Parabilis MEDICINES



November 2026

***Creating Extraordinary Medicines***

*Drugging Previously Undruggable Intracellular Drivers of Serious Diseases*

# Forward-looking statements & disclaimer

This presentation contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. All statements other than statements of historical fact are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “on track,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements in this presentation include, without limitation, statements regarding: the design, timing and conduct of the planned Phase 3 PEDESTAL trial of zolucatetide, including initiation in the first half of 2027 and topline data anticipated in 2029; the Company’s alignment with the FDA on the PEDESTAL trial design; the potential therapeutic benefit, safety, tolerability and differentiation of zolucatetide and the Company’s other product candidates; the timing of anticipated data in FAP, ACP and HCC, and potential paths to registration, including tumor-agnostic development; the Company’s clinical collaboration with Revolution Medicines; the timing of ERG, AR and β-catenin degrader program; the size of potential patient populations and market opportunities; and the Company’s expected cash runway into 2030.

These forward-looking statements are based on management’s current expectations and beliefs, are not guarantees of future performance, and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied, including, among others: the interim and preliminary nature of the Phase 1/2 data presented, which involve a limited number of patients, including single-patient case studies, and may change as patients are followed longer and data undergo additional review, verification and audit; the risk that results of preclinical studies and earlier clinical trials may not be predictive of results in later trials, including PEDESTAL; the non-binding nature of FDA feedback and the risk that the FDA or other regulators may disagree with the Company’s trial designs or interpretation of data or require additional trials; delays or difficulties in initiating trials, activating sites or enrolling patients, unexpected adverse events or other safety findings; the Company’s substantial dependence on the success of zolucatetide; competition, and the market acceptance, pricing and reimbursement of any approved product; the Company’s ability to obtain, maintain and enforce intellectual property protection; the Company’s need for substantial additional capital and the risk that its cash runway estimate, which is based on assumptions that may prove wrong, is inaccurate; and general economic, market, geopolitical and regulatory conditions. For a further discussion of these and other risks, refer to “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the most recent quarter and its subsequent filings with the Securities and Exchange Commission. You should not place undue reliance on forward-looking statements, which speak only as of the date of this presentation. The Company expressly disclaims any obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

**Investigational status.** Zolucatetide and the Company’s other product candidates are investigational and have not been approved by the FDA or any other regulatory authority. Their safety and efficacy have not been established.

**Comparisons.** Comparisons to other products or product candidates are based on separate trials that differed in design, patient population, stage of development, timing and methodology, and certain figures were derived by the Company from published data using assumptions. No head-to-head trials have been conducted, and the results may not be directly comparable.


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# Parabilis:
# From platform breakthrough to advancing unique Helicon medicines

**2015:** Company founded; built on15 years of α-helix research at Harvard's Verdine Lab to drug the "undruggables"

**2018:** First successful *de novo* hit discovery screen on the Helicon™ platform

**2021:** First *in vivo*-active Helicons targeting β-catenin

**2023:** Mathai Mammen joins as CEO, President & Chairman of the Board

**2023:** Zolucatetide (FOG-001) IND

**2024:** Platform expansion into targeted protein degradation to further broaden pipeline

**2025:** Zolucatetide Ph1/2 clinical signals across desmoid tumors and other Wnt/β-catenin-driven tumors

**2026:** Zolucatetide further demonstrates strong efficacy and tolerability in desmoid tumors; clear path to FAP, ACP

**2027 & Beyond: Building the next chapter**
Zolucatetide advancing toward Ph3 registrational trials; expanding pipeline of novel Helicon candidates

***Pioneering the Novel Helicon Platform*** → ***Clinical Proof of Concept*** → ***Portfolio Expansion & Deepening of Patient Impact***


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# Led by an experienced leadership team and Board

## LEADERSHIP TEAM



**Mathai Mammen, M.D., Ph.D.**
Chairman, Chief Executive Officer & President

- **21 approved medicines** across career
- Former Global R&D Head, **J&J;** Research Head, **Merck**
- Co-founder & R&D Head, **Theravance, Innoviva**
- 40+ acquisitions/licenses; 350+ strategic collaborations
- Boards: **Sandoz, Xaira, Kelonia** ($7B Lilly acquisition); advisor, **General Atlantic**



**Helen Ho, Ph.D.**
Chief Business and Strategy Officer



**Teresa Jurgensen, J.D.**
EVP, General Counsel



**Thomas Kotarakos**
Chief Financial Officer



**Rohin Mhatre, Ph.D.**
Chief Technical Operations Officer



**Kristen Stants**
Chief People Officer



**Markus Haeberlein Ph.D.**
EVP, Discovery Science



**Jonathan Hurov, Ph.D.**
EVP, Discovery Biology



**John McGee, Ph.D.**
Scientific Co-Founder and EVP, Head of Platform



**Hannah Walter**
Enterprise Strategic Operations, Chief of Staff to the CEO

## BOARD OF DIRECTORS

**Mathai Mammen, M.D., Ph.D.**

**Alexis Borisy**
*Lead Independent Director*
*Founded/led 15+ biotech companies | 10 Nasdaq-listed companies*

**Edward Fitzgerald**
*Former ARIAD CFO (14 years) | 40+ years in finance*

**Rick Klausner, M.D.**
*Former NCI Director | Co-founder of GRAIL, Juno Therapeutics & Altos Labs*

**Alan Sebulsky**
*Former Adage Capital Partner | $2B+ Biotech Portfolio*

**Jake Simson, Ph.D.**
*Partner, RA Capital Management*

**Craig Tendler, M.D.**
*Former Head, Oncology Clinical Development, Johnson & Johnson | Contributed to the development of 15 oncology medicines and 30+ approvals*

**Barbara Weber, M.D.**
*Former CEO, Tango | Former Novartis Oncology R&D Leader*

**Krishna Yeshwant, M.D.**
*General Partner, GV | GV founding team member | Flatiron, Foundation Medicine, Relay & Beam*


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# 2026 has been an inflection year for Parabilis

*Entering the next chapter to build an enduring, fully integrated biopharmaceutical company*

## REALIZING THE HELICON POSSIBILITIES WITH ZOLUCATETIDE

**72.2%**

**Landmark ORR in desmoid tumors at 32 weeks[1]**

100% disease control rate; no discontinuations due to TRAEs

### Desmoid Phase 3 PEDESTAL

FDA-aligned trial design; initiation in 1H 2027

### FAP

Compelling early observations of duodenal polyp reductions; dose-ranging study underway

### ACP

Encouraging antitumor activity in 3 patients; more data 1H 2027

**More to come:**

HCC, CRC and other Wnt/β-catenin-driven tumors

Strong progress across Helicon research programs including β-catenin, ERG and allosteric AR$^{ON}$ degrader programs

## VALUE-CREATING PARTNERSHIPS

### Regeneron

Strategic collaboration on antibody-Helicon conjugates beyond oncology

$125M upfront and equity

Up to $2.2B in milestones

### Revolution Medicines

Clinical collaboration: zolucatetide + zoldonrasib + cetuximab in 2L/3L RAS G12D mutant MSS CRC

## FUELED FOR GROWTH

**$1.1B in cash[2]**

**Runway into 2030**

**$770.5M**

IPO on Nasdaq (PBLS) · June

**$305M**

Series F financing · January

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1. Objective response rate among response-evaluable patients with starting dose of ≥450 mg; data cutoff June 22, 2026.
2. Cash as of September 30, 2026.

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# Our growth strategy focused on relentless pursuit of key priorities

**1**

## Deliver on Zolucatetide Anchors

*Anchor indications: Desmoid, FAP and ACP*

- **Desmoid:** Initiating Phase 3 PEDESTAL registrational study
- **FAP:** Dose-ranging study ongoing
- **ACP:** Exploring a rapid path toward registration

**2**

## Expand the β-Catenin Franchise

*Advance zolucatetide in additional indications and progress next-gen β-catenin degraders*

- **Additional Wnt-driven tumors for zolu:** HCC and tumor-agnostic path
- **CRC:** Zolucatetide + RevMed's zoldonrasib + cetuximab
- **Next-gen β-catenin degraders:** To expand and extend the franchise

**3**

## Advance Helicon Research Pipeline

*Building a prostate cancer portfolio and pursuing other previously undruggable targets*

- **Prostate cancer:** ERG and $AR^{ON}$ degraders targeting key drivers
- **Additional targets:** Cyclin D1, p53, other undisclosed targets

**4**

## Broaden the Helicon Modalities

*Built to repeat, scale, and expand*

- **New modalities:** Degraders, induced proximity and AHCs
- **Regeneron:** Antibody-Helicon conjugates outside of oncology


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# Our pipeline of differentiated Helicon therapeutic candidates

| PROGRAMS | INDICATIONS | DISCOVERY | IND-ENABLING | PHASE 1 | PHASE 2 | PHASE 3 | ANTICIPATED UPCOMING MILESTONES |
|---|---|---|---|---|---|---|---|
| **Zolucatetide** β-catenin:TCF Inhibitor | ***Desmoid Tumors*** | | | | | | • Phase 3 PEDESTAL registrational study initiation 1H 2027 |
| | ***Familial Adenomatous Polyposis (FAP)*** | | | | | | • Additional FAP data Q1 2027 |
| | ***Adamantinomatous Craniopharyngioma (ACP)*** | | | | | | • Additional Ph1 ACP data 1H 2027 |
| | ***WPAM+ HCC, CRC*, Tumor-Agnostic Basket*** | | | | | | • Additional Ph1 HCC data Q1 2027 |
| **ERG Degrader** | ***ERG Fusion+ Prostate Cancer*** | | | | | | • IND filing 2H 2027 |
| **Allosteric AR$^{ON}$ Degrader** | ***AR-Dependent Prostate Cancer*** | | | | | | • IND filing 2H 2027 |
| **β-Catenin Degrader** | ***WPAM+ Tumors*** | | | | | | • Initiation of IND-enabling activities 2H 2027 |
| **Multiple Discovery Programs** | ***Additional previously "undruggable" targets*** | | | | | | |
| **5 Programs, including AHCs** | ***Multiple indications outside of oncology*** | REGENERON | | | | | |

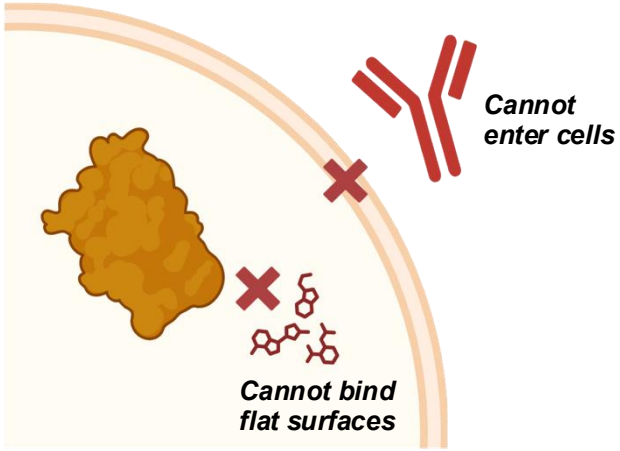
* Clinical collaboration with RevMed to evaluate zolucatetide + zoldonrasib + cetuximab in 2L/3L RAS G12D mutant MSS CRC
WPAM+: Wnt-pathway activating mutations; AHCs: Antibody-Helicon Conjugates

# **Helicons:** Redefining what is druggable inside a cell

*Antibody-like control of disease-driving intracellular targets*

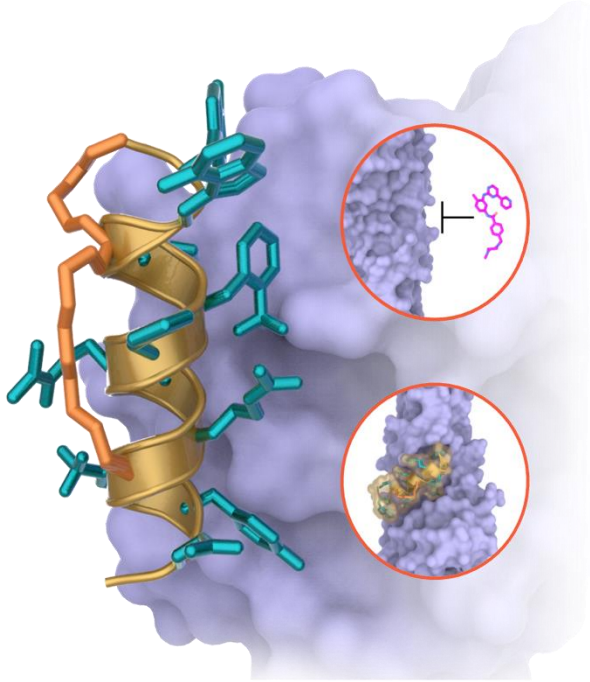
## The Challenge: Undruggable Biology

- Estimated 80% of biologically validated disease targets are considered undruggable
- The majority are intracellular proteins with relatively flat surfaces
- Small molecules can enter cells but cannot selectively bind these surfaces
- Antibodies can bind flat surfaces, but cannot enter the cells



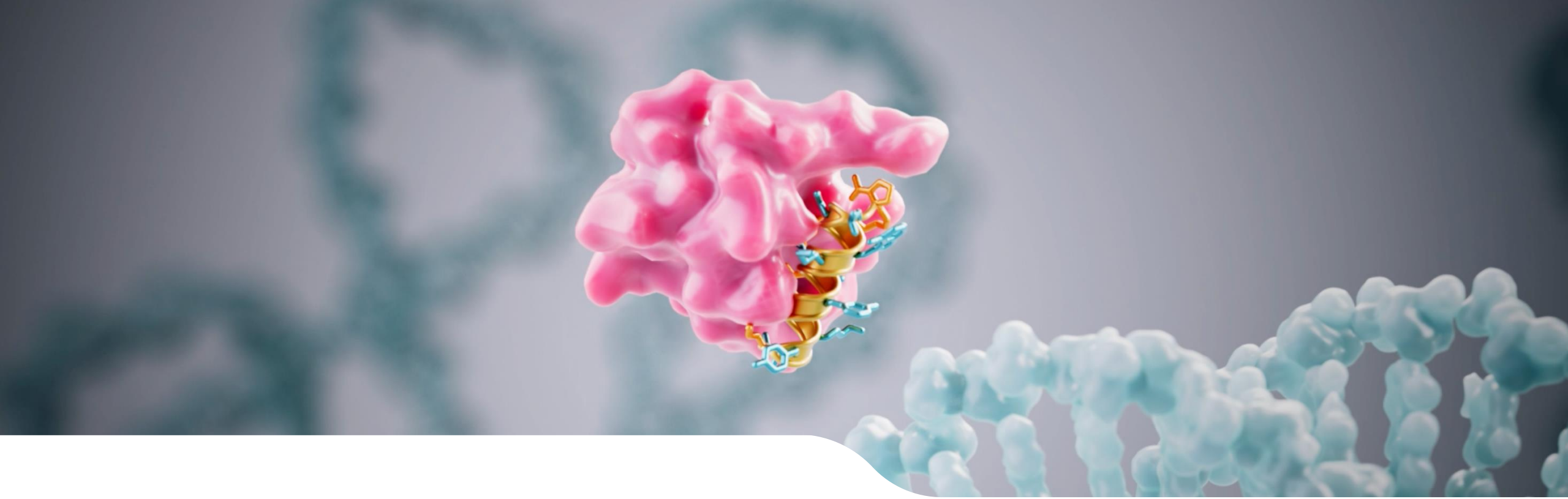

## Our Solution: Helicons

Stabilized α-helical peptides combine the precision of antibodies with the intracellular access and tunability of small molecules



- ✓ Engineered for cell penetration
- ✓ Bind to flat intracellular surfaces
- ✓ Tunable potency, selectivity, and pharmacokinetic & pharmacologic properties
- ✓ Expandable modality:
  - Inhibition
  - Targeted degradation
  - Targeted modulation and payload delivery


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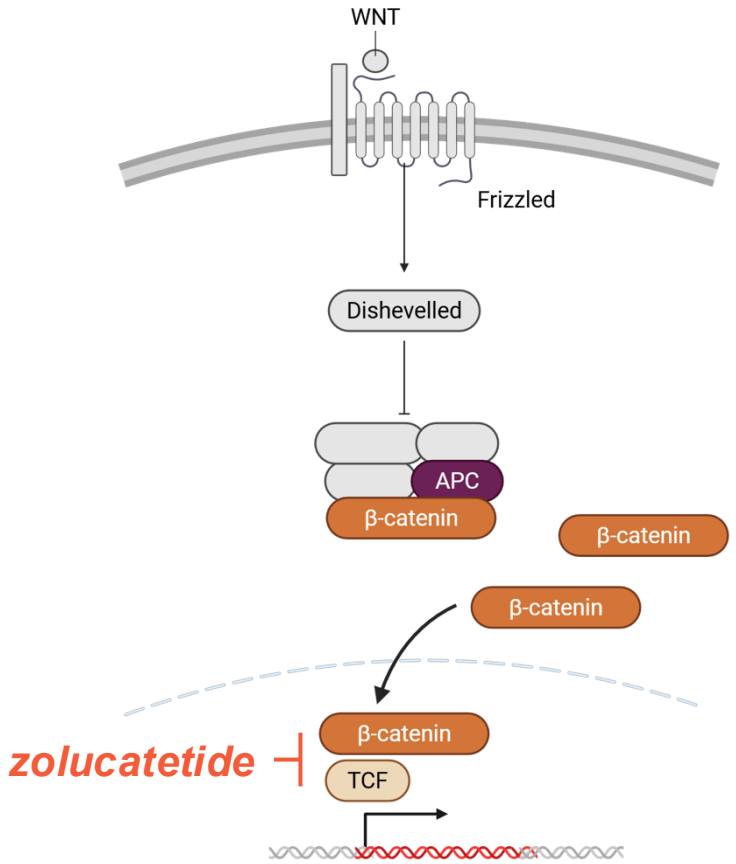
# **Zolucatetide:**
Directly targeting the causal driver of Wnt/β-Catenin-driven diseases

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# Zolucatetide: The first and only β-catenin:TCF inhibitor

*Pursuing a pipeline-in-a-product strategy for zolucatetide*

## Zolucatetide acts downstream of β-catenin or APC mutations




| | | INDICATIONS | MUTATIONS |
|---|---|---|---|
| ANCHOR INDICATIONS | 1 | Desmoid Tumors | β-Catenin, APC |
| | 2 | Familial Adenomatous Polyposis (FAP) | APC |
| | 3 | Adamantinomatous Craniopharyngioma (ACP) | β-Catenin |
| ADDITIONAL INDICATIONS | 4 | Hepatocellular Carcinoma (HCC) | β-Catenin |
| | 5 | Colorectal Cancer (CRC) | APC |
| | 6 | Additional Wnt/β-catenin driven indications | β-Catenin, APC |



Zolucatetide is an investigational product candidate that has not been approved by the FDA or any other regulatory authority for any use. Its safety and efficacy have not been established.

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# Desmoid tumors are invasive tumors with chronic, life-altering burden

## Desmoid tumors are driven by genetic mutations in CTNNB1 (β-catenin) or APC

### Sizable, chronic patient population

- **~11K patients actively managed** in the U.S.
- **30K** prevalent population
- **2x** as prevalent **in females**
- Typically diagnosed in **young adults** with peak incidence at age 30-40[1]

### Substantial symptomatic and functional burden

- **Chronic pain, functional loss, and psychological impact** that patients describe as controlling their daily lives

### High medical need despite existing therapies

- **Gaps remain in both efficacy and tolerability of GSIs**, including ovarian toxicity, rash and diarrhea

### Key unmet needs to address for desmoid tumor patients:

- Higher response rate
- Improved safety and tolerability profile
- Shorter time to response



1. Alman B, et al., (2020). 2. Kasper et al., (2017).

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# Phase 1/2 data demonstrate compelling efficacy, safety & tolerability profile for zolucatetide in desmoid tumors

## Objective Response at 32 Weeks

**72.2%**

**(13/18)**

Among all response-evaluable patients with starting dose of ≥450 mg and a scan at the landmark

Underscores impact of targeting causal driver of disease biology

Continues to show potential for differentiation from GSIs

## Disease Control

**100%**

Among all 46 response-evaluable patients with starting dose of ≥450 mg

No progression events or resistance

## Safety

**Favorable safety and tolerability profile**

TRAEs largely grade 1-2

None of the 76 participants enrolled discontinued due to TRAEs

## Registrational Study

**On track to initiate Ph3**

Registrational trial design aligned with the FDA

Induction dose of 450mg QW x 4 months + maintenance dose of 300mg Q2W selected

Topline data readout anticipated in 2029



Data cutoff: June 22, 2026

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# Zolucatetide early landmark ORRs compared with GSIs

| ORR Comparison to GSIs by RECIST 1.1 | | | |
|---|---|---|---|
| | GSI data derived from publications^ | | Reported in publications+ |
| **Treatment** | **24-week landmark** | **32-36-week landmark#** | **88-90 weeks** (Primary Analysis) |
| **Zolucatetide ≥ 450 mg*** | **61.9%** (13/21) | **72.2%** (13/18) | TBD |
| Nirogacestat* (DeFi) | 24.6% (17/69) | 34.8% (24/69) | 41% (29/70) |
| Varegacestat* (RINGSIDE) | 21.5% (17/79) | 40.5% (32/79) | 55.7% (44/79) |

- **Magnitude of early zolucatetide responses supports hypothesis of differentiated activity**
- **Zolucatetide data consistent with 74% ORR demonstrated in zolucatetide Feb 2026 data of patients with ≥2 scans with median time on treatment of 36 weeks**

Zolucatetide June 22, 2026 data cut; nirogacestat data published in NEJM (Gounder et al., 2023); varegacestat data published at ASCO 2026; ^ The data is derived from the aforementioned publications. Certain assumptions were made to derive this data. The Phase 3 trials of nirogacestat and varegacestat described above were conducted at a later stage in the development process using different trial designs than our Phase 1/2 clinical trial of zolucatetide. These trial results may not be directly comparable to those we have observed in our clinical trial of zolucatetide to date; # Zolucatetide scan at 32 weeks; nirogacestat and varegacestat at 36 weeks; + Nirogacestat primary analysis: Gounder M et al., NEJM 2023 (DeFi); varegacestat primary analysis: Gounder M, ASCO 2026 (RINGSIDE) and Immunome press release 30 May 2026


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# Zolucatetide shown to be well-tolerated at selected Phase 3 doses

| TRAEs in ≥20% of Study Participants | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **TRAEs, n (%)** | **150 mg (n=16)*** | | **300 mg (n=12)** | | **450 mg (n=46)** | | **900 mg (n=2)** | | **All patients (N=76)** | |
| | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** |
| **Any TRAE** | 15 (93.8) | 1 (6.3) | 8 (66.7) | 0 | 44 (95.7) | 6 (13.0) | 2 (100) | 2 (100) | 69 (90.8) | 9 (11.8) |
| **TRAEs (any grade) in ≥20% of pts** | | | | | | | | | | |
| Fatigue | 7 (43.8) | 0 | 4 (33.3) | 0 | 27 (58.7) | 1 (2.2) | 2 (100) | 0 | 40 (52.6) | 1 (1.3) |
| Alopecia | 5 (31.3) | 0 | 1 (8.3) | 0 | 21 (45.7) | 0 | 2 (100) | 0 | 29 (38.2) | 0 |
| Nausea | 4 (25.0) | 0 | 3 (25.0) | 0 | 21 (45.7) | 0 | 1 (50.0) | 0 | 29 (38.2) | 0 |
| Epistaxis | 4 (25.0) | 0 | 1 (8.3) | 0 | 16 (34.8) | 0 | 0 | 0 | 21 (27.6) | 0 |
| AST increased | 1 (6.3) | 0 | 0 | 0 | 17 (37.0) | 1 (2.2) | 2 (100) | 1 (50.0) | 20 (26.3) | 2 (2.6) |
| Blood bilirubin increased | 1 (6.3) | 0 | 0 | 0 | 15 (32.6) | 1 (2.2) | 2 (100) | 1 (50.0) | 18 (23.7) | 2 (2.6) |
| Myalgia | 3 (18.8) | 0 | 0 | 0 | 15 (32.6) | 0 | 0 | 0 | 18 (23.7) | 0 |
| **Any serious TRAE** | | | | | | | | | 2 (2.6)[1] | |
| **TRAE leading to discontinuation of treatment** | | | | | | | | | 0 | |
| **TRAEs leading to death (Grade 5)** | | | | | | | | | 0 | |

***Findings support favorable safety and tolerability profile and clear potential for differentiation vs. current therapies***

- **No treatment discontinuations due to TRAEs**
- **Not associated with ovarian toxicity**
- **No high-grade skin or GI toxicities**

1. Events were one each of grade 1 fever and grade 2 peripheral sensory neuropathy

*300 mg Q2W AUC-matched to 150mg QW, optimized to biweekly, which will support patient convenience within the study

Data cutoff: 22-Jun-2026; AST – Aspartate aminotransferase; TRAE – Treatment-related adverse event



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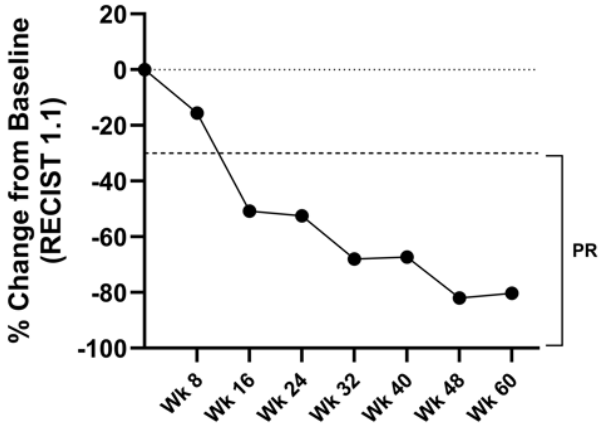
# Patient vignettes from the ongoing Phase 1/2 trial

## Case #1 (Pre-GSI): A patient w/ no prior systemic therapy

### 39-yo female with tumor in her left leg

- Diagnosed Dec ’24; began dosing at 450mg QW in Mar ‘25
- Declined nirogacestat due to ovarian toxicity concerns
- No systemic therapy prior to joining the trial
- Achieved a partial response at 16 weeks of treatment
- Remains on treatment at 150mg Q2W

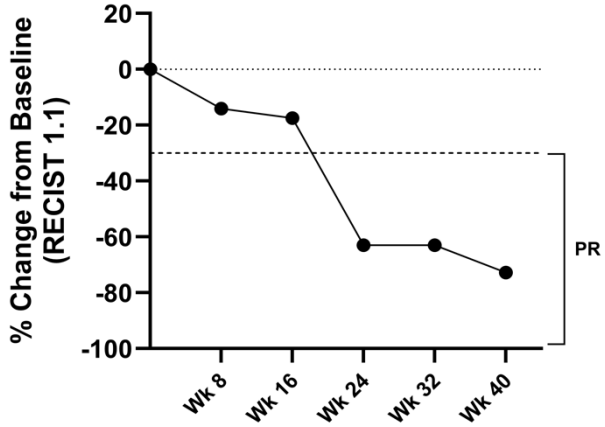
*“At enrollment, patient was experiencing pain and numbness in her leg and foot and had difficulty walking. [Prior to her 16-week scan], significant improvement in terms of pain – no further pain related to the tumor.” – Principal Investigator*




## Case #2 (Post-GSI): A heavily pre-treated patient

### 32-yo female with tumor in her left shoulder

- Diagnosed May ’12; began dosing at 450mg QW in Jul ‘25
- Previously treated with 5 therapies – sulindac/tamoxifen, vinblastine/methotrexate, imatinib, sorafenib, and nirogacestat – with progressive disease on each
- Achieved a partial response at 24 weeks of treatment
- Remains on treatment at 300mg Q2W






PR: partial response; QW: weekly dosing; Q2W; every-other-week dosing; Wk: week

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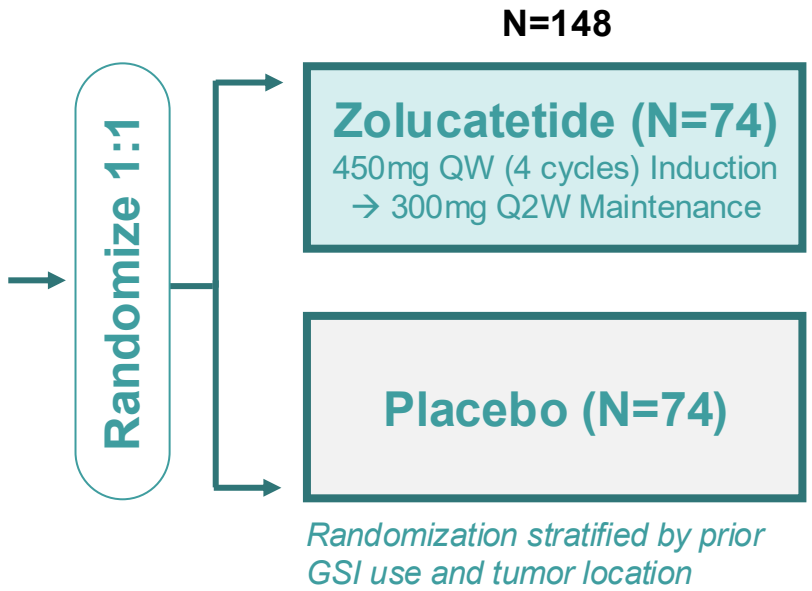
# Aligned with FDA on Phase 3 registrational study design

## Phase 3 PEDESTAL Trial

### Study Population

Treatment-naïve, recurrent, or refractory patients with desmoid tumor

Active disease: ≥20% tumor growth in the 12 months prior to screening




### Key Endpoints

**Primary:**
- PFS (RECIST 1.1)

**Secondary:**
- ORR
- MRI Tumor Volumetrics
- DOR, TTR, DCR
- PROs

**Exploratory:**
- MRI T2 hyperintensity/cellularity
- PD/Biomarkers

Study allows for cross-over to open-label extension (OLE) of participants in placebo arm after RECIST 1.1 disease progression per independent central review

**Phase 3 topline data read-out projected in 2029**

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GSI: gamma secretase inhibitor; PFS: progression-free survival; PRO: patient reported outcome; QW: weekly; Q2W: every two weeks; SoC: Standard of care

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# FAP patients face a lifetime of disease burden and fear of developing cancer, with no approved drug therapy

## FAP is 100% driven by germline APC mutations

### AGE 10-15

**Childhood and teens: Active surveillance**

- >34K patient prevalence in US[1]
- Diagnosed via family history, or *de novo* in ~30% of cases
- Colonoscopies begin around age of 10-15
- Near-inevitable progression to CRC if polyps are not managed[2]

### AGE 15-25

**Late teens/young adults: Major GI surgery**

- Colectomy is often performed to reduce polyp burden and colorectal cancer risk
- Often results in permanent ostomy or pouch
- Life-altering impact on fertility, continence, and quality of life

### AGE 25+

**Rest of adult life: Lifelong management**

- Continued polyp formation in GI tract (e.g., duodenum) in up to 90% of patients[3]
- Cancer risk persists post-colectomy, requiring life-long endoscopic surveillance and potentially additional surgeries



1. Across all ages; 2. Yen T, et al., (2022). 3. Johnson JC, et al., (2004).

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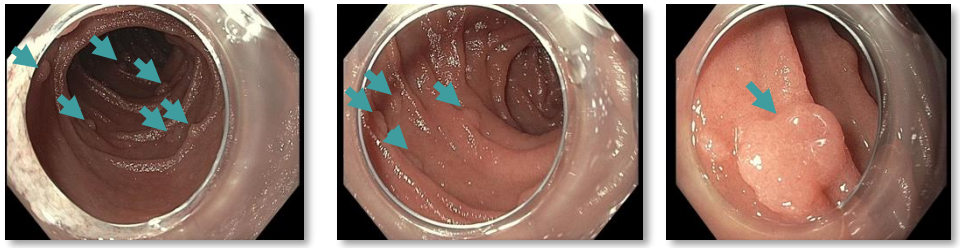
# Zolucatetide demonstrates potential to reduce pre-cancerous polyp burden

- Two desmoid tumor patients with FAP enrolled in the ongoing Phase 1/2 study of zolucatetide
- Both with APC mutation and history of FAP, post colectomy; findings from routine duodenal endoscopy

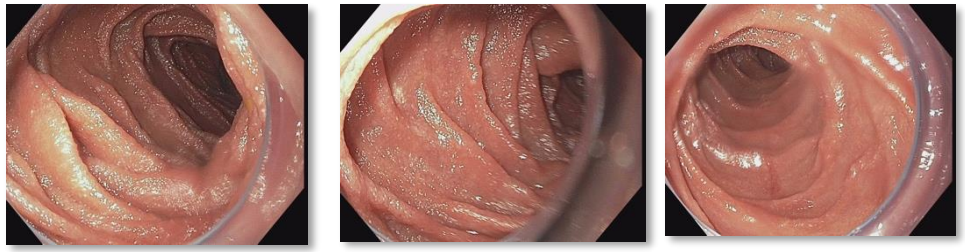
## Case 1: Spigelman Stage 2 → Stage 1

- **Clear reduction in duodenal polyp burden[1]**

**Baseline: 24-Jul-2023**



**On treatment: 21-Oct-2025**



## Case 2: Spigelman Stage 4 → Normal duodenum

- **Significant reduction in duodenal polyp burden at 10 weeks**

**Baseline: 28-Oct-2025**



**10 weeks on treatment: 7-Apr-2026**



**Anticipate sharing case studies in additional FAP/desmoid patients in Q1 2027**

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1. Klempner SJ, et al. Zolucatetide (FOG-001), a first-in-class direct β-catenin:TCF inhibitor. Poster #78. Presented at the InSiGHT Biennial Meeting; March 4–7, 2026; Singapore.

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# ACP is a debilitating, chronic disease with significant morbidity and no approved systemic therapy

## ACP is driven by genetic mutations in CTNNB1 (β-catenin)

### A lifelong disease driven by a single acquired mutation

- Slow-growing tumor near the pituitary and hypothalamus
- Estimated 620 new CP US cases annually; ACP is the majority[1]
- Bimodal age distribution with peaks in children (5-14) and older adults (55-74)
- Near-normal life expectancy; need for chronic treatment

### Lifelong multi-systemic complications

- Vision loss, hypothalamic obesity, and cognitive/mental health deficits
- Brain pressure symptoms: headaches, nausea, and lethargy
- Hormone deficiencies requiring replacement therapy

### No approved systemic therapy

- Surgery remains primary treatment; radiotherapy used as adjuvant
- Chemotherapy has shown limited efficacy
- Recurrence is common with current management approaches
- Lifelong surveillance amid repeat surgery and re-irradiation



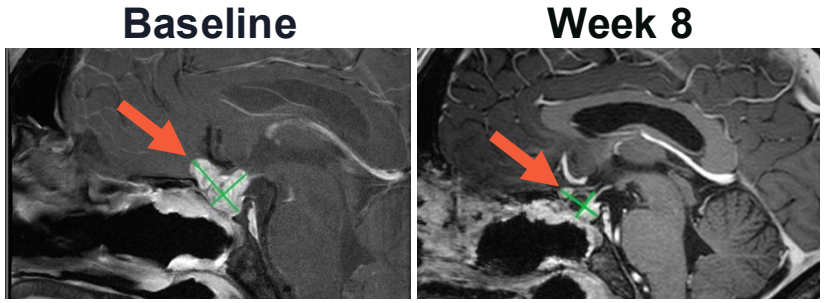
1. CBTRUS

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# Compelling tumor reductions observed in 3 patients with ACP

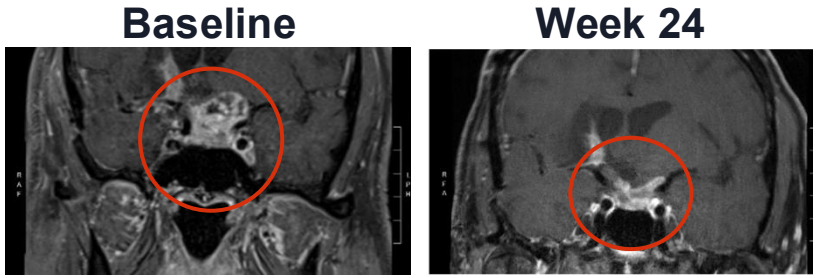
## Patient 1:

Partial response of -56% at week 16 (confirmed PR)



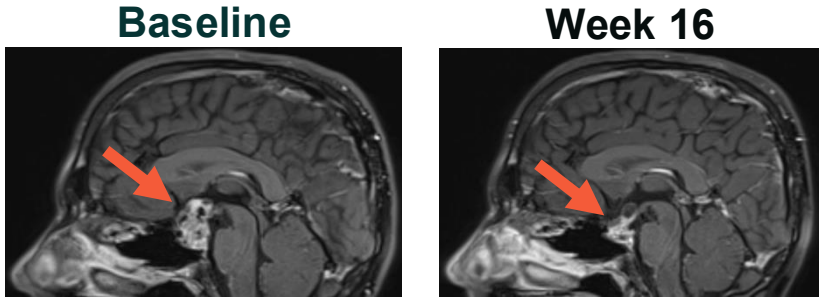

## Patient 2:

Has maintained stable disease for over 48 weeks, with a best tumor reduction of -19.2%; patient remains on study since initial dosing in August 2024




## Patient 3:

Partial response of -48% at week 16 (confirmed PR)




**Anticipate sharing clinical data from additional ACP patients in 1H 2027**

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Data cut off date of Aug 11, 2025
Data presented as an oral presentation at SNO 2025 by Kyriakos Papadopoulos et al.

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# Single-patient clinical activity in hepatocellular carcinoma (HCC) consistent with expected β-catenin biology

**β-catenin activating mutations seen in ~30% of HCC patients**

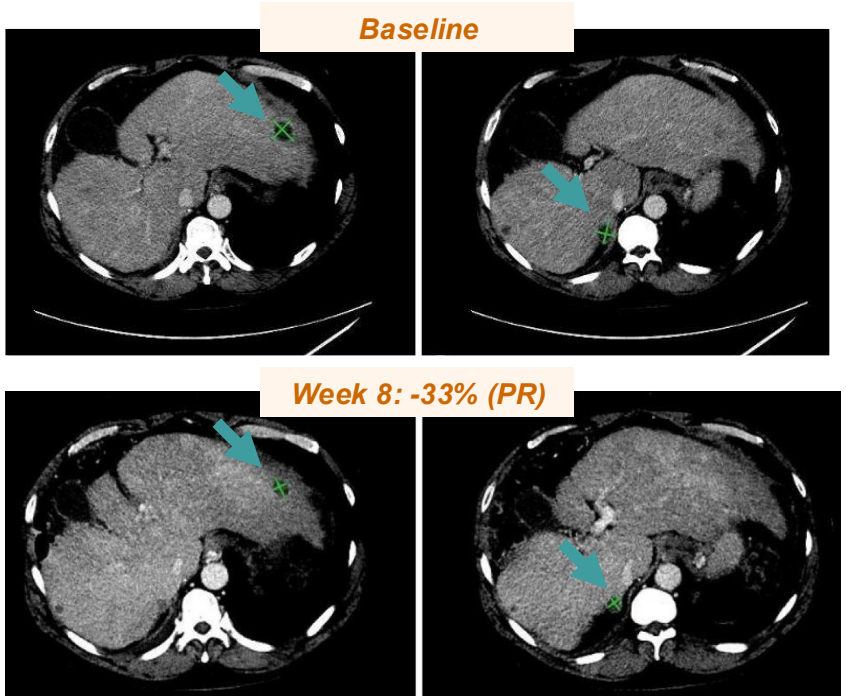
- Present across both viral and alcoholic etiologies
- ~700K-800K new HCC cases annually worldwide, with Asia accounting for over half of global cases

**Case study**

- Heavily pre-treated HCC patient with history of cirrhosis
- 4 pathogenic mutations (incl. β-catenin), 4 prior lines of therapy

**Clinical course on zolucatetide**

- Starting dose of 450 mg
- PR at Week 8 and confirmed PR by Week 16; tumor reduction continued to deepen over time
- PR maintained at last scan but off study due to underlying cirrhosis
- Deep molecular response at C2D1, with clearance of ctDNA

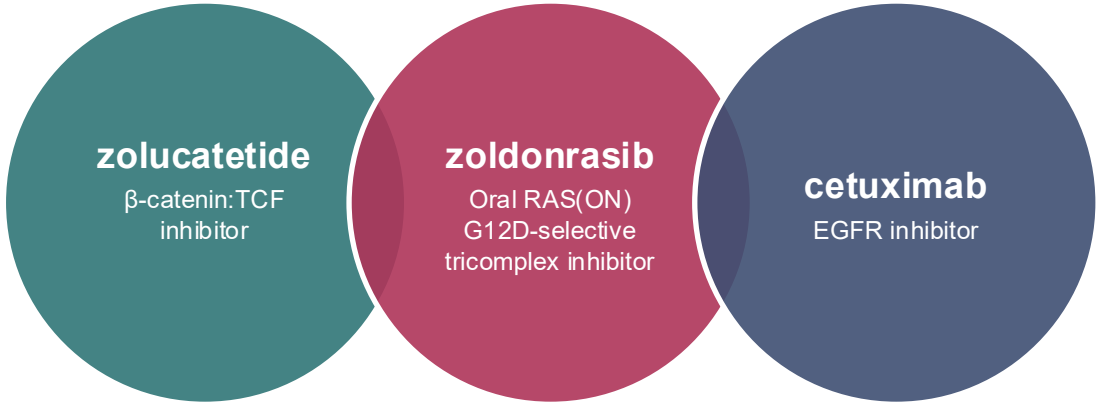



**Anticipate sharing additional HCC data at a medical meeting in Q1 2027**


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# Revolution Medicines Clinical Collaboration: Rational combination targeting RAS and Wnt in colorectal cancer

Parabilis MEDICINES + Revolution Medicines




In **2L/3L RAS G12D mutant** microsatellite stable (MSS) metastatic colorectal cancer*

- **Strong biological rationale:**
  - KRAS inhibition increases β-catenin transcriptional activity in patient-derived systems^
  - Inhibiting β-catenin:TCF deepens and extends durability of KRAS inhibition^
  - Significantly better efficacy of zolucatetide + zoldonrasib than either single agent in patient-derived xenograft (PDX) mouse model
- **Shared investment:** Parabilis conducts the study; RevMed supplies shares study costs equally

^ Centonze A, et al. Cancer Discovery. 2026;16:320–344. doi:10.1158/2159-8290.CD-25-0679.
* Zolucatetide and zoldonrasib are investigational agents that have not been approved by the FDA or any other regulatory authority. Their safety and efficacy have not been established.
Use of cetuximab in combination with these agents is investigational.


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# Responses across multiple Wnt/β-catenin-driven tumor types highlights opportunity for a tumor-agnostic development pathway

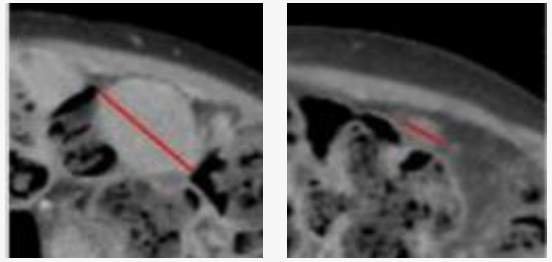
## *Examples of patient vignettes across tumor types*

### SPN

**−77.3%**

Best tumor change · Week 16

Baseline | Week 8 (-69.3%)



**Age / sex**
43 F

**Prior therapy**
Surgery and 4 prior systemic therapies

**Starting Dose**
450 mg*

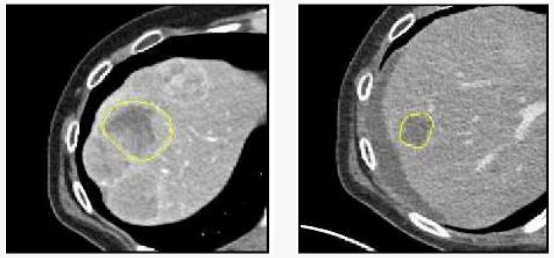
**Mutation**
β-Catenin

### pNEC

**−38.8%**

Best tumor change · Week 16

Baseline | Week 16 (-38.8%)



**Age / sex**
46 F

**Prior therapy**
RT and 8 prior systemic therapies

**Starting Dose**
450 mg

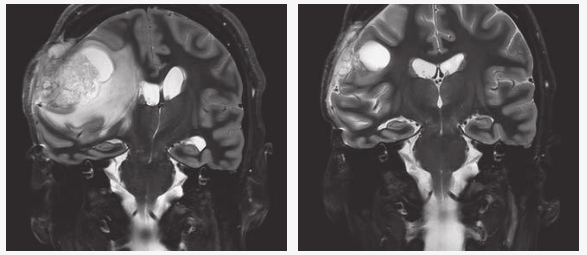
**Mutation**
β-Catenin

### Ameloblastoma

**−55.9%**

Best tumor change · Week 72

Baseline | Week 8 (-34.3%)



**Age / sex**
29 M

**Prior therapy**
Multiple surgical debulkings

**Starting Dose**
900 mg*

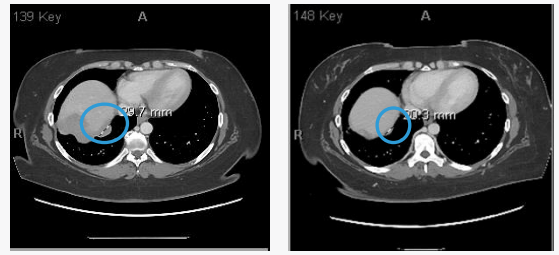
**Mutation**
APC

### Endometrial

**−40.8%**

Best tumor change · Week 24

Baseline | Week 8 (-30.6%)



**Age / sex**
40 F

**Prior therapy**
RT and 3 prior systemic therapies

**Starting Dose**
450 mg

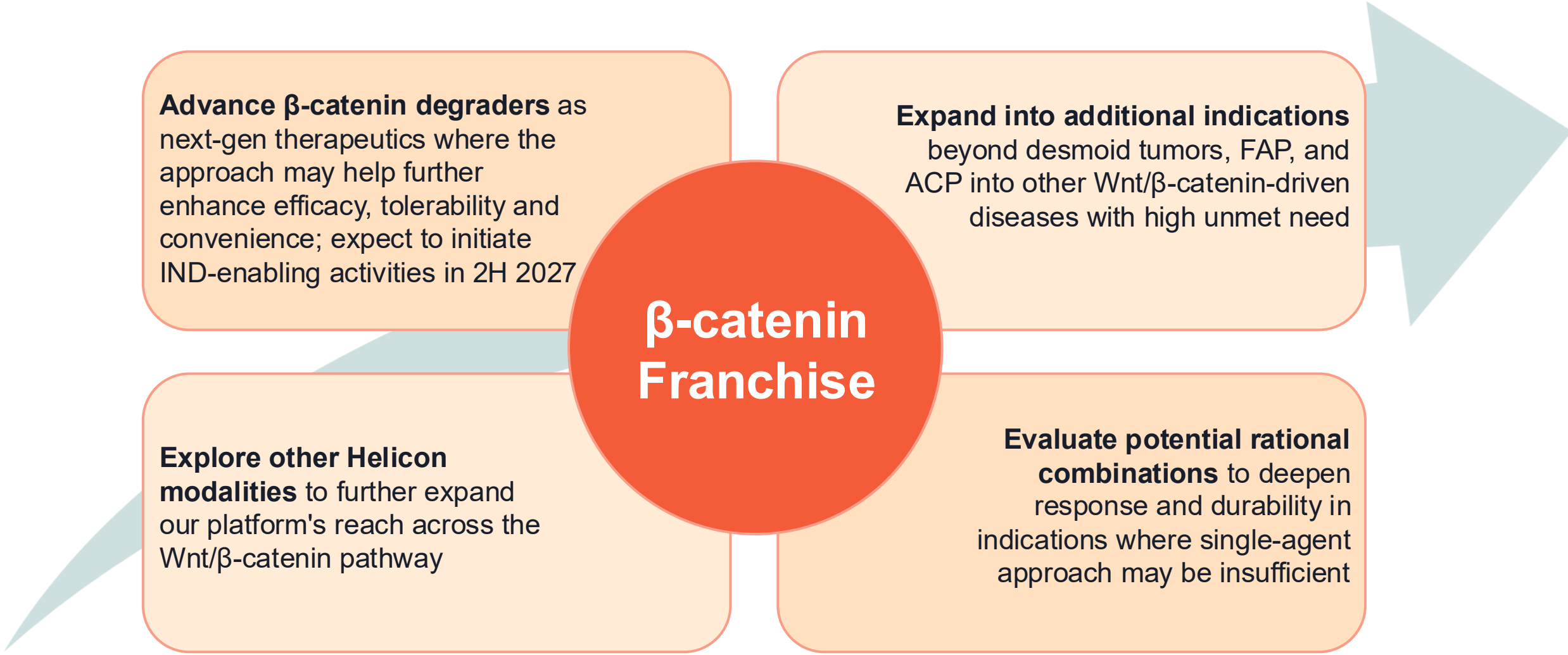
**Mutation**
β-Catenin

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SPN: solid pseudopapillary neoplasm of the pancreas; pNEC: neuroendocrine carcinoma of the pancreas; RT: radiation therapy
Ameloblastoma images: Klempner SJ, et al. N Engl J Med 2026;394:2168-70 (Figure 1, Panels A and C)
* Fixed dose equivalent of BSA based dose

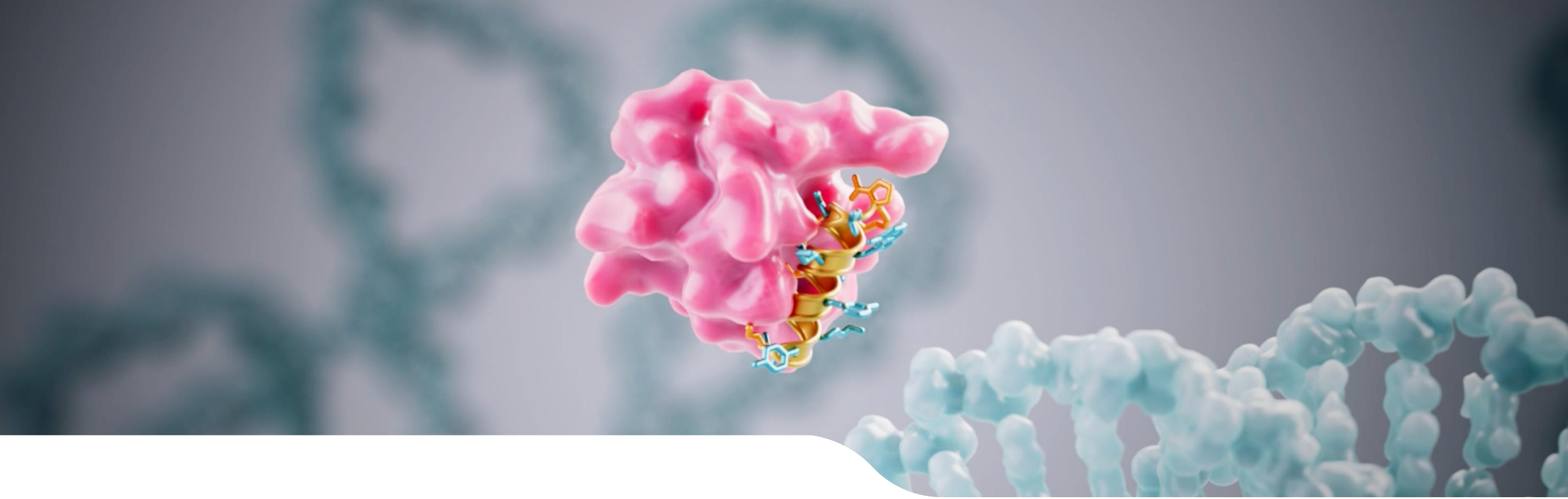
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# Building a lasting β-catenin franchise with a relentless focus on patient impact





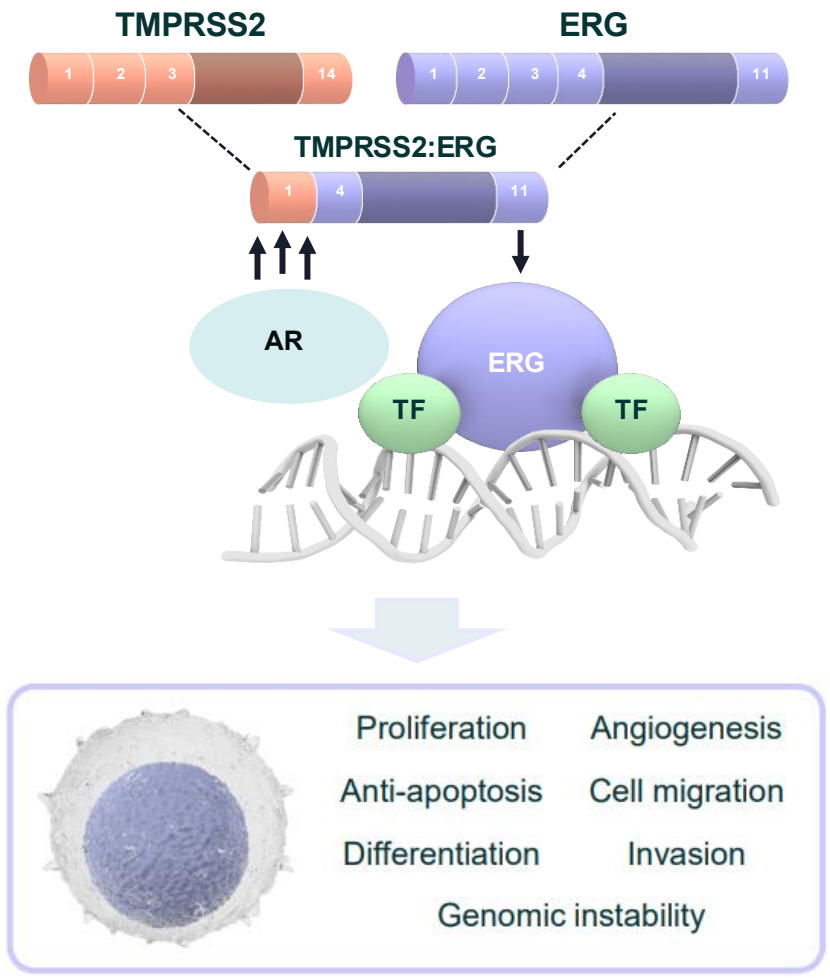
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**Research Pipeline & Platform:**
Addressing additional previously undruggable targets

Parabilis MEDICINES

# ERG Degrader: Potential first-in-class ERG degrader targeting a long-recognized, yet historically undruggable, cancer driver




## Why is ERG a critical target to drug?

- TMPRSS2:ERG is the most prevalent genomic alteration in prostate cancer, present in 40-50% of the patients across stages of disease
- AR drives high levels of ERG expression via TMPRSS2 promoter
- No approved therapies targeting this population – ERG has been historically undruggable despite industry efforts
- Estimated >15K new U.S. patients with ERG fusion-positive mAPMR (mCRPC) prostate cancer each year

## Our ERG degrader Helicons

- Potent, selective degradation with demonstrated tumor dependence, 60–95% TGI across multiple models
- Single-agent activity exceeding enzalutamide; additive in combination



ERG: ETS-related gene; TMPRSS2: transmembraneserine protease 2:; AR: androgen receptor; mCRPC: metastatic castration-resistant prostate cancer; TGI: tumor growth inhibition

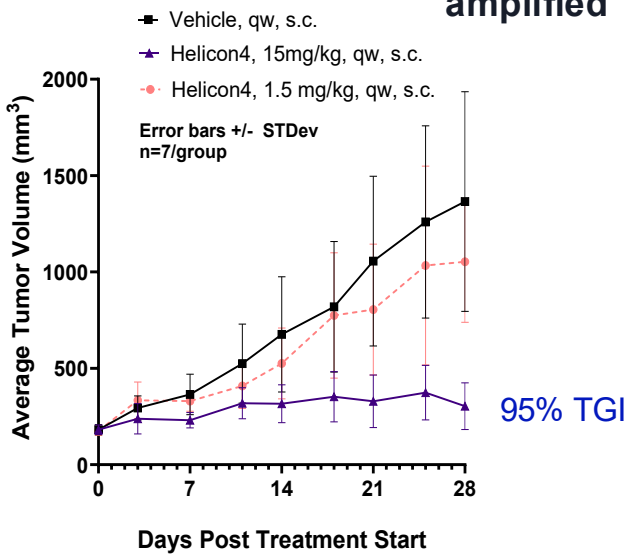
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# ERG Degrader: Dose-dependent, single-agent anti-tumor activity in ERG-fusion models; synergy in combination with enzalutamide

## Preclinical anti-tumor activity seen in ERG+ xenograft models

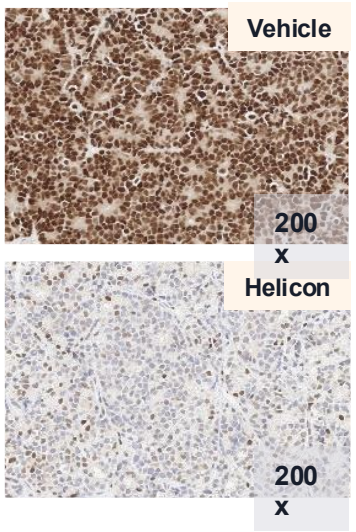
### Single agent anti-tumor activity in VCaP CDX model

**VCaP Xenograft Efficacy: ERG-fusion+, mCRPC AR amplified**



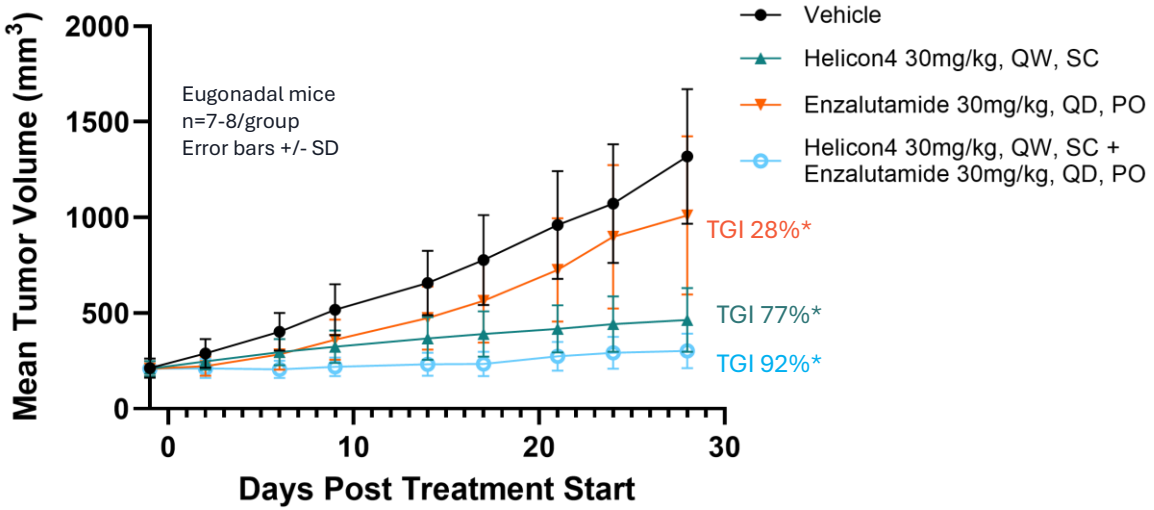

95% TGI

IHC-based ERG detection




### Single agent and combination anti-tumor activity in an enzalutamide-resistant PDX model#

**Patient Derived Xenograft Efficacy: ERG-fusion+, AR amplified, AR mutant H875Y**

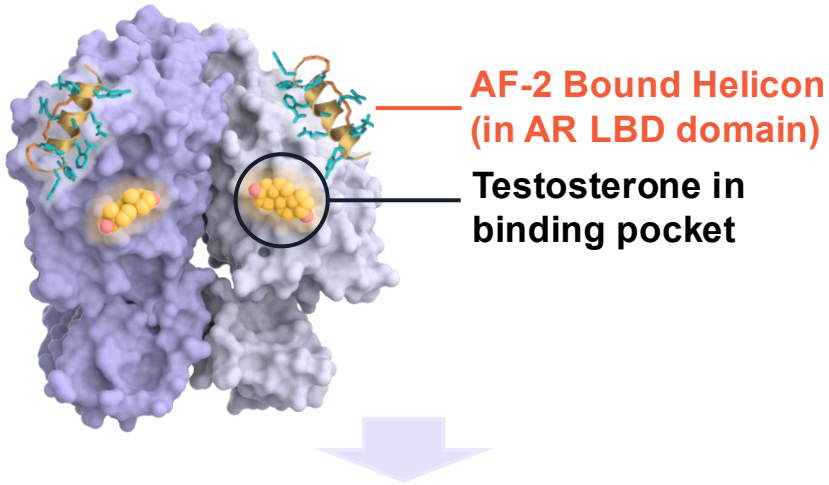



*Adjusted p-values relative to vehicle: 0.029, 0.012, 0.002

# Vasudevamurthy et al. Clinical Genitourinary Cancer, 2016


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# Allosteric $AR^{ON}$ Degrader: Differentiated target with the potential to combine with standard of care and overcome resistance




- ✓ Binding to the unique AF-2 pocket enables selective degradation of the $AR^{ON}$ agonist-bound pool
- ✓ Binding to distinct pool from all other AR targeting agents enabling combination
- ✓ $AR^{ON}$ degraders are not susceptible to common LBD mutations that confer resistance to $AR^{OFF}$ agents

## Why continue to target AR in Prostate Cancer?

- AR is the lineage defining transcription factor for prostate cancer, driving tumor cell survival and proliferation
- Current AR targeted therapies target $AR^{OFF}$ (inactive) pool yielding insufficient pathway suppression, allowing disease progression and emergence of resistance
- **~330K+** newly diagnosed patients; AR pathway dependence maintained in vast majority of patients including post-ARPI

## Why target the "ON" form of AR allosterically?

- $AR^{ON}$ is the active testosterone-bound pool that drives transcription; targeting requires novel binding site outside the testosterone binding pocket
- Combination of $AR^{ON}$ and $AR^{OFF}$ targeting agents with ADT has potential to yield deeper, more durable efficacy across stages of disease

## Our allosteric $AR^{ON}$ degrader Helicons

- **84% TGI** in AR-amplified xenograft; additive effects with enzalutamide



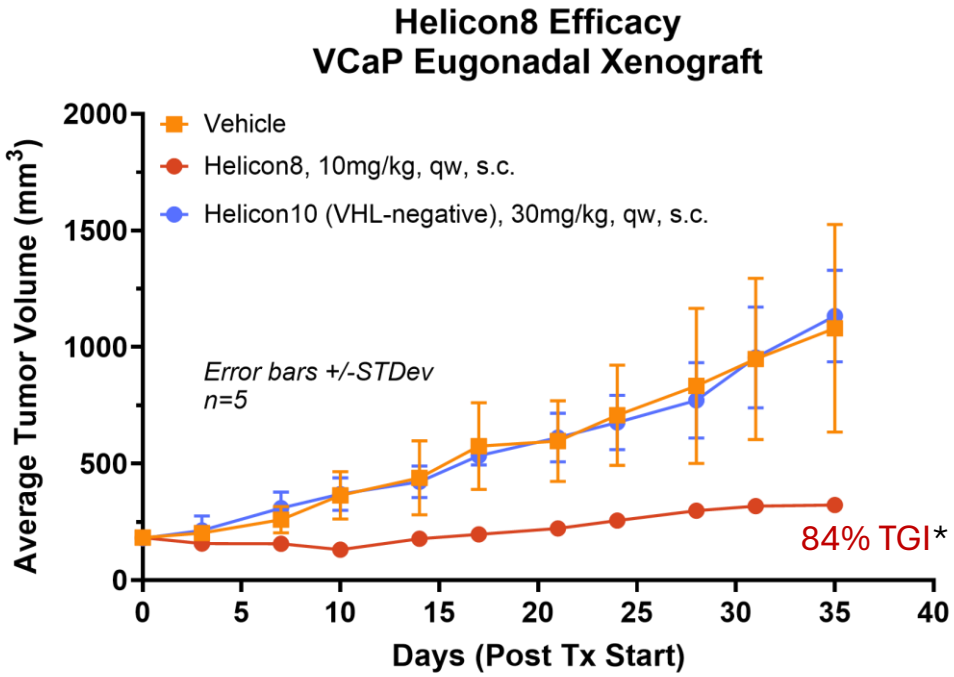
AR: androgen receptor; ARPIs: androgen receptor pathway inhibitors; mCRPC: metastatic castration-resistant prostate cancer; AF-2: activation function-2; LBD: ligand-binding domain; TGI: tumor growth inhibition

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# Allosteric AR$^{ON}$ Degrader: Early signals of single-agent activity and additivity in combination with enzalutamide

## Preclinical data from *in vivo* and *in vitro* AR amplified VCaP models

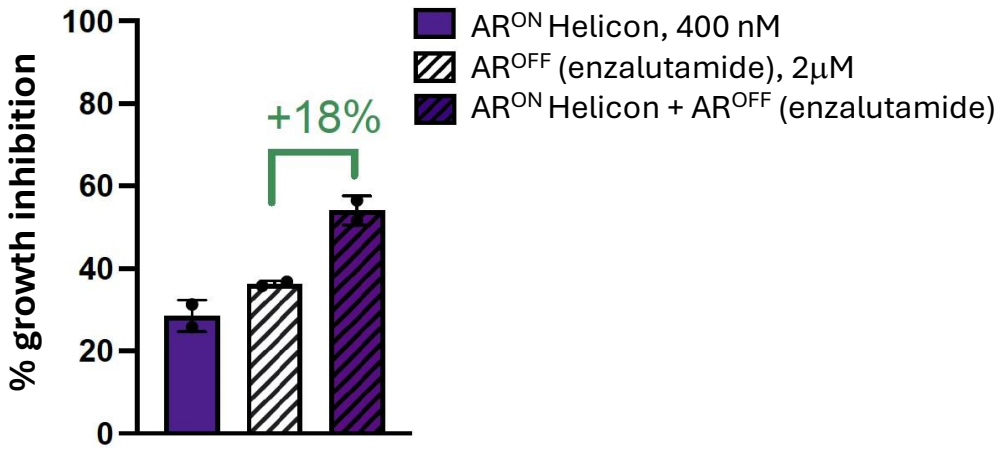
### Single agent anti-tumor activity in VCaP CDX model




*Mixed-effect 2-way ANOVA test
p<0.05 for Helicon 8 dosing

### Combination additivity with enzalutamide in vitro

Additive effects of AR$^{ON}$ and AR$^{OFF}$ combination in AR-amplified prostate cancer cells (VCaP)




Pattabiraman DR, et al. Cancer Res 2026;86(8_Suppl):Abstract LB070

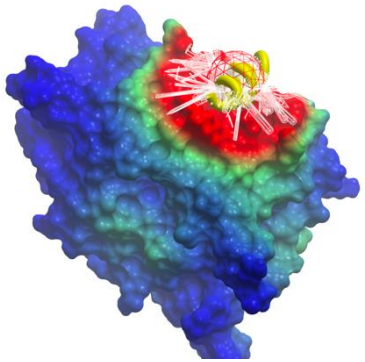

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# Helicon Platform: Fully integrated and AI-enabled

*Repeatable, scalable, and hard to replicate*

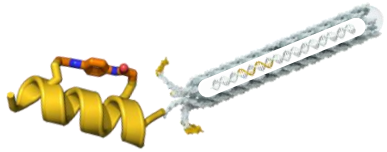
- ✓ **Enabled by a decade of high-volume proprietary data generation**
- ✓ **AI models trained on proprietary in-house data, proprietary industry leading complex peptide synthesis**
- ✓ **Extensive platform IP and accumulated know-how**

## Target Selection

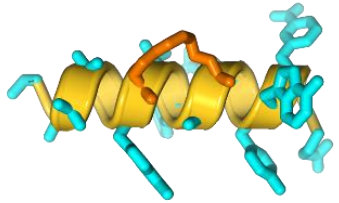


- **ML-Based Prediction of Helicon Binding Sites**

## Hit Discovery

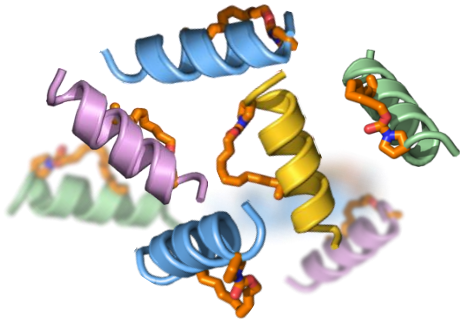


- **Highly Parallelized Phage & mRNA Display**



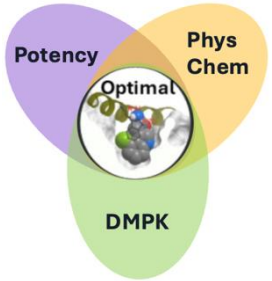
- **In Silico *De Novo* Helicon Design**

## Hit-to-Lead

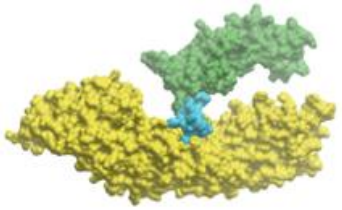


- **Multiplexed Mass Spec Library Screening**
- **1000s of non-canonical amino acids**
- **100s of covalent bridges**

## Lead Optimization




- **Generative Design**

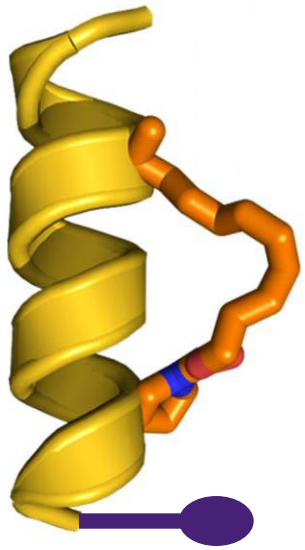


- **Molecular Simulations**


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# One integrated synthesis platform reaches broad chemical space, synthesizes compounds faster, and learns more each cycle

## Differentiated Building Blocks Reach a Broader Design Space



***1,300+***
***customized amino acids***

***275+***
***staples***

***675+***
***E3 ligands and linkers***

- ✓ **Proprietary chemistry few can access**

## Automated Peptide Synthesis at a Scale Rare Outside Pharma

**12 automated peptide synthesizers**



**Syro II**



**CEM Liberty Blue**

- ✓ **Rapid, scalable, streamlined synthesis**
- ✓ **Integrated peptide and small molecule teams**

## A DMTA Cycle Measured in Weeks

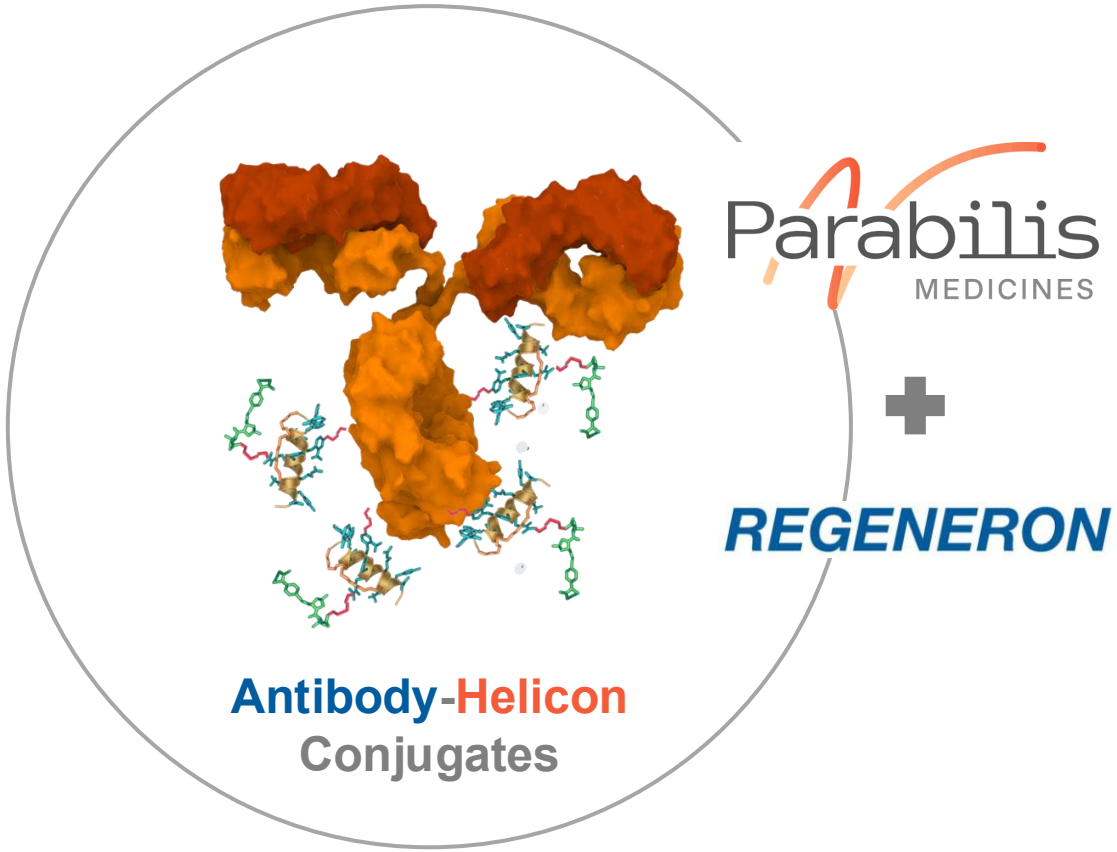
**2-week synthesis turnaround time**
**~90,000 singletons synthesized**
**200,000+ assay data points**




- ✓ ***Sophisticated design with steep compound progression***


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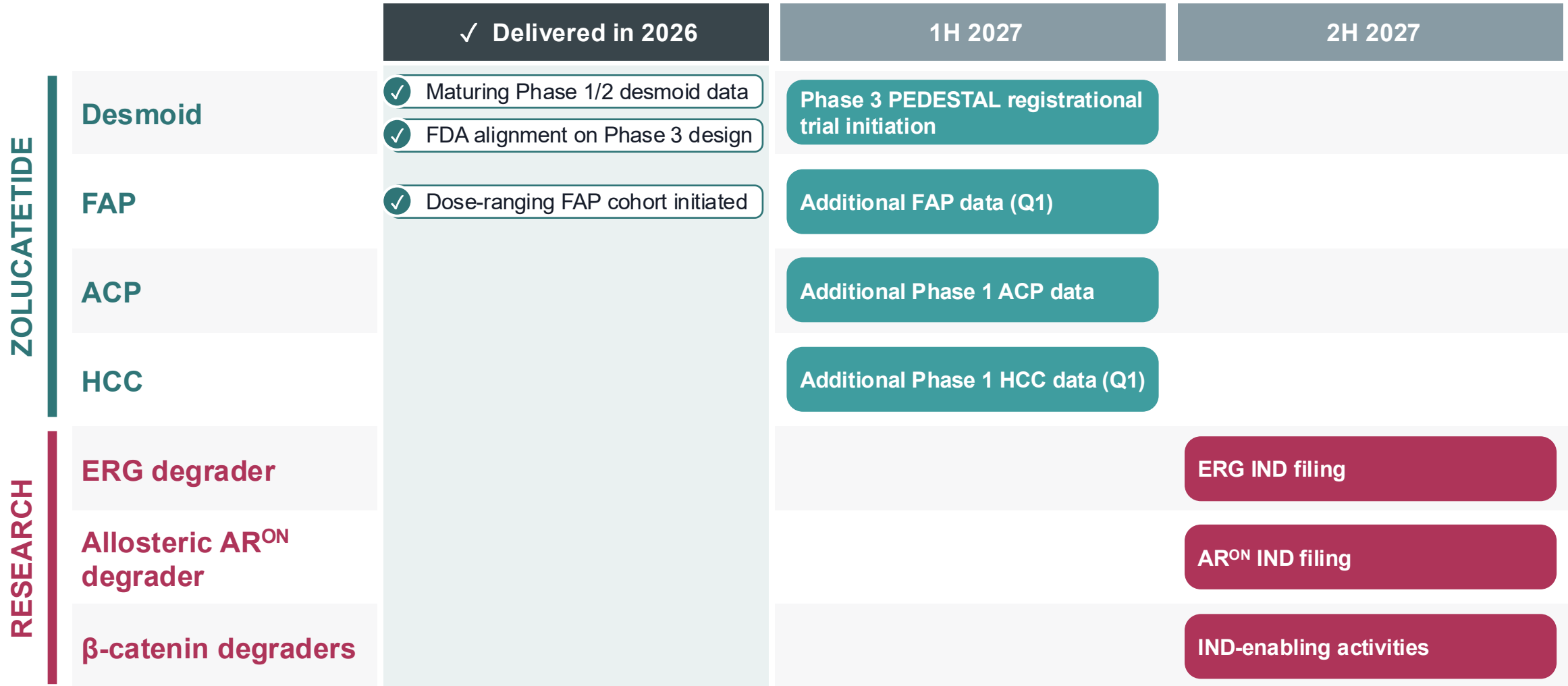
# Regeneron Collaboration: Expanding our Helicon platform into new therapeutic areas and modalities with strong deal economics




- **Unlocking a novel class of Helicon therapeutics** targeting historically undruggable and challenging intracellular targets via antibody-Helicon conjugates (AHCs)
- **Enables expansion into non-oncology areas** where Regeneron brings deep expertise
- **Leverages complementary expertise**: Parabilis leads Helicon discovery and chemistry; Regeneron leads biology validation, preclinical development, and path to market
- **High-margin deal economics:** $125M in upfront and equity investment; potential for up to $2.2B in milestone payments plus tiered royalties


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# Strong momentum in delivering our strategy, with multiple value-creating catalysts expected across the portfolio





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