Discovery of precision degrader antibody conjugates (pDACs) employing novel SMARCA2/4 degrader payloads

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Degrader-Antibody Conjugates (DACs): Recent Developments, Challenges, and Opportunities
American Chemical Society Spring 2026 (Atlanta)
Symposium sponsored by PharmaBlock

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Disclosures & Financial Relationships

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Financial Relationships

Andrew Buesking is an employee and shareholder of Prelude Therapeutics Incorporated.

To date, ADCs deliver meaningful benefit but fall short of “magic bullet” ideal

- “Magic bullet” concept (Ehrlich, 1900’s) continues to inspire targeted drug design
- Currently, 14 FDA-approved are helping patients
- ADCs improve efficacy compared to unconjugated payload but possess similar MTD
- Tumor enrichment observed but inefficient targeting results in vast majority of ADC distributing to non-target tissues
- Notable adverse events observed across ADC clinical trials

Continued innovation can advance scope and tolerability of ADCs

AI-generated image (ChatGPT 5.2 Thinking)

1) Shen, W.-C. Antibdody-Drug Conjugates: A Historical Review. *Antibody-Drug Conjugates: The 21st Century Magic Bullets for Cancer*; Springer, 2015; pp 3–7. 2) Colombo, R.; Rich, J. R. *Cancer Cell.* **2022**, *40*, 1255. 3) Bensch, F.; et al. *Theranostics.* **2018**, *8*, 4295. 4) Casi, G.; Neri, D. *J. Med. Chem.* **2015**, *58*, 8751. 5) Zhu, Y.; et al. *J. Hematol Oncol.* **2025**, *18*, 71.

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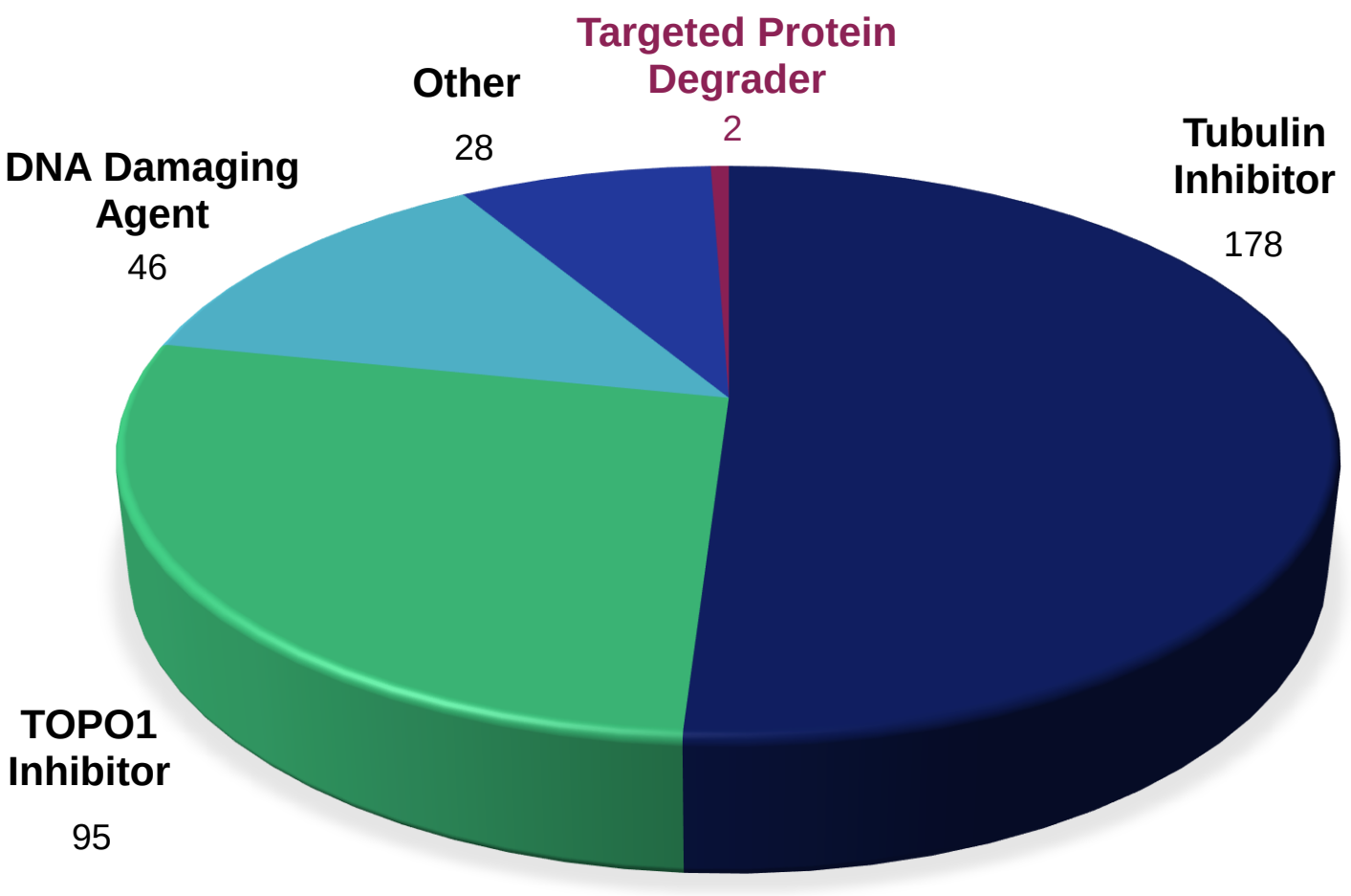
Degraders remain under-represented payload class



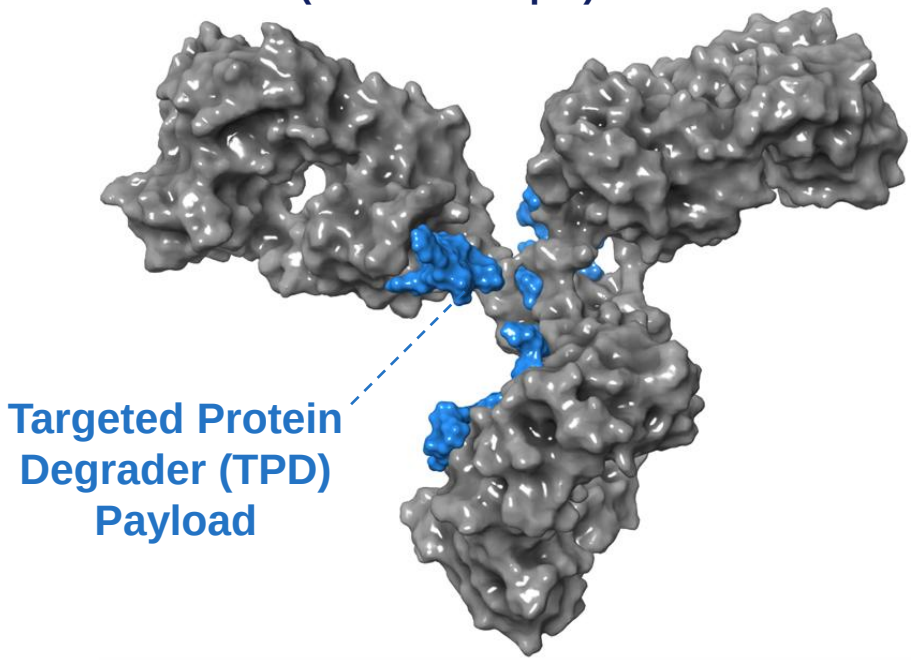
Data source: Morris, J. Beacon ADC by HansonWade. “Analyzing the ADC Boom: Landscape Review.” World ADC (San Diego). November 2024. Denotes Payload MOA for clinical stage assets currently in development at time of analysis.

- Most next-gen, clinical ADCs use just three classes of cytotoxic payloads
- TPD payloads offer exceptional potency and opportunities for additional benefits of precision
- TPD properties can be designed to limit undesired exposure through clearance and cell-penetration
- TPD payloads offer potential to avoid genotoxicity liabilities
- TPDs can expand reach of ADCs to cancers and other therapeutic areas beyond traditional cytotoxics

Precision degrader antibody conjugates (pDACs) represent next generation of ADCs

Model of Precision DAC

(DAR 4 example)



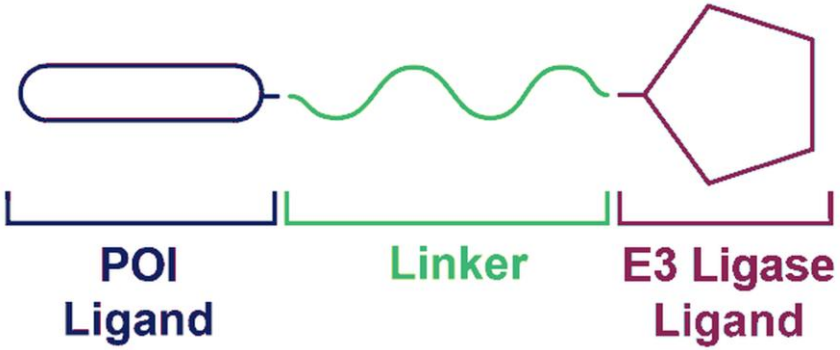
Property	Traditional ADC	Precision DAC
Potency	☑	☑
Antibody Selectivity	☑	☑
Payload Selectivity	X	☑
PD Marker - Payload	X	☑
Non-Genotoxic	X	☑

- **Precision DACs enable improved selectivity in two ways**
  - ✓ **Antibodies** target tumor-specific cell surface antigens sparing healthy cells
  - ✓ **Targeted Protein Degraders** address critical proteins in validated biological pathways
- **Potential to deliver both improved efficacy and improved tolerability**

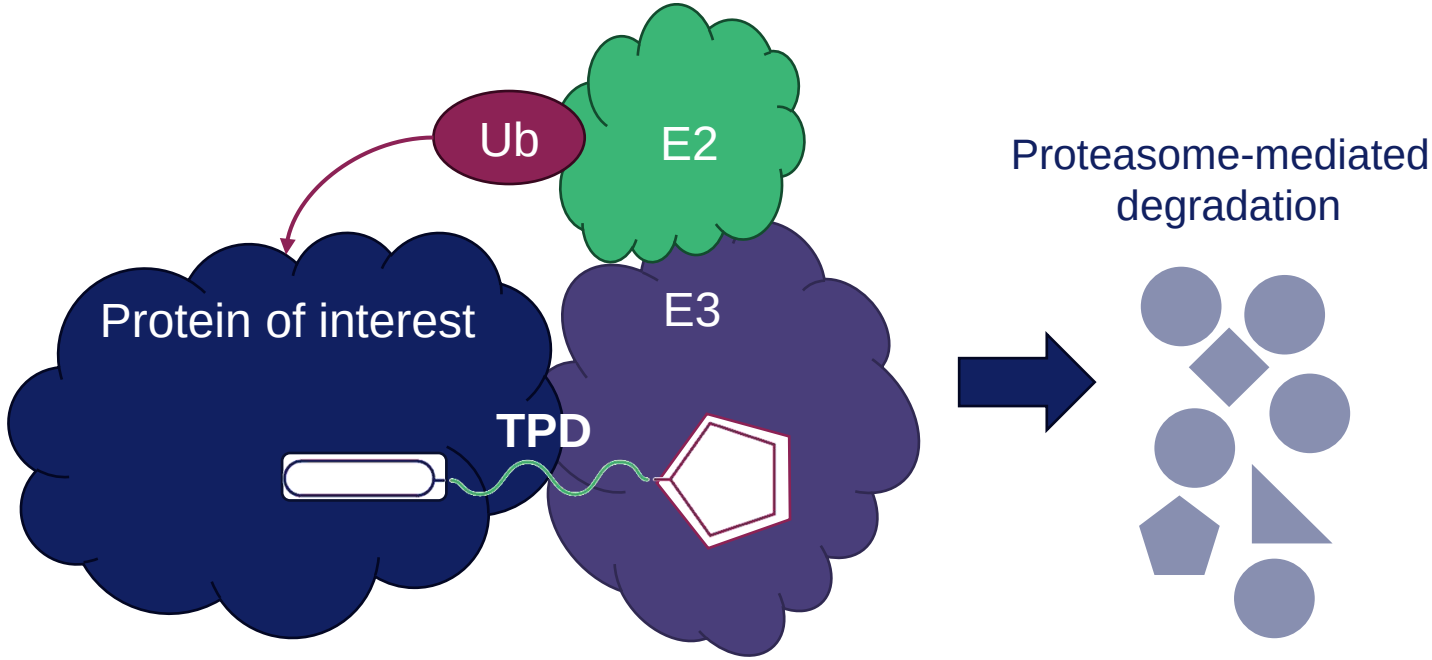
For a review of ADCs, see Fu, Z., Li, S., Han, S. *et al. Sig Transduct Target Ther* **7**, 93 (2022).

Targeted protein degraders represent emerging therapeutic class with unique advantages as payloads

Components of heterobifunctional degrader



Mechanism of ubiquitin-proteasome degradation



Advantages of Targeted Protein Degrader (TPD) Technology

- Excellent potency and catalytic activity (event-driven pharmacology)
- Prolonged pharmacodynamic effects resulting from protein resynthesis
- Possibility for enhanced pharmacology beyond enzymatic function including targeting protein-protein interactions and disrupting protein complex assembly

For select, recent reviews, see 1) Zhang, C. et al. *Sci. Bulletin* **2024**, *69*, 1776. 2) Hong, K. B.; An, H. *J. Med. Chem.* **2023**, *66*, 140.

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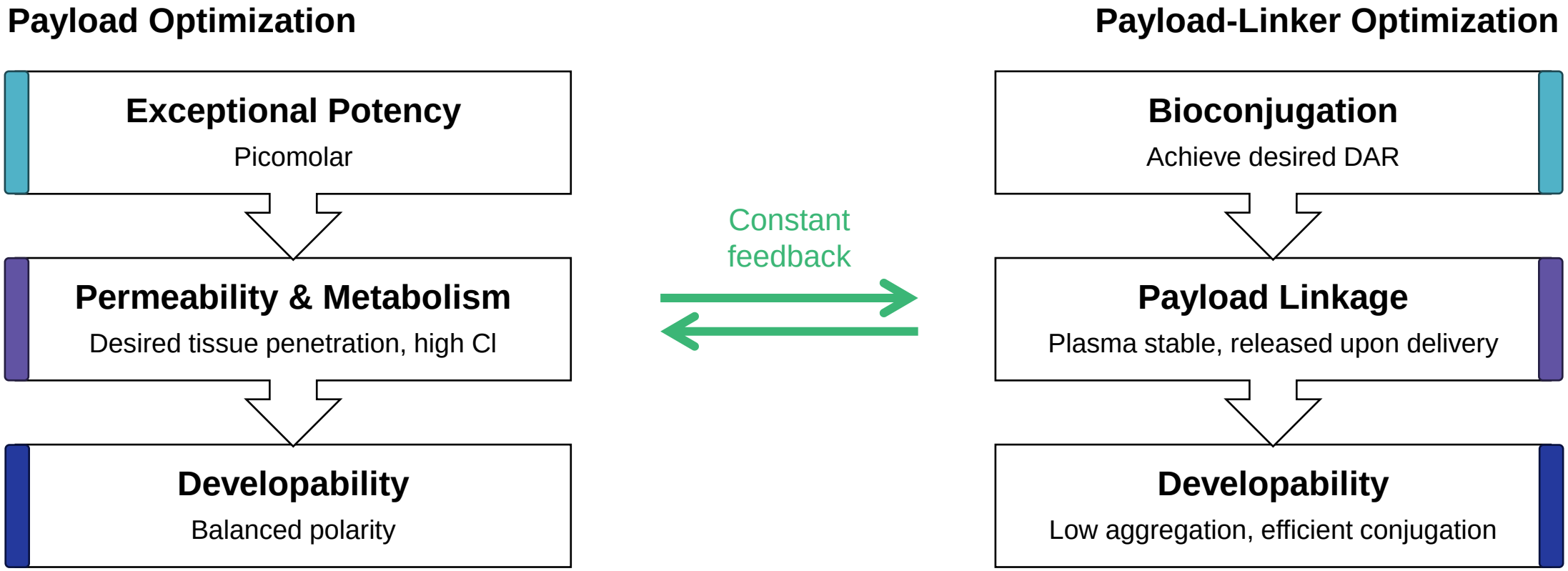
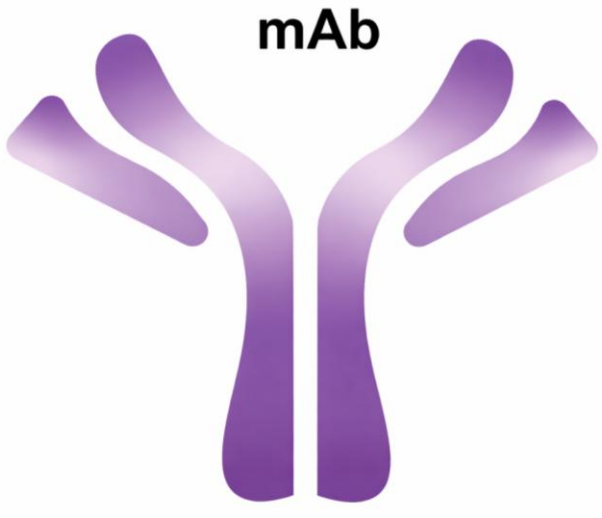
Medicinal chemistry drives integrated payload and payload-linker optimization



- Integrated design-build-test cycles accelerate discovery of payloads, payload-linkers, and pDACs
- Iterative workflows provide continuous feedback across platform to identify best pDAC candidates

Leveraging directed antibodies and targeted SMARCA2/4 degraders to generate pDACs

Directed delivery



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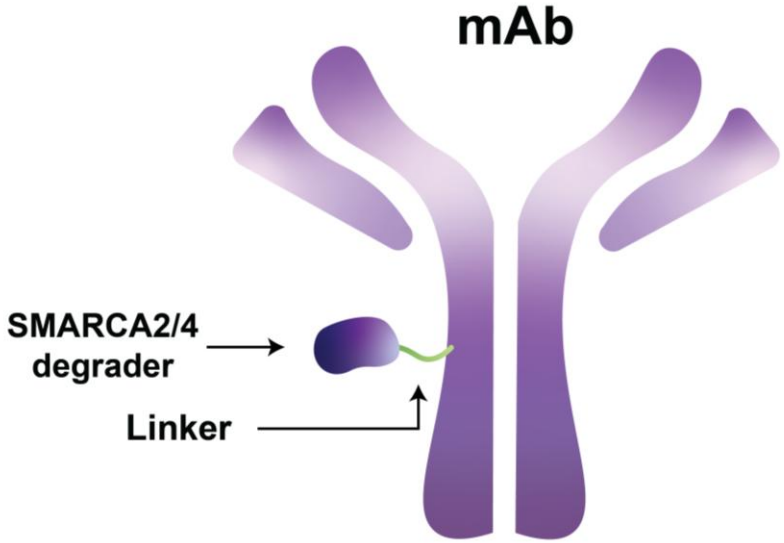
Targeted agent

SMARCA2/4 dual degrader

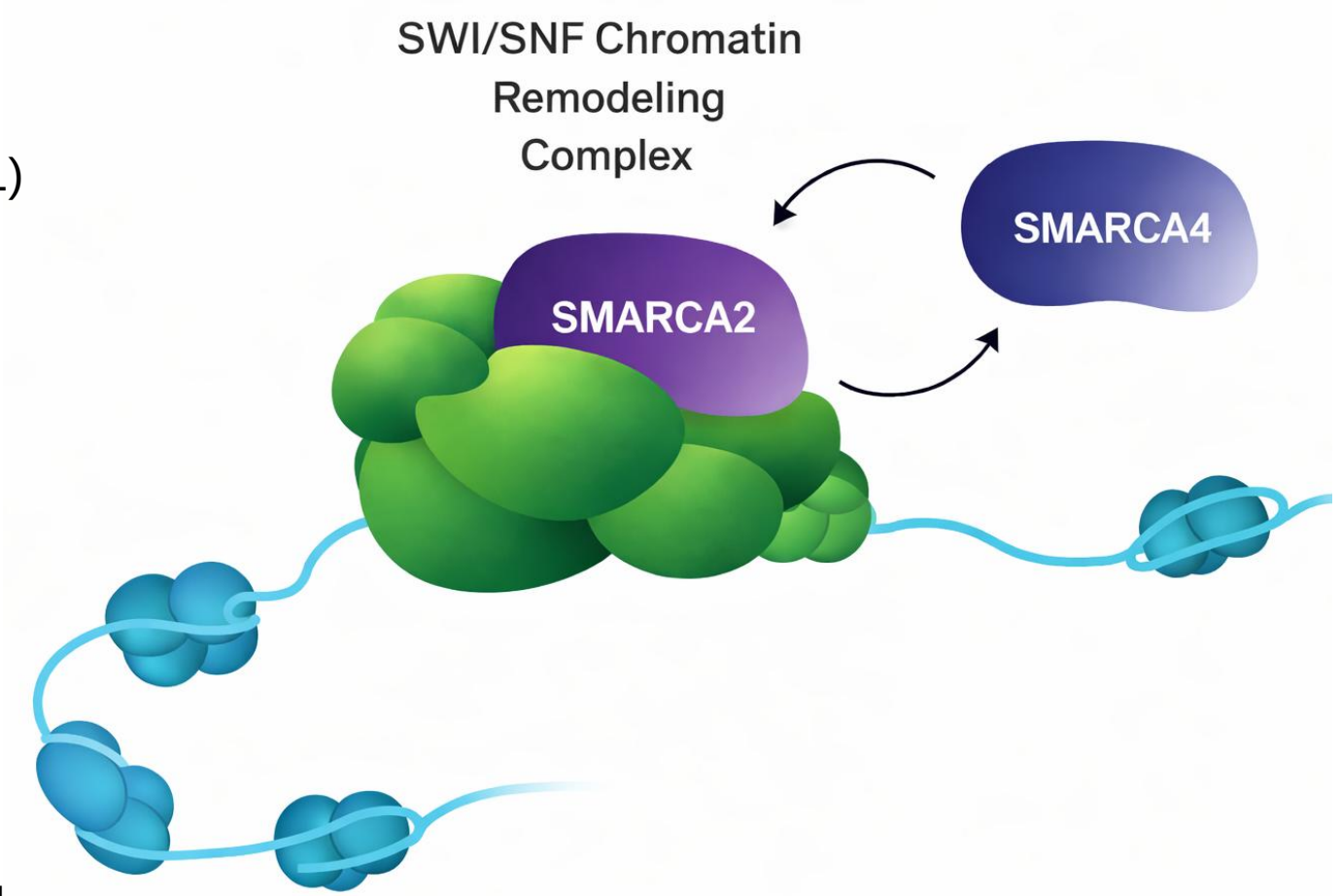
Precision DACs (pDACs)



Harnessing this double targeting holds potential to unlock new era of precision medicine

Utilizing SWI/SNF dependence to build precision ADCs with SMARCA2/4 payloads

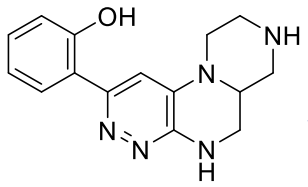
- SWI/SNF complex is a major chromatin remodeling complex containing ATPase catalytic subunit
  - Either SMARCA2 (BRM) or SMARCA4 (BRG1)
- Transcription factor (TF)/enhancer-driven cancers including prostate cancer highly dependent on SWI/SNF chromatin remodeling complex
  - SMARCA2/4 dual inhibitors/degraders suppress specific types of cancers
  - Selecting these SMARCA2/4-dependent indications imparts layer of precision
- pDAC approach could provide balance of deep responses and tolerability
  - Dual inhibitor/degraders not well tolerated as systemic agents due to dependence of normal cells on SMARCA2/4

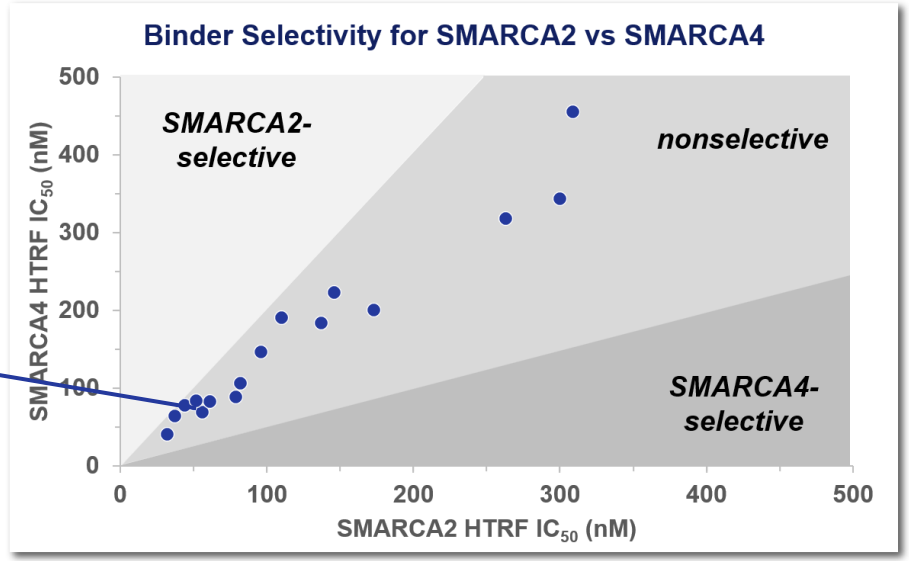


1) Gourisankar, S.; et al. *Nat Rev Genet.* **2024**, *25*, 340. 2) Xiao, L.; et al. *Nature.* **2022**, *601*, 434.
3) Xiao, L.; et al. *Nature* **2022**, *601*, 434. 4) He, T.; et al. *Caner Cell*. **2024**, *42*, 1336.

Tricyclic SMARCA2/4 binder enables early lead degrader identification

Binder identification

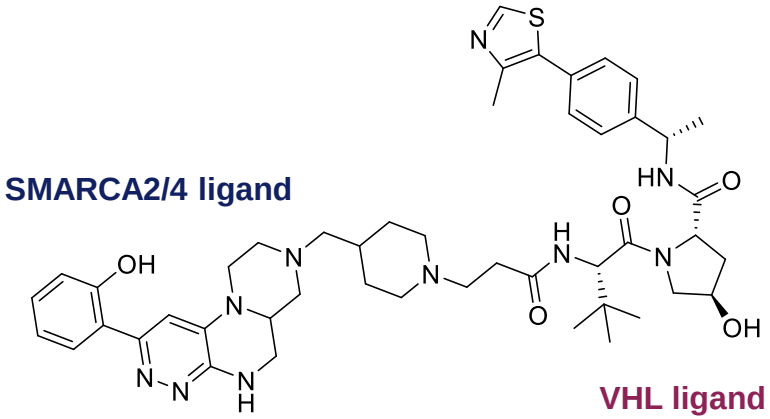




HTRF	1
SM2 IC_{50} (nM)	51
SM4 IC_{50} (nM)	80
Selectivity	1.6

VHL-based degrader

SMARCA2/4 ligand



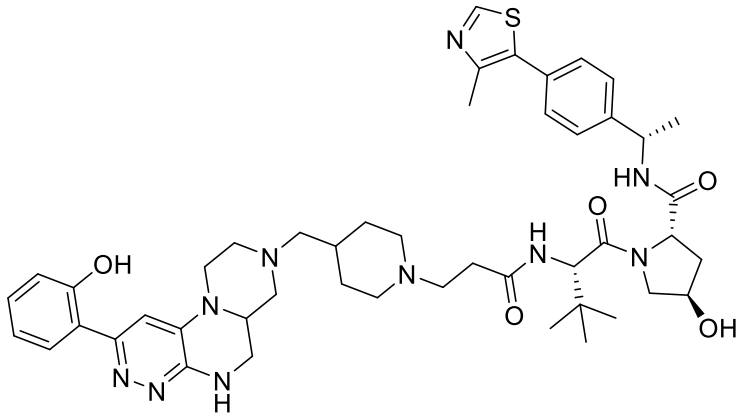
VHL ligand

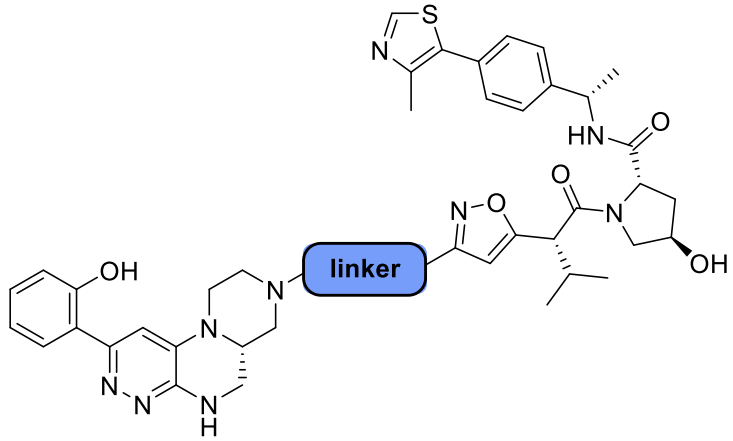
HiBit	2
SM2 DC_{50} (nM) (D_{max})	304 (88%)

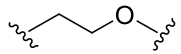
- Medicinal chemistry campaign identified non-selective, tricyclic binder **1** of SMARCA BRD domain
- Linking to VHL ligand provided promising degrader **2** for further exploration

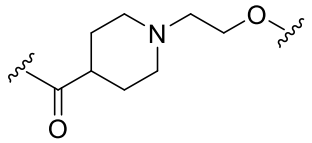
Basch, C. H. ACS Spring Meeting, March 2025

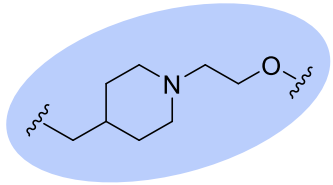
VHL ligand and linker SAR drive three-order of magnitude potency increase











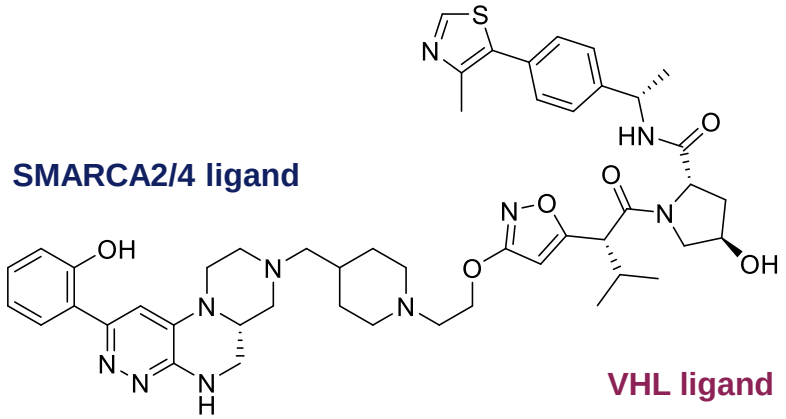
HiBit	2
SM2 DC_{50} (nM) (D_{max})	304 (88%)
SM4 DC_{50} (nM) (D_{max})	--
Selectivity	--

3	4	5
3.9	4.4	0.37
60	6.8	2.7
15x	1.5x	7.3x

- Isoxazole-containing VHL ligand improved degradation potency
- Linker structure influenced both potency and selectivity
- Very potent, dual SMARCA2/4 degrader **5** selected for further investigation as payload

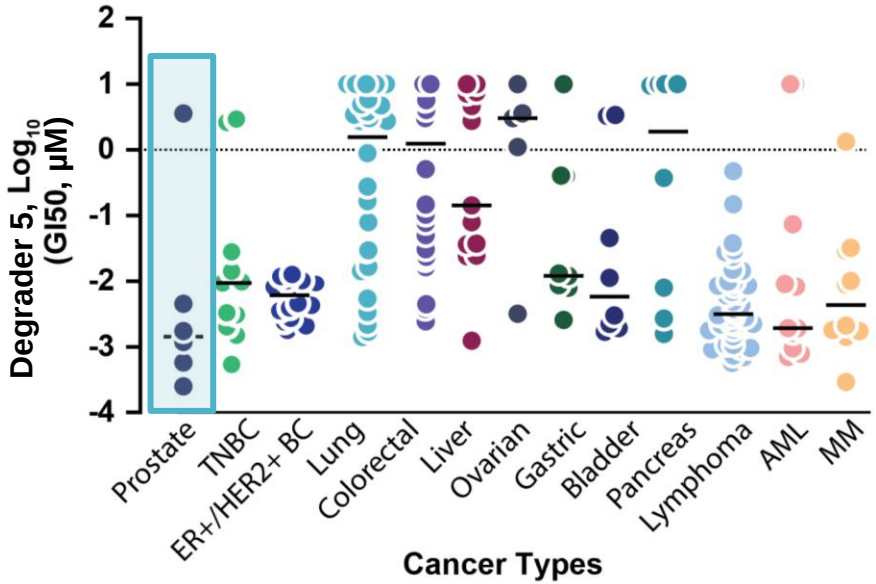
Basch, C. H. ACS Spring Meeting, March 2025

Novel SMARCA2/4 dual degrader payload demonstrates potency and precision

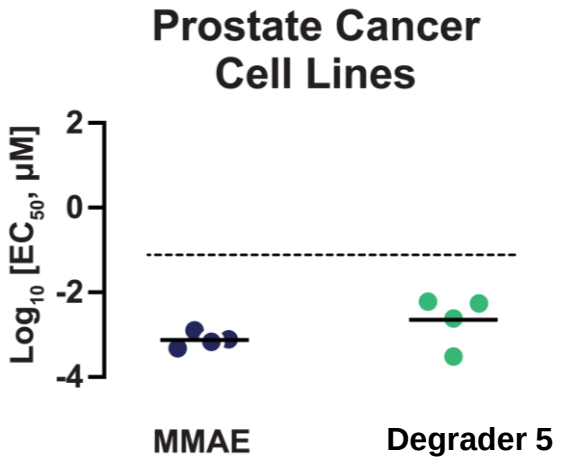


Potency & selectivity assays	5
HeLa HiBit SM2 DC_{50} (pM) (D_{max})	370 (97%)
HeLa HiBit SM4 DC_{50} (pM) (D_{max})	2,700 (96%)
Fold Selectivity SM4/SM2	7.3x
LNCaP prolif EC_{50} (pM)	210 (96%)
hIntCl HLM mL/min/kg (%HBF)	16 (77%)

GI_{50} in cancer cell panel



EC_{50} in prostate cell panel



- Identified potent, dual SMARCA2/4 degrader **5** with exceptional potency in prostate cancer cells
- High clearance to limit prolonged systemic exposure that could erode therapeutic index
- Consistent with targeted approach, range of activity in other cancer types (even >1 µM in some cases)
- Potency comparable to cytotoxic payload MMAE in prostate cancer cells

1) Buesking, A.W. Novel Conjugates Summit, March 2025. 2) Carter, J. et al. *E. J. Cancer.* **2024**, *211*, 114688. (36th EORTC-NCI-AACR Symposium)

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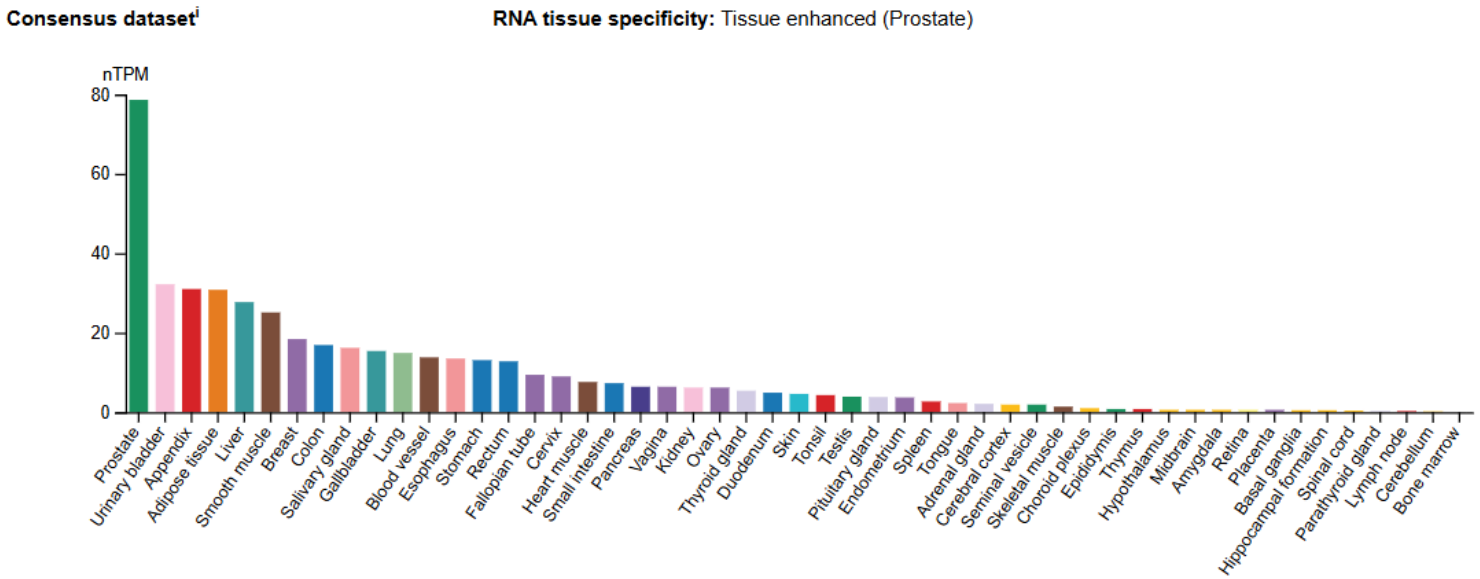
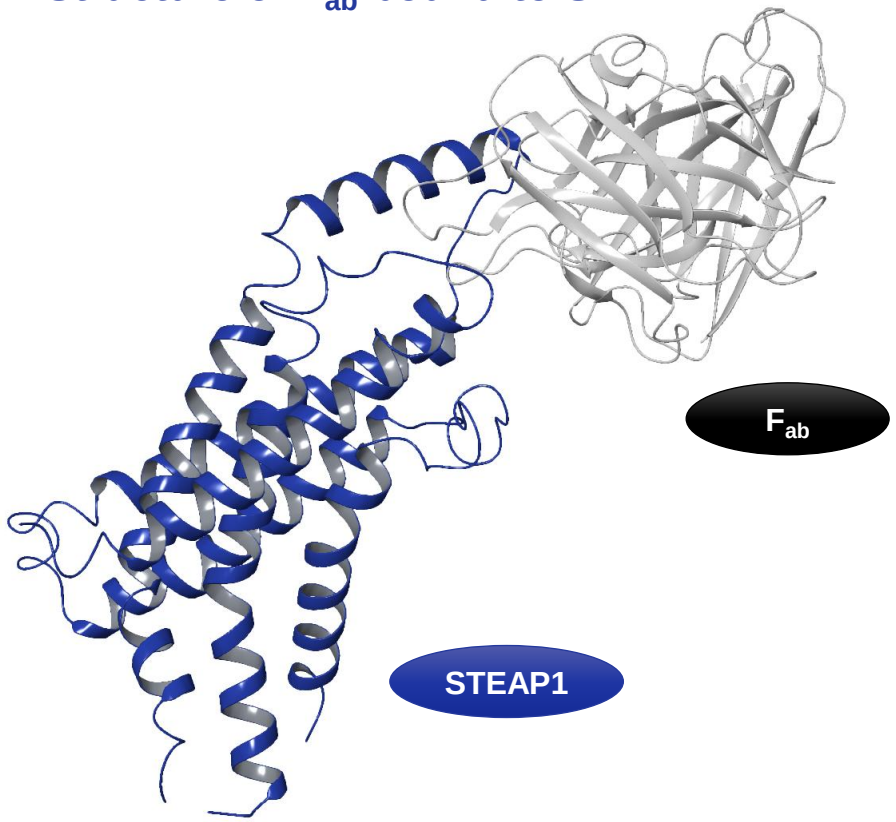
Six-transmembrane epithelial antigen of prostate 1 (STEAP1): Representative antigen target for novel SMARCA2/4 pDACs

STEAP1 transcript expression across tissue types



Structure of F_{ab} bound to STEAP1



- STEAP1 is a transmembrane metalloreductase and expressed in >85% prostate cancer
- STEAP1 transcript expression enriched in prostate tissue with less expression in other normal tissues
- Antibodies including vandortuzumab recognize extracellular domain and used in clinical ADCs

1) “ENSG00000164647 (STEAP1).” https://www.proteinatlas.org (graph extracted Feb 2026) 2) Sing, R.; Kyte, J. A. *Trends in Cancer*, **2025**, *11*, 722-725.
3) Structure visualized using PDB code 6Y9B.

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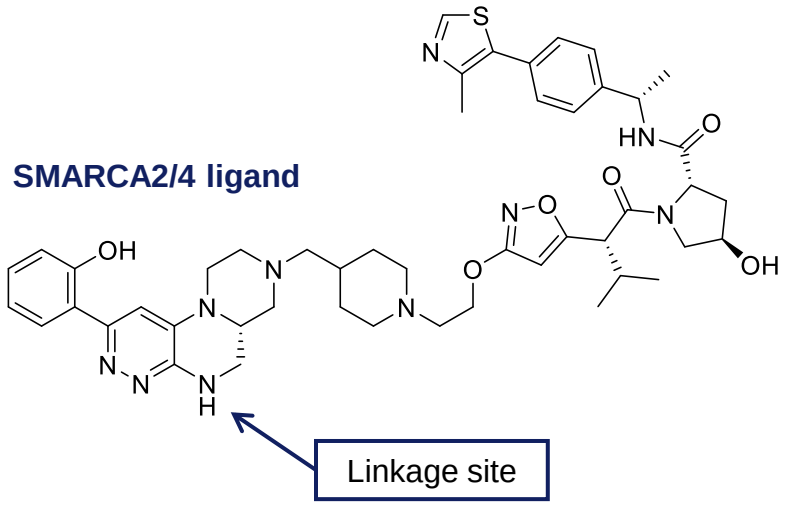
Design of SMARCA2/4 payload-linker utilizes *N*-linkage and state-of-art linker



Potency & selectivity assays	5
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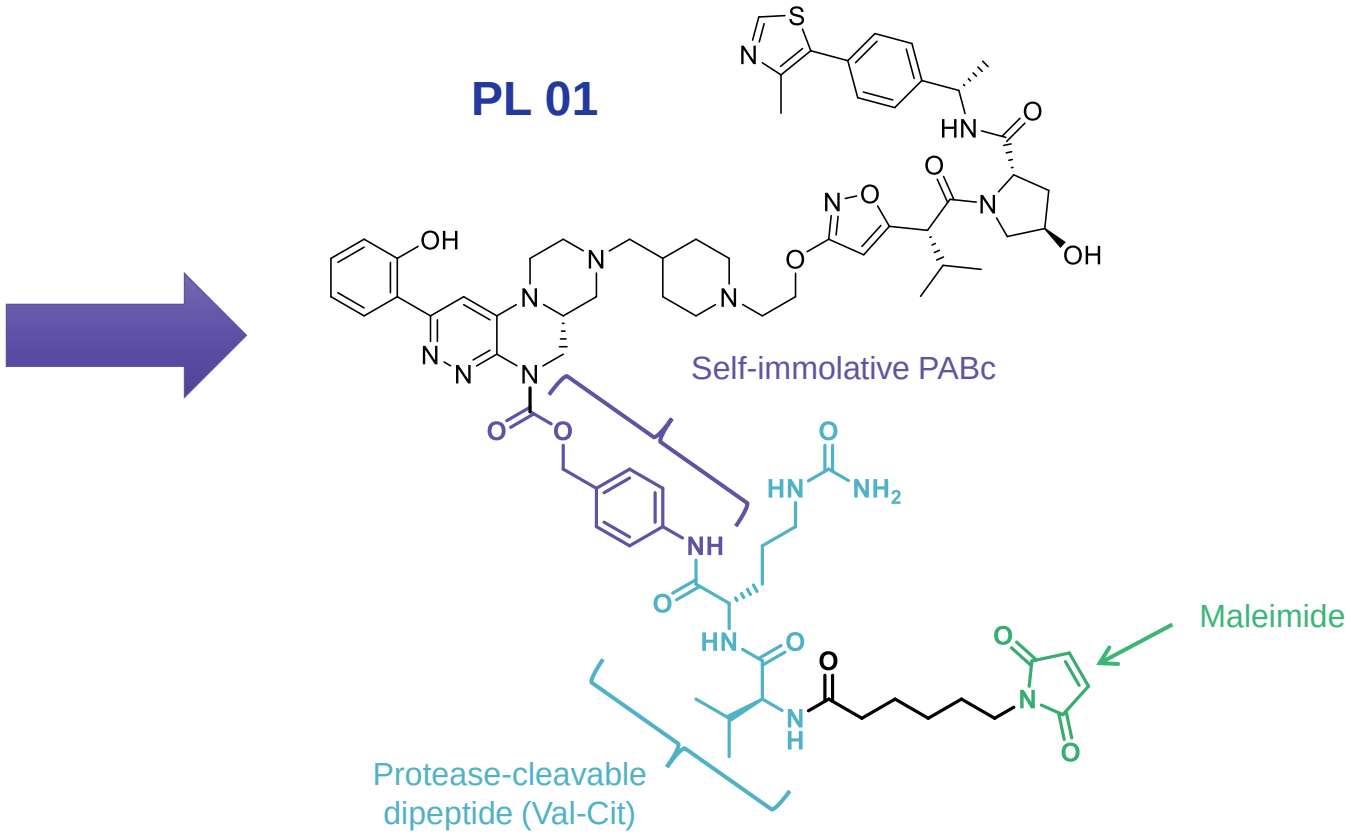
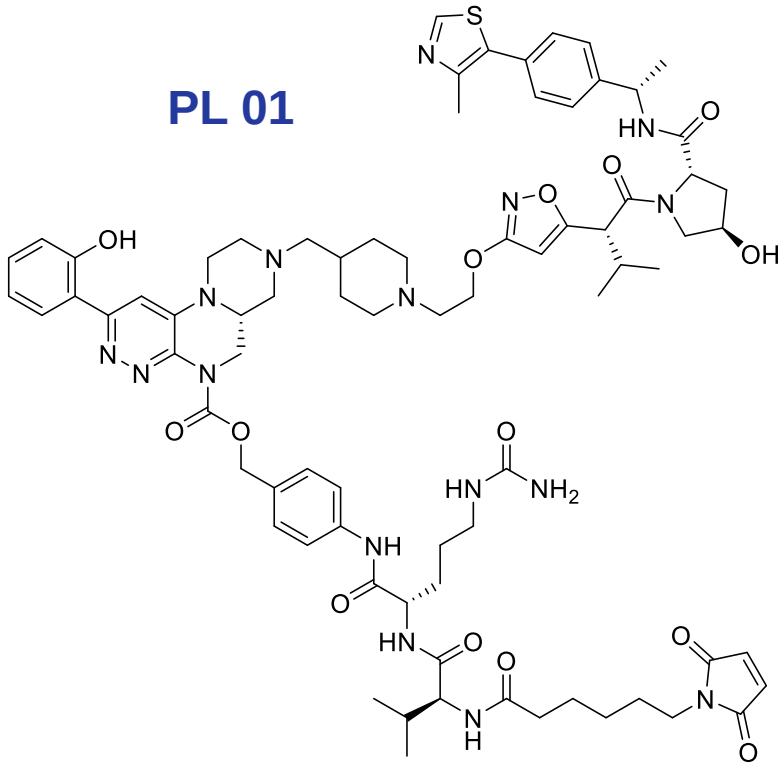
LNCaP prolif EC_{50} (pM) (E_{max})	210 (96%)



- SMARCA2/4 binder N–H selected as facile site of linker attachment
- Initially selected protease-cleavable, dipeptide linker with self-immolative PABc

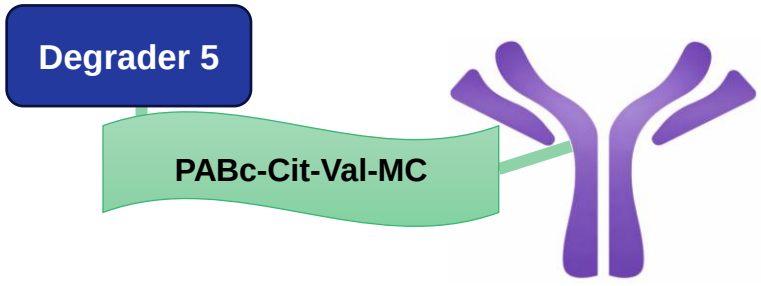
Facile conjugation of payload-linker affords STEAP1 x SMARCA2/4 pDAC

PL 01



conjugation

polishing



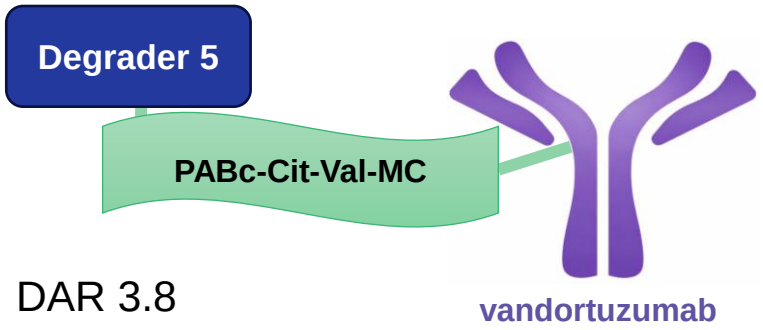
vandortuzumab

Property	DAC 01
Initial aggregation (%)[a]	27
DAR (average)	3.8
Monomeric purity (%)	97

[a]Aggregation (%HMWS) under standard, unoptimized conditions. An early metric for developability.

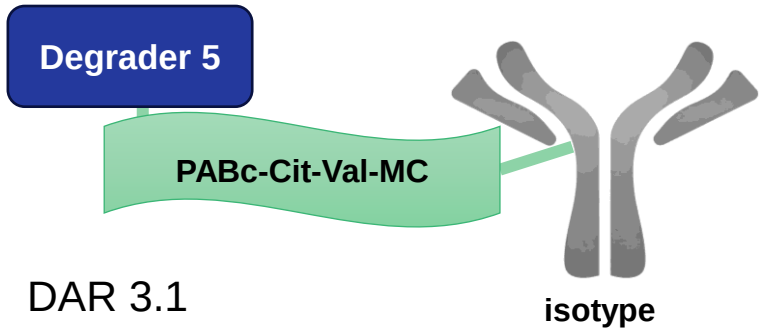
- **PL 01** conjugated via stochastic, native-cysteine conjugation
- Anti-STEAP1 antibody vandortuzumab selected as case study
- Bioconjugation provided ADCs with acceptable DAR and properties

Initial payload modestly active when conjugated to vandortuzumab



DAR 3.8

vandortuzumab



DAR 3.1

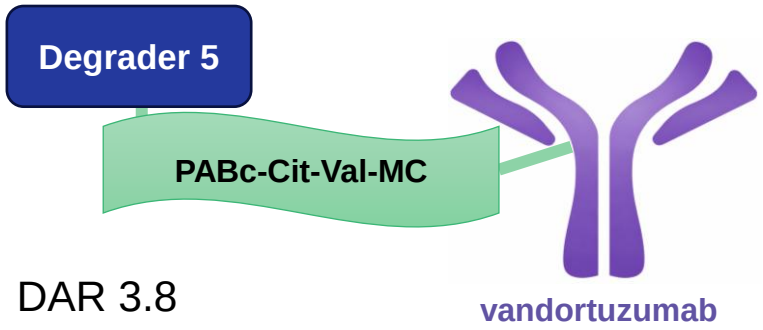
isotype

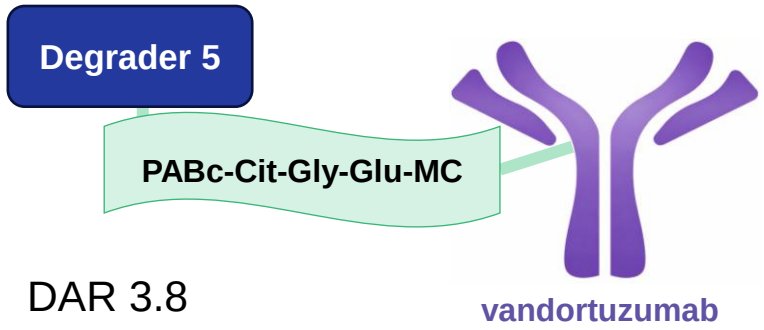
Potency (ng/mL)	DAC 01	DAC 02
LNCaP SM2 DC_{50} (D_{max})	75 (88%)	1000 (55%)
LNCaP SM4 DC_{50} (D_{max})	2700 (50%)	>1200 (7%)
LNCaP prolif EC_{50} (E_{max})	460 (86%)	610 (75%)

LNCaP STEAP1+.

- Acceptable SMARCA2 degradation and modest SMARCA4 degradation observed for DAC **01**
- Isotype control suggested degradation activity was differentiated from background
- Antiproliferation activity observed but indistinguishable from isotype control

Varying linker composition provided comparable degradation potencies





Potency (ng/mL)	DAC 01	DAC 03
LNCaP SM2 DC_{50} (D_{max})	75 (88%)	87 (85%)
LNCaP SM4 DC_{50} (D_{max})	2700 (50%)	930 (82%)
LNCaP prolif EC_{50} (E_{max})	460 (86%)	135 (91%)

LNCaP STEAP1+.

- Additional cleavable peptide sequences possessed similar degradation potency
- Appeared to rule out inefficient release as major factor
- Hypothesized that additional payload potency could be required to drive pDAC activity

Myth 1

Off-the-shelf MYTH

Degrader payloads are catalytic, so they do not need to be as potent

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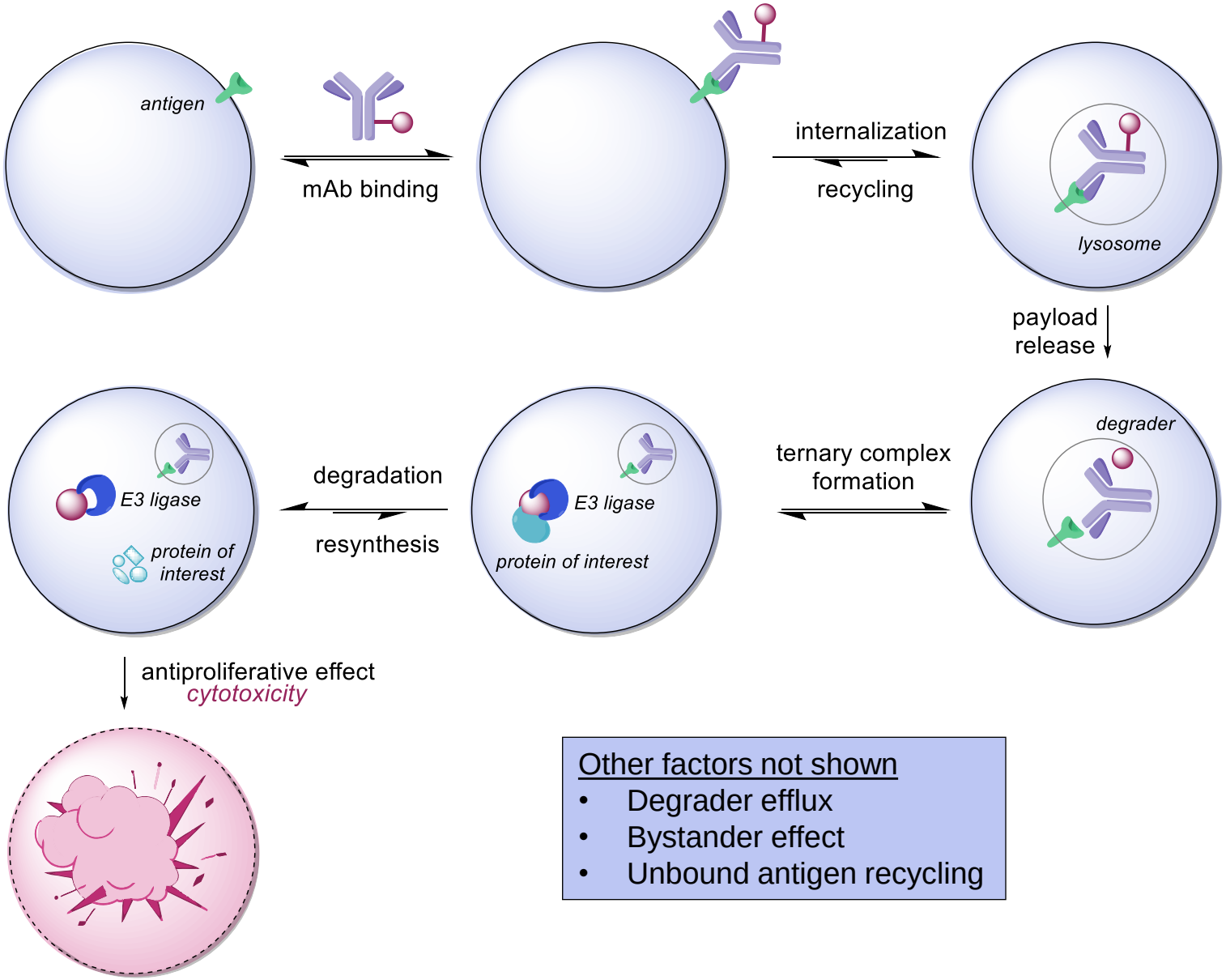
Exceptional potency to support complex mechanism



Other factors not shown
- Degrader efflux
- Bystander effect
- Unbound antigen recycling

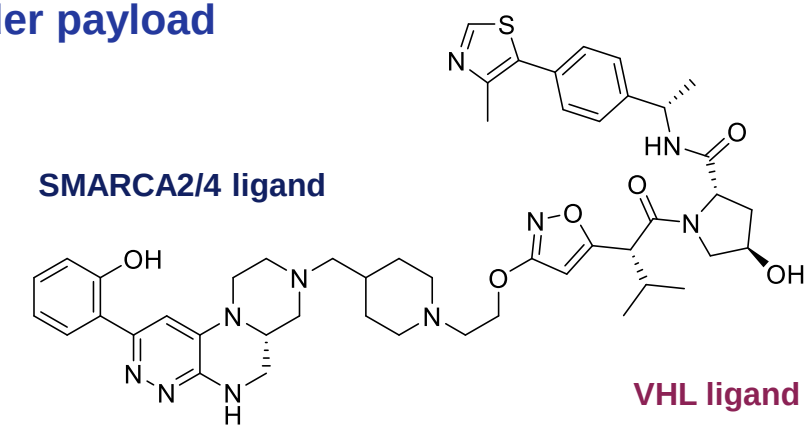
Rationale

- Delivery efficiency
  - Payload delivery <1%
- Unique, kinetic mechanism
  - Induced proximity
  - Catalytic activity
  - Time-dependent degradation
  - Resynthesis required
- Translation
  - Degradation triggers cytotoxicity
  - Target-specific degradation threshold

1) Hong, K. B.; An, H. *J. Med. Chem.* **2023**, *66*, 140.
2) Bensch, F.; et al. *Theranostics.* **2018**, *8*, 4295.
3) Casi, G.; Neri, D. *J. Med. Chem.* **2015**, *58*, 8751.

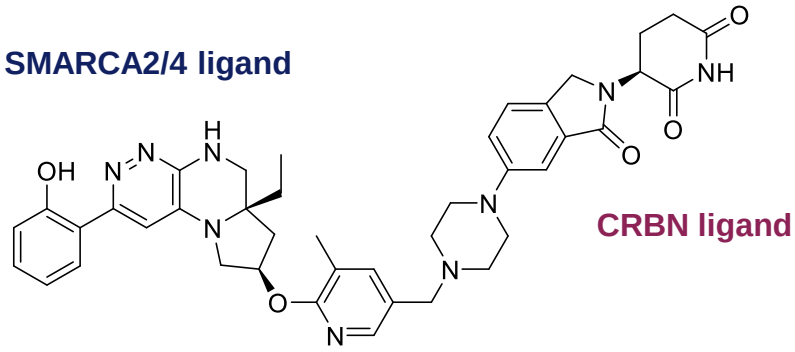
CRBN-based degrader payload more potent than VHL-based payload

VHL-based degrader payload



Potency assays	5
HeLa HiBit SM2 DC_{50} (pM) (D_{max})	370 (97%)
HeLa HiBit SM4 DC_{50} (pM) (D_{max})	2,700 (96%)
Fold Selectivity SM4/SM2	7.3x
LNCaP prolif EC_{50} (pM) (E_{max})	210 (96%)
hIntCl HLM mL/min/kg (%HBF)	16 (77%)

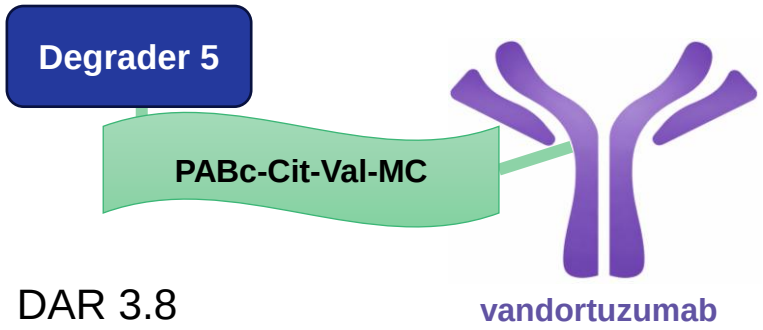
CRBN-based degrader payload

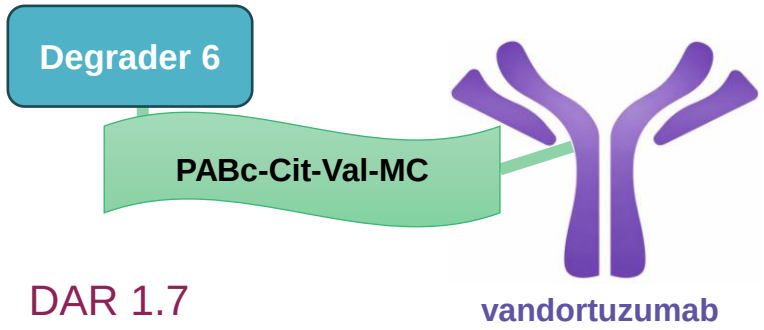


6
40 (97%)
90 (97%)
2x
74 (93%)
19 (90%)

- CRBN-based degrader **6** provided additional potency over degrader VHL-based payload **5**
- Difference most notable in SMARCA4 with 30-fold increase in degradation potency
- Maintained high clearance to minimize free payload exposures

Initial CRBN-based degrader conjugates hampered by lower DAR



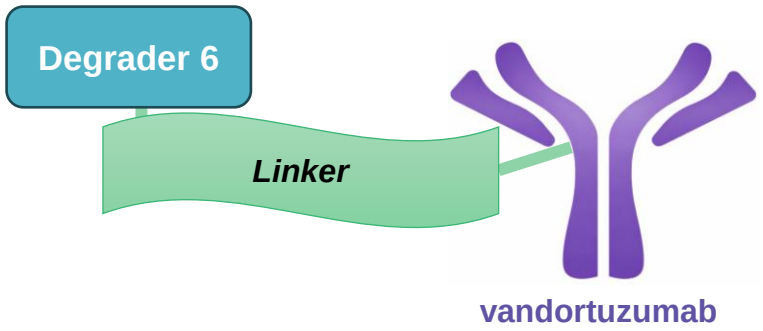


Potency (ng/mL)	DAC 01	DAC 05
LNCaP SM2 DC_{50} (D_{max})	75 (88%)	290 (82%)
LNCaP SM4 DC_{50} (D_{max})	2700 (50%)	2600 (60%)
LNCaP prolif EC_{50} (E_{max})	460 (86%)	2300 (86%)

LNCaP STEAP1+.

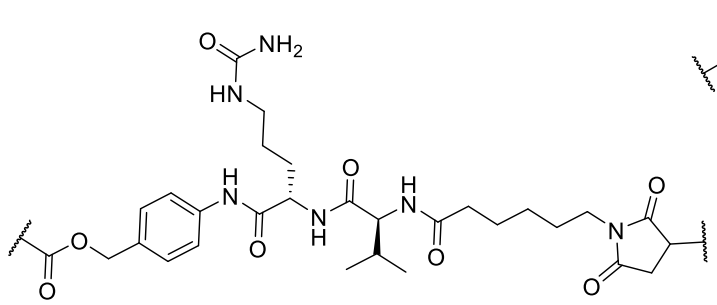
- Properties of payload **6** and initial dipeptide linker limited conjugation to DAR 2
- Resulting pDAC notably less potent both in SMARCA4 degradation and antiproliferation
- Suggested payload-linker physicochemical needed to be adjusted

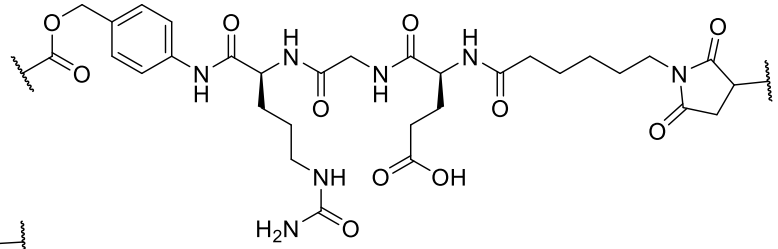
Exceeding DAR 2 with traditional peptide linkers proved challenging

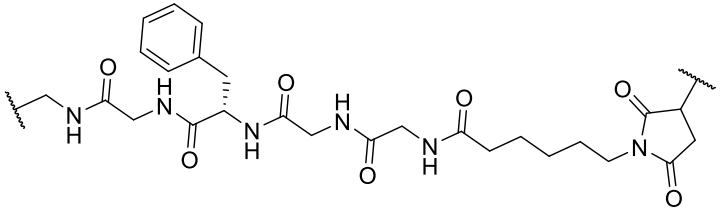


- Modification of peptide sequence reduced aggregation during conjugation
- Aggregation associated with calculated lipophilicity of payload-linker
- These modifications did not afford isolable DAR > 2

Linker







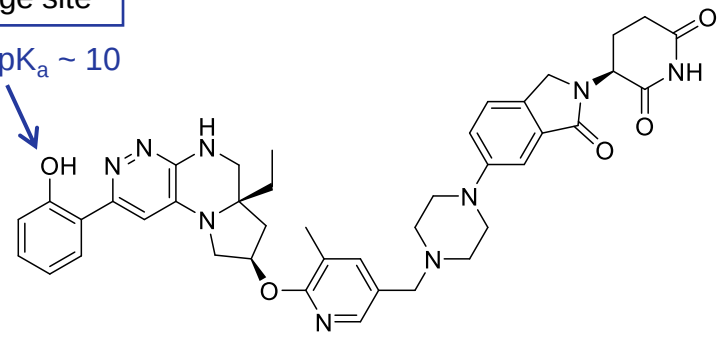
	DAC 05	DAC 06	DAC 07
Linker designation	**PABc-Cit-Val-MC**	**PABc-Cit-Gly-Glu-MC**	**AMA-Gly-Phe-Gly-Gly-MC**
XLogP[a]	**5.1**	**0.74**	**2.7**
Initial aggregation[b]	**23%**	**8%**	**6%**
Isolated DAR	**1.7**	**1.7**	**1.7**

[a]Calculated logP of payload-linker. [b]Aggregation (%HMWS) under standard, unoptimized conditions. An early metric for developability.

Next-gen design of SMARCA2/4 payload-linkers utilizing *O*-linkage

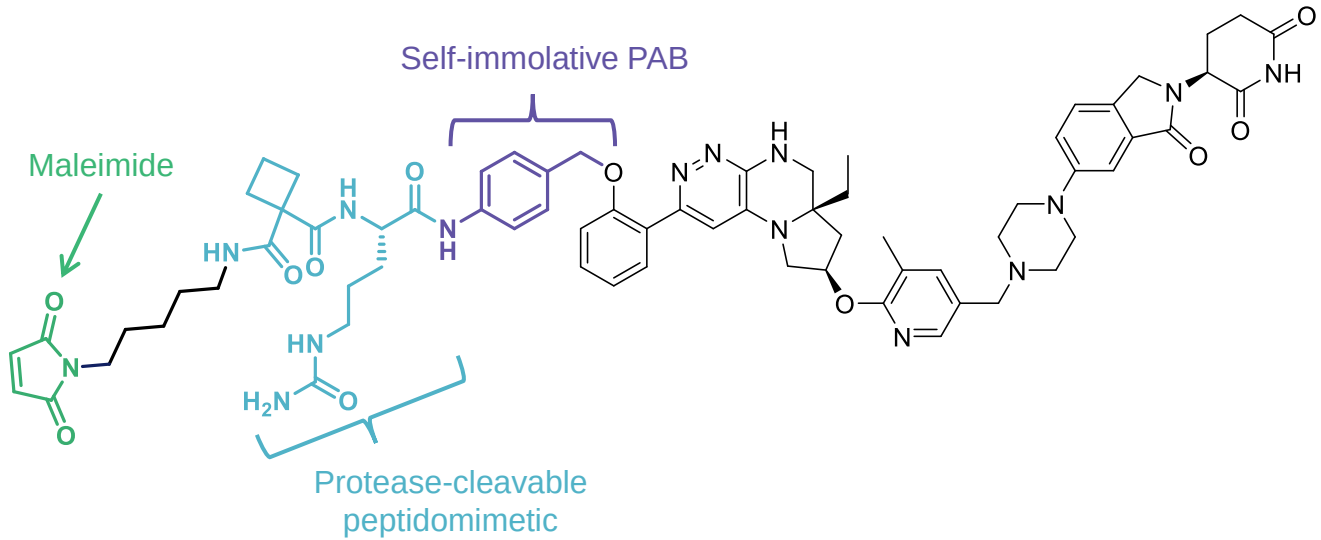
Linkage site

phenol pK_a ~ 10



Potency & selectivity assays	6
HeLa HiBit SM2 DC_{50} (pM) (D_{max})	40 (97%)
HeLa HiBit SM4 DC_{50} (pM) (D_{max})	90 (97%)
LNCaP prolif EC_{50} (pM) (E_{max})	74 (93%)

PL 02

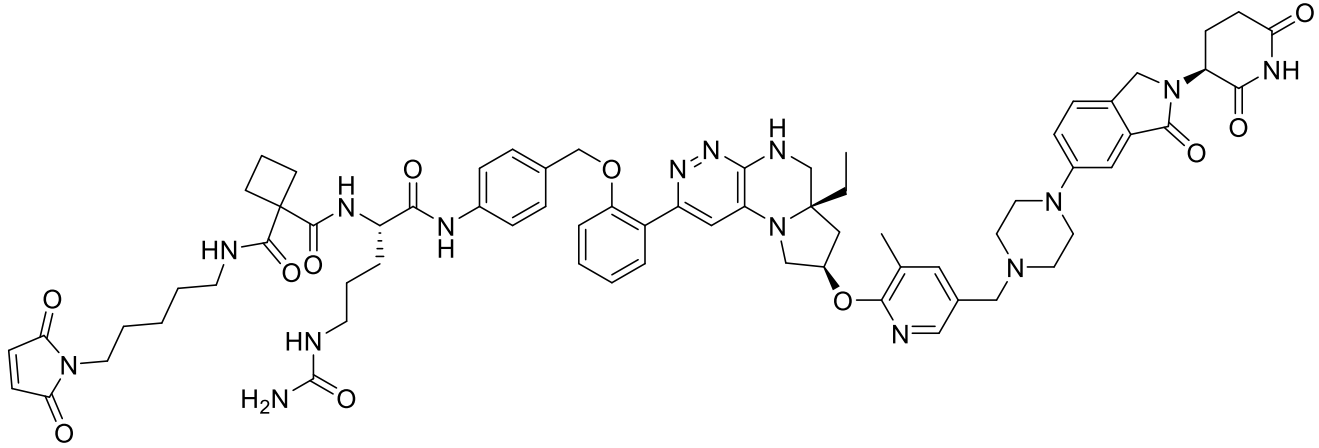


- Explored chemically diverse architecture with unique properties to improve conjugatability
- Acidic O–H of degrader phenol selected as new linker attachment site
- Identified protease-cleavable, peptidomimetic linker with self-immolative PAB

1) Zhang, D.; et al. *Bioconjugate Chem.* **2018**, *29*, 267. 2) Wei, B.; et al. *J. Med. Chem.* **2018**, *61*, 989.

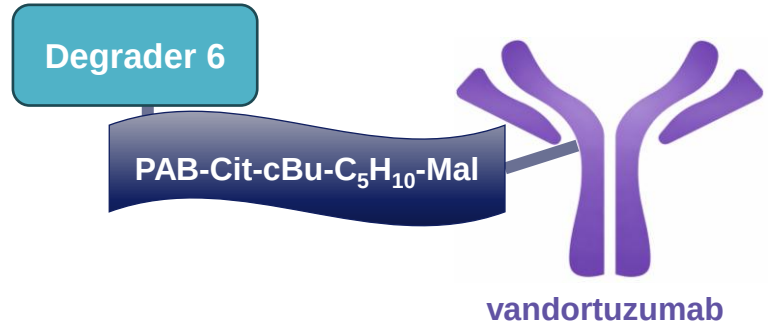
Conjugation of chemically diverse payload-linker afforded pDAC with higher DAR

PL 02



conjugation

polishing

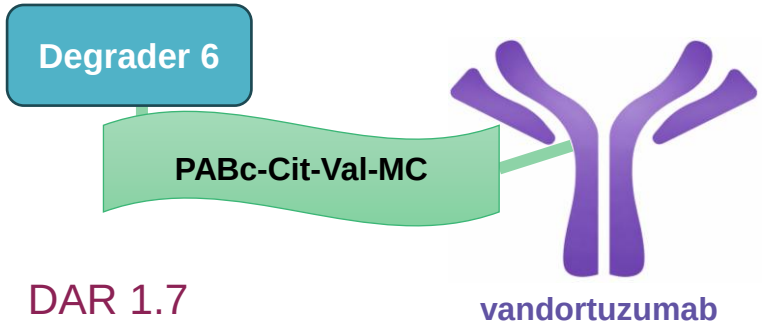


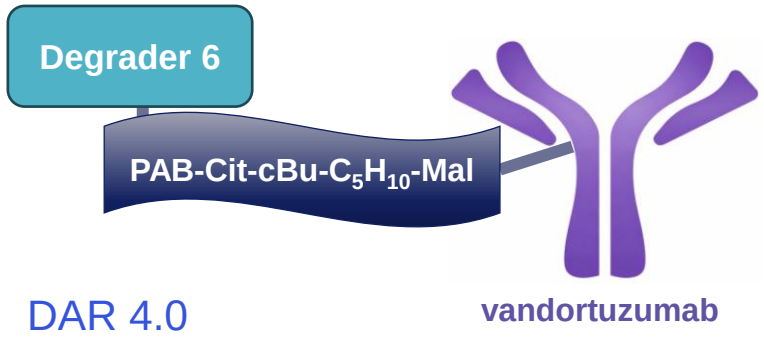
Property	DAC 08
Initial aggregation (%)[a]	<1
DAR (average)	4.0
Monomeric purity (%)	99

[a]Aggregation (%HMWS) under standard, unoptimized conditions. An early metric for developability.

- **PL 02** conjugated via stochastic, native-cysteine conjugation
- Bioconjugation provided pDAC with DAR 4 and good properties

Higher DAR improves degradation potency but not antiproliferation activity





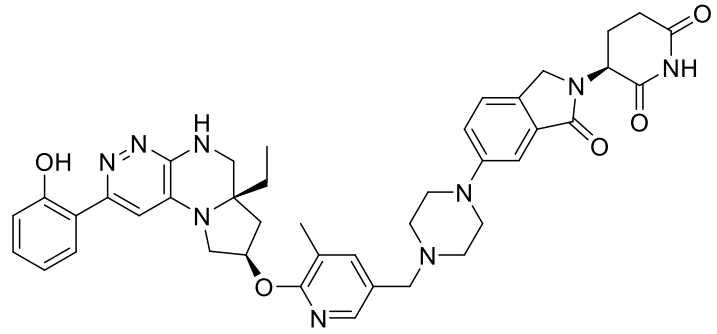
Potency (ng/mL)	DAC 05	DAC 08
LNCaP SM2 DC_{50} (D_{max})	290 (82%)	35 (82%)
PC3 SM2 selectivity	10x	290x
LNCaP SM4 DC_{50} (D_{max})	2600 (60%)	340 (75%)
PC3 SM4 selectivity	3x	>29x
LNCaP prolif EC_{50} (E_{max})	2300 (86%)	7300 (60%)

LNCaP STEAP1+; PC3 STEAP1-.

- Increasing drug loading notably improved degradation potency, especially for SMARCA4
- New linkage also confers improved degradation selectivity in antigen-low cell line
- Proliferation activity remained poor despite exceptional payload activity

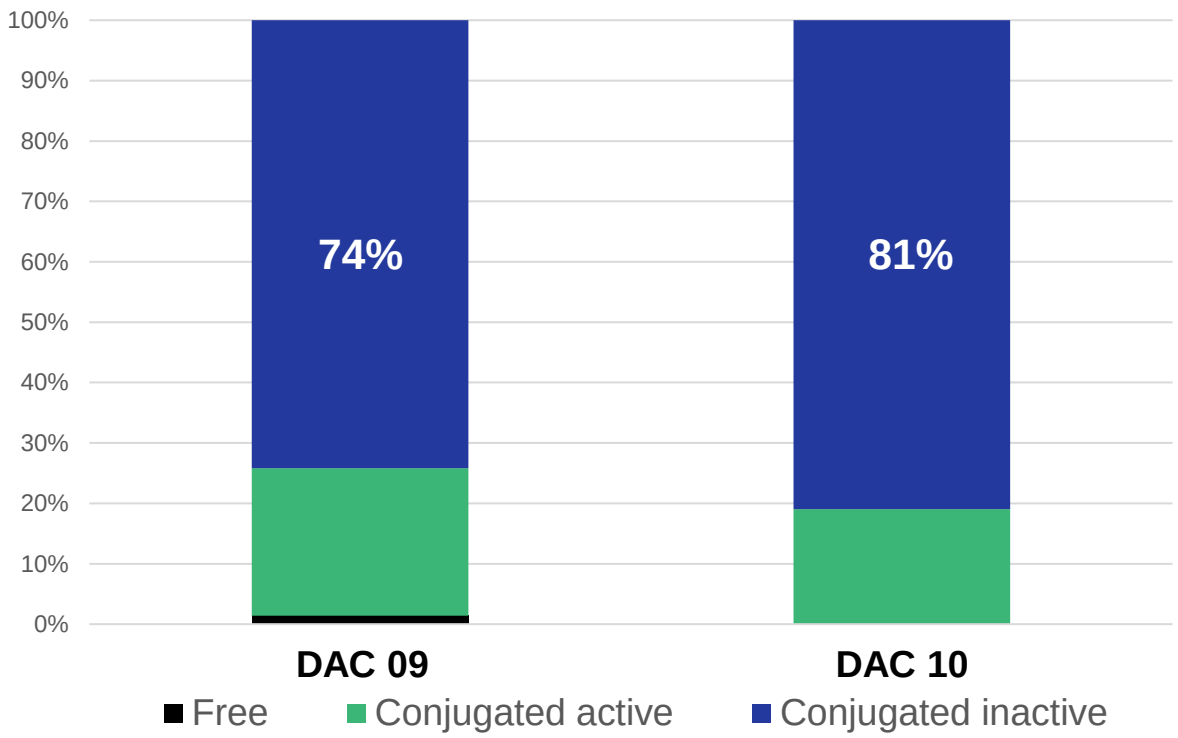
Degrader payload 6 demonstrates on-antibody hydrolysis in human plasma

Payload stability upon aging in plasma



	6
hPlasma stability, $t_{1/2}$ (d)	1.4
mPlasma stability, $t_{1/2}$ (d)	1.4

Payload species upon aging pDAC in plasma (2 d)



- In plasma, payload **6** hydrolyzes both alone as free drug and on-antibody as a conjugate
- Hydrolysis produces inactivated payload, which represents major conjugated species after just 2 d
- To advance more potent pDACs improved plasma stability proved essential

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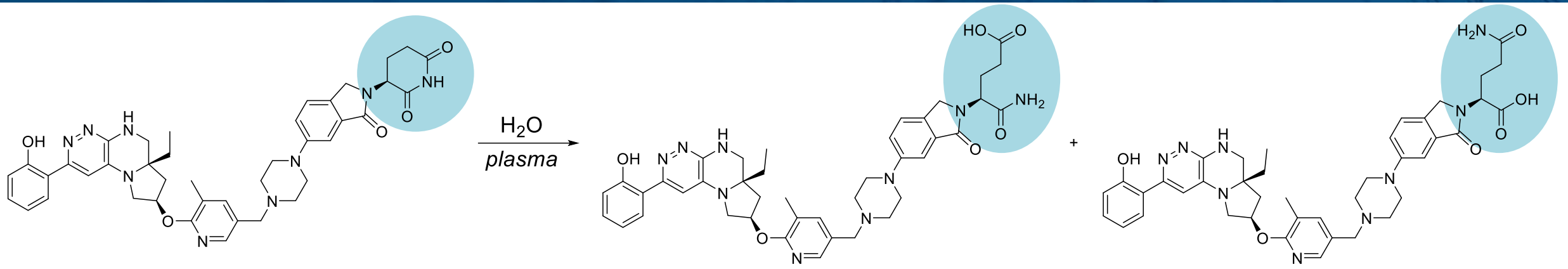
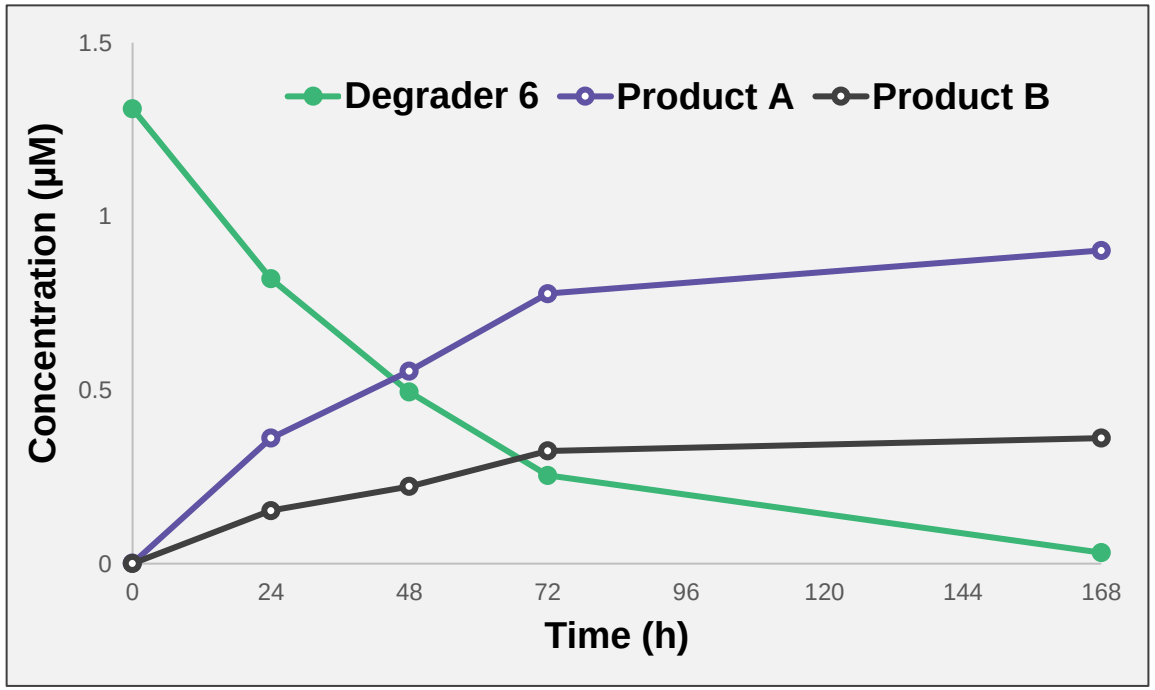
Mechanism of payload inactivation involves glutarimide hydrolysis



Degrader **6**

Product **A**
Major

Product **B**
Minor



- Two regioisomeric hydrolysis products observed in plasma
- Hydrolysis proceeds to near-quantitative conversion (7 d)
- Additional stability desired for pDAC payload

1) Schumacher, H.; et al. *Brit. J. Pharmacol.* **1965**, *25*, 324.
2) Kumar, G.; et al. *Cancer Chemother. Pharmacol.* **2009**, *63*, 1171.
3) Hoffman, M.; et al. *Cancer Chemother. Pharmacol.* **2013**, *71*, 489.

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Myth 2

Analogy MYTH

Good small molecules parameters translate to good payload qualities

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Design of ADCs requires consideration of modality-specific features

Dosing

- Once monthly dosing
- $t_{1/2}$ ~ 7 d

Storage

- Aqueous buffer
- Intentionally hemi-labile (cleavable)
- Shelf-life considerations

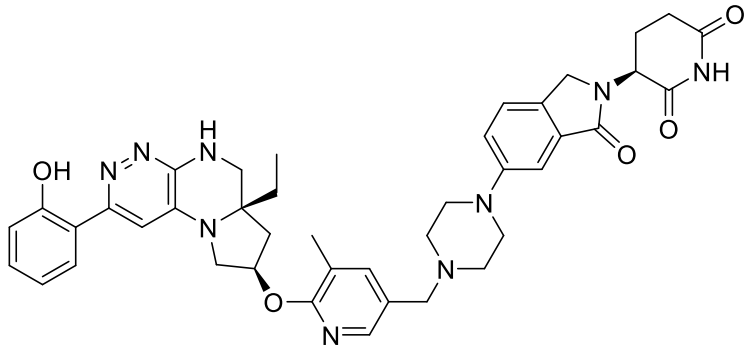
Composition

- Heterogeneous mixture
- Stochastic distribution of species

1) López de Sá, A.; et al. *J. Hematol. Oncol.* **2023**, *16*, 118. 2) Buecheler, J. W.; et al. *J. Pharm. Sci.* **2020**, *109*, 1611.

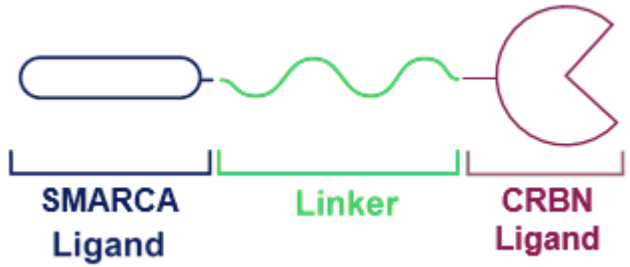
Medicinal chemistry approach extended payload stability in plasma

Initial CRBN-based degrader payload



Potency assays	6
HeLa HiBit SM2 DC_{50} (pM) (D_{max})	40 (97%)
HeLa HiBit SM4 DC_{50} (pM) (D_{max})	90 (97%)
Fold Selectivity SM4/SM2	2x
In vitro ADME	
hPlasma stability, $t_{1/2}$ (d)	1.4

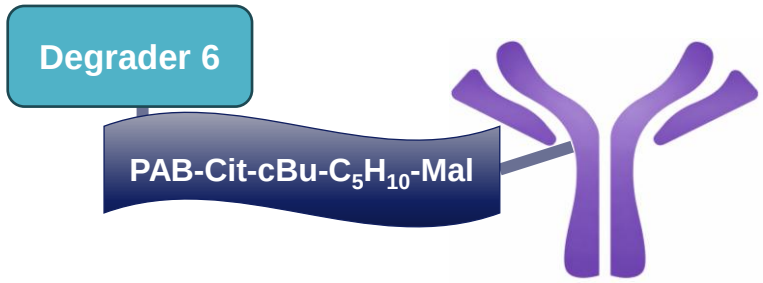
Plasma-stable CRBN-based degrader payload



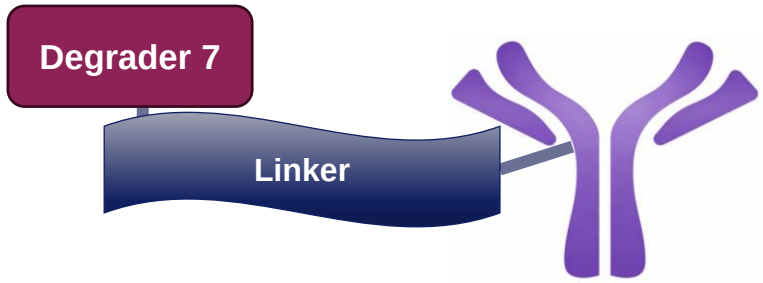
7
26 (93%)
35 (96%)
1x
10

- Payload stability investigation informed additional degrader discovery campaign
- Focused on maintaining exceptional potency while limiting hydrolysis in plasma
- Identified degrader **7** with excellent potency and improved human plasma stability

More stable payload delivers more potent pDACs with desired activity profile



DAR 4.0 vandortuzumab



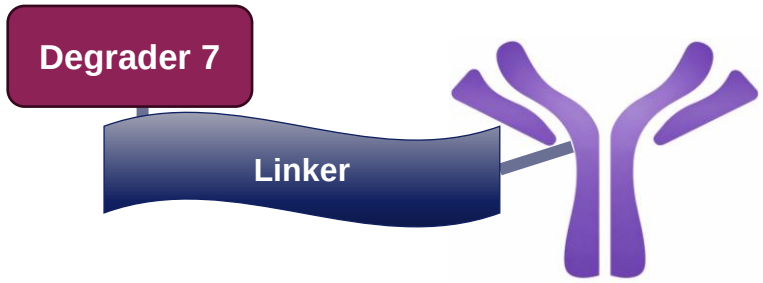
DAR 3.7 vandortuzumab

Potency (ng/mL)	DAC 08	DAC 11
LNCaP SM2 DC_{50} (D_{max})	35 (82%)	36 (89%)
PC3 SM2 selectivity	290x	150x
LNCaP SM4 DC_{50} (D_{max})	340 (75%)	53 (80%)
PC3 SM4 selectivity	>29x	160x
LNCaP prolif EC_{50} (E_{max})	7300 (60%)	210 (82%)

LNCaP STEAP1+; PC3 STEAP1-.

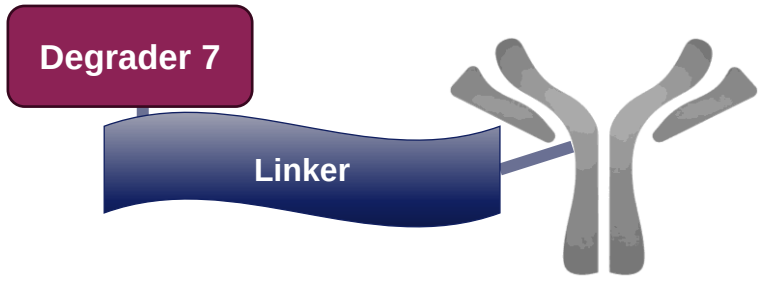
- Payload-linkers containing more stable degrader **7** conjugated to anti-STEAP1 antibody
- Resulting pDACs demonstrated superior SMARCA4 degradation and antiproliferative activity

Potent STEAP1 x SMARACA2/4 pDAC demonstrates antigen-selective activity



DAR 3.7

vandortuzumab



DAR 3.9

isotype

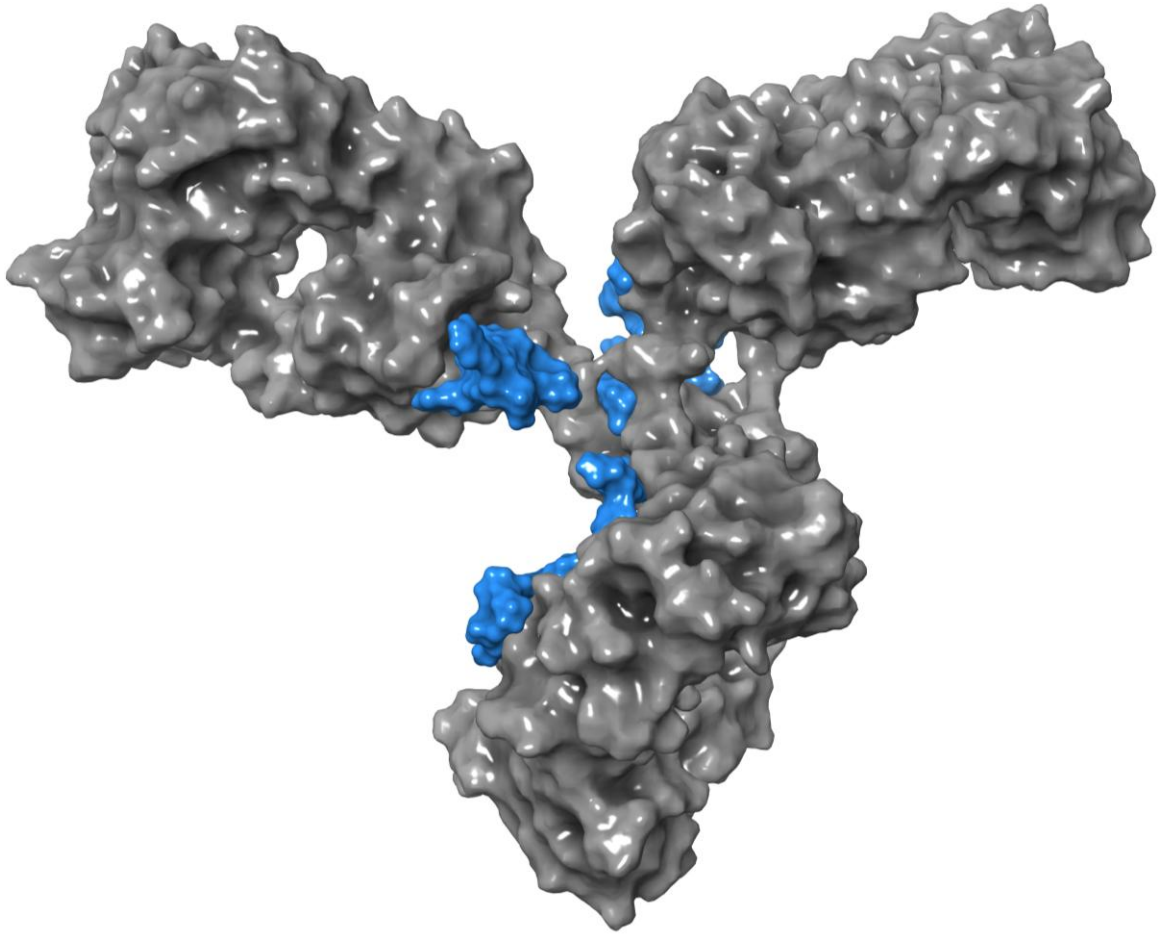
Potency (ng/mL)	DAC 11	DAC 12
LNCaP SM2 DC_{50} (D_{max})	36 (89%)	--
PC3 SM2 selectivity	150x	--
LNCaP SM4 DC_{50} (D_{max})	53 (80%)	>1200 (14%)
PC3 SM4 selectivity	160x	n/a
LNCaP prolif EC_{50} (E_{max})	210 (82%)	>1200 (14%)

LNCaP STEAP1+; PC3 STEAP1-.

- DAC **11** demonstrates exceptional antigen-selective activity
- Two-order of magnitude selectivity in antigen-negative PC3 cell lines
- Degradation and antiproliferation activity not observed for isotype control

Identification of STEAP1 x SMARCA2/4 pDACs highlights key design features

Model of precision DAC with Degrader 5 payload

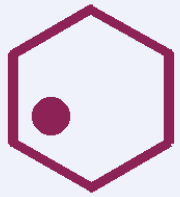


- Medicinal chemistry identified three potent, dual SMARCA2/4 degrader payloads
- Exceptional payload potency and long-term payload stability proved critical parameters
- Payload-linker composition and physicochemical properties affected pDAC developability and activity metrics
- Resulting pDACs demonstrated potent and antigen-selective activity in vitro

Case studies highlight nuances in extending SMARCA2/4 payloads to other antigens

Case Study 1

STEAP1
vandortuzumab



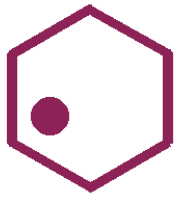
SMARCA2/4 degrader
Degrader 7

Good pDAC activity

Matched payload and antigen

Case Study 2

CEACAM5
tusamitamab



SMARCA2/4 degrader
Degrader 7

Poor pDAC activity

Same payload,
mismatched activity

Case Study 3

PSMA
rosopatamab

SMARCA2/4 degrader
Degrader 5

Good pDAC activity

Different antigen tolerates
less potent payload

Myth 3

Copy-and-Paste MYTH

Payload-linkers work for any antigen target

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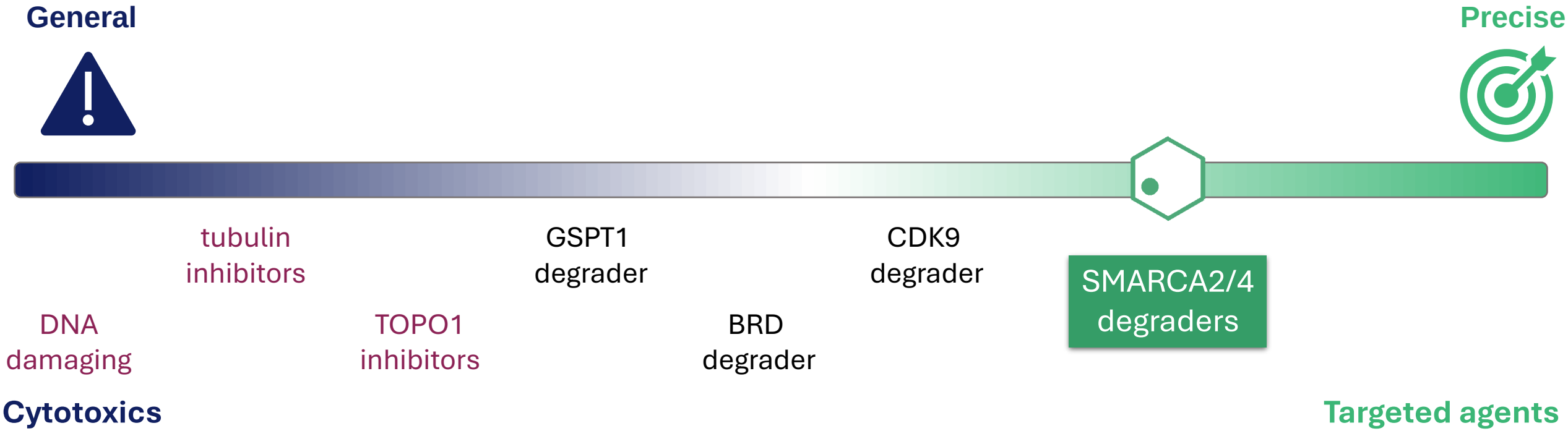
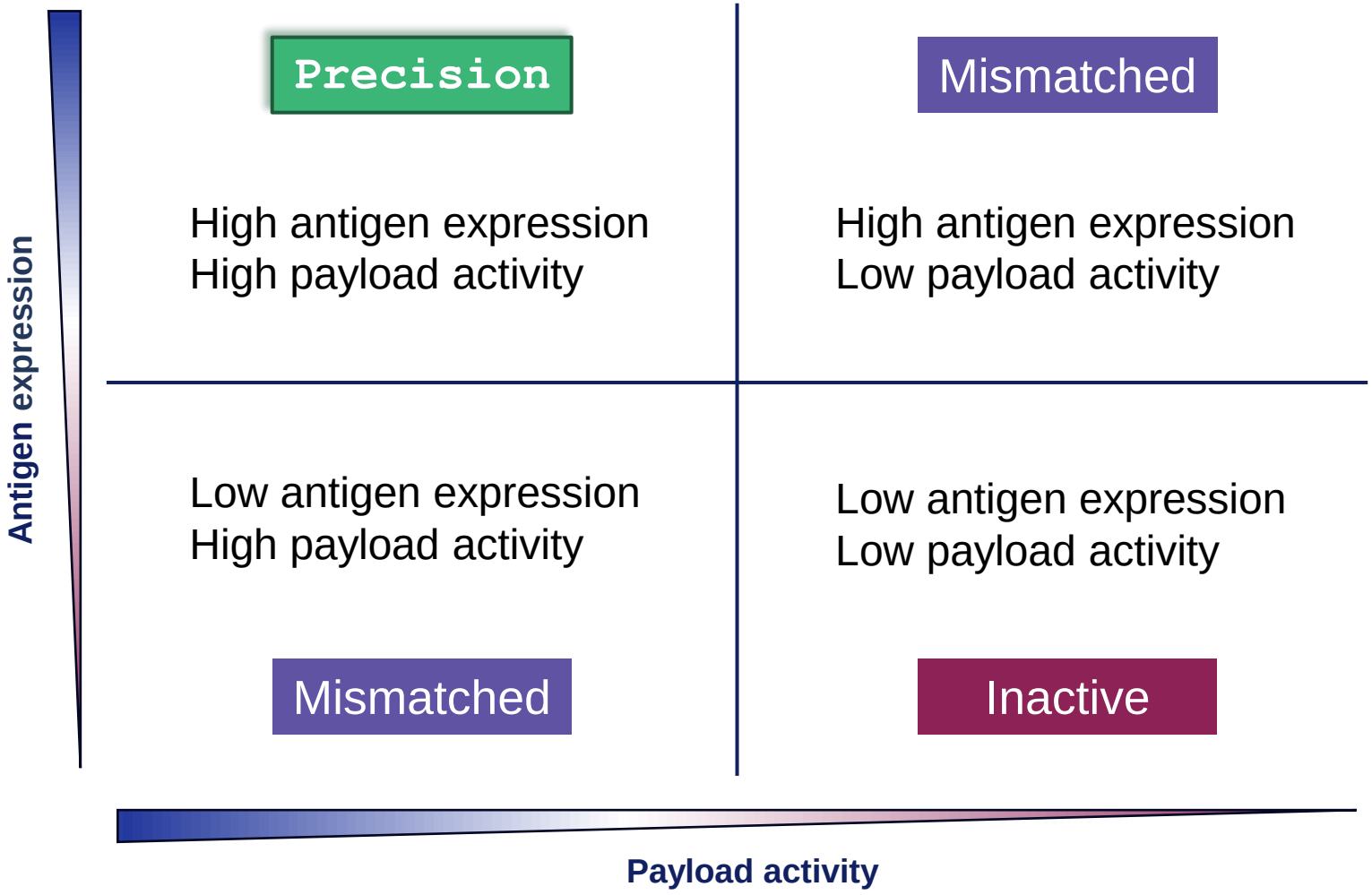
Dialing in payload precision influences downstream ADC design and properties



- Precision exists along spectrum from broad cytotoxics to highly indication-specific targeted agents
- Precision narrows application (generality) but offers potentially improved safety (therapeutic index)

For reviews of degrader-antibody conjugates, see 1) Hong, K. B.; An, H. *J. Med. Chem.* **2023**, *66*, 140. 2) Guo, Y.; et al. *E. J. Med. Chem.* **2024**, *268*, 116216.
Note: Payload classes are plotted for illustration purposes only. Location and spacing should be viewed as arbitrary.

Precision approach requires matching payload activity with antigen biology



Selection Criteria

- **Antigen biology**
  - Sufficient expression
  - Productive internalization
  - Disease context is key
- **Payload fit**
  - Intrinsic sensitivity to the payload mechanism of action
  - Degradation translation to antiproliferation/cytotoxicicity
  - Cross-check against antigen expression

Case Study 2: Degradation to antiproliferative translation hinders CEACAM5 x SMARCA2/4 pDAC

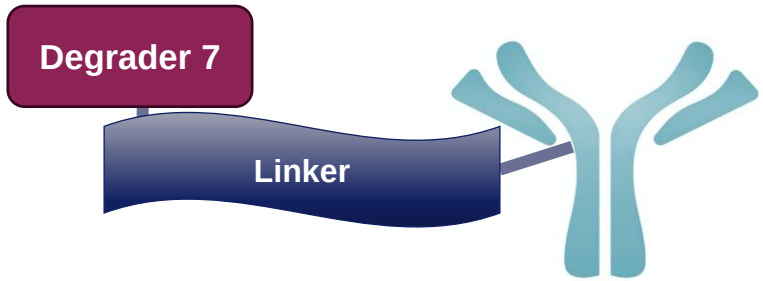
Case Study 2

tusamitamab x Degrader 7

CEACAM5 antigen
High surface expression[a]
Antibody internalization confirmed

SMARCA2/4 degrader translation
Degrader **7**: No antiproliferative activity[b]
Poor ADC antiproliferative activity

Same payload, mismatched activity



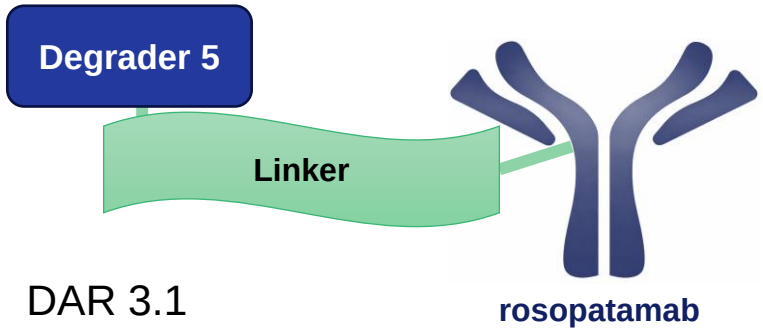
DAR 6.4

Cellular potency (ng/mL)	DAC 13
MKN45 SM2 DC_{50} (D_{max})	58 (77%)
MKN45 SM4 DC_{50} (D_{max})	44 (74%)
MKN45 proliferation EC_{50}	>10000

MKN45 CEACAM5+.

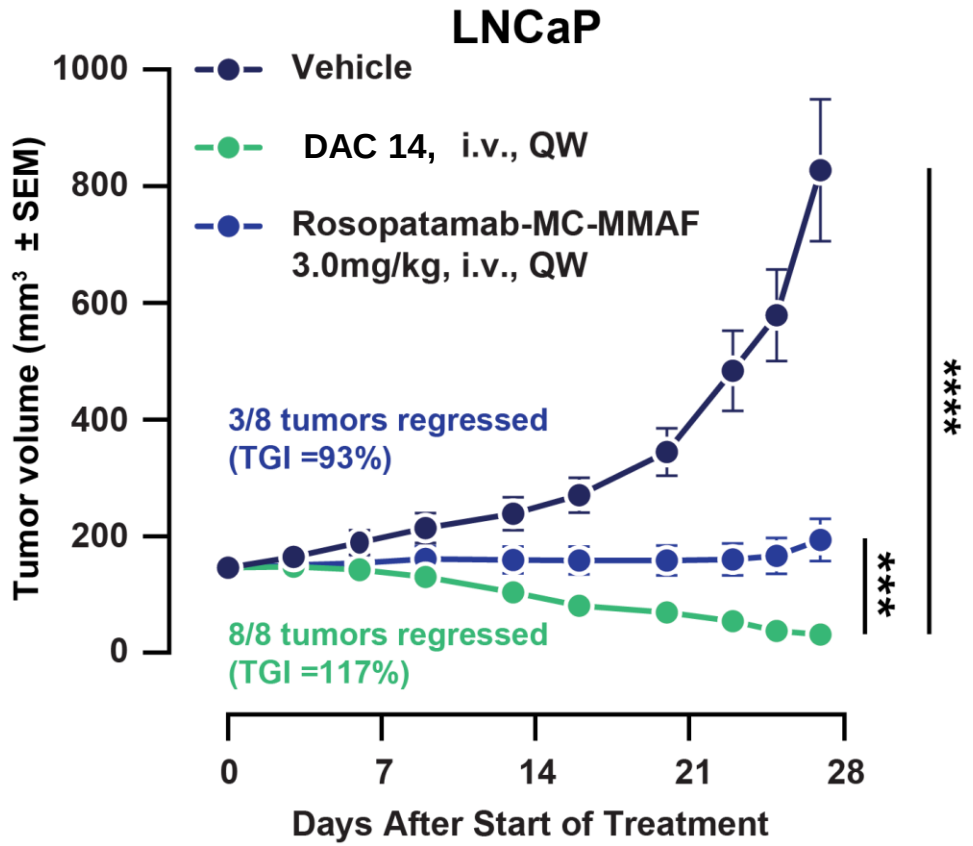
[a]MKN45 cell line: surface receptor number >400k. [b]Degradation DC_{50} < 1 nM; antiproliferation EC_{50} >1000 nM.

Case Study 3: PSMA x SMARCA2/4 pDAC demonstrates regressions and exceeds cytotoxic ADC benchmark



Cellular potency (ng/mL)	DAC 14
LNCaP SM2 DC_{50} (D_{max})	6.9 (87%)
PC3 SM2 selectivity	32x
LNCaP SM4 DC_{50} (D_{max})	26 (90%)
PC3 SM4 selectivity	57x
LNCaP proliferation EC_{50} (E_{max})	57 (92%)

LNCaP PSMA+; PC3 PSMA-.

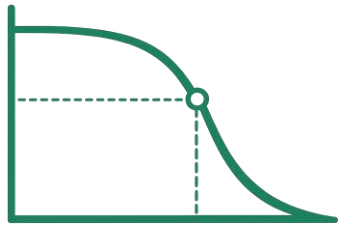


- pDAC incorporating less potent degrader **5** demonstrates good potency and antigen-selective degradation
- Anti-proliferative activity of DAC **14** comparable to MMAF benchmark ADCs
- In vivo, DAC **14** induces regressions and exceeds efficacy of MMAF benchmark ADC

1) Buesking, A.W. Novel Conjugates Summit, March 2025. 2) Carter, J. et al. *E. J. Cancer.* **2024**, *211*, 114688. (36th EORTC-NCI-AACR Symposium)

Identifying pDACs requires criteria that embrace the modality's complexities

Degrader payloads…



Must be highly potent
to achieve ADC activity

Picomolar potency

Should remain stable
in aqueous media & plasma

Stable for weeks

Require pairing
with right antigen target
for desired indication

Right combination matters

Acknowledging the Prelude Team

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