of new Molecular Glues through intramolecular protein editing



GSPT1, STAT3 GlueSEEKER screening



Molecular modelling from hit space



Questions?



CDD, VAULT[®]
Complexity Simplified



Inventory

Keep track of samples,
biologicals and compounds



Activity & Registration

Store and organize your
research data



Visualization

Plot datasets and mine them



Deep Learning

Computer aided
design



ELN

Document all your
research.
Build Data Rooms
Digitalize your lab

Learn More:

Personalized Demo & Free Trial: