Frontier Medicines

JPMorgan Healthcare Conference
January 13, 2026

Chris Varma, PhD
Co-founder, Chair & CEO

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Unlocking the proteome to deliver next-generation covalent medicines

The Frontier™ Platform

Powered by chemoproteomics and AI for covalent drug discovery

- Proprietary dataset of >300M compound-protein interactions across the proteome, experimentally measured *in living cells*
- Unparalleled covalent library w/ >40 warheads represented, built in house through AI optimization
- Proprietary AI tools enable delivery of development candidates in under 24 months

Next Generation Covalent Medicines

Pipeline of clinical and near-clinical stage assets for multiple cancers including lung, pancreatic, and colon — representing vast commercial opportunities

- Synergistic and potential best-in-class RAS pathway portfolio
- Potential first-in-class portfolio of transcription factor programs, including partnered with AbbVie
- Multiple anticipated value inflection points for 2026 across the pipeline

Backed by a strong investor syndicate

ARROWMARK PARTNERS · PCVC | Bio · DEEP TRACK CAPITAL · DEERFIELD Advancing Healthcare · DRIEHAUS CAPITAL MANAGEMENT · DROIA oncology ventures · Galápagos · MPM · RACAPITAL · SPHERA ASPIRE HIGHER · WOODLINE PARTNERS

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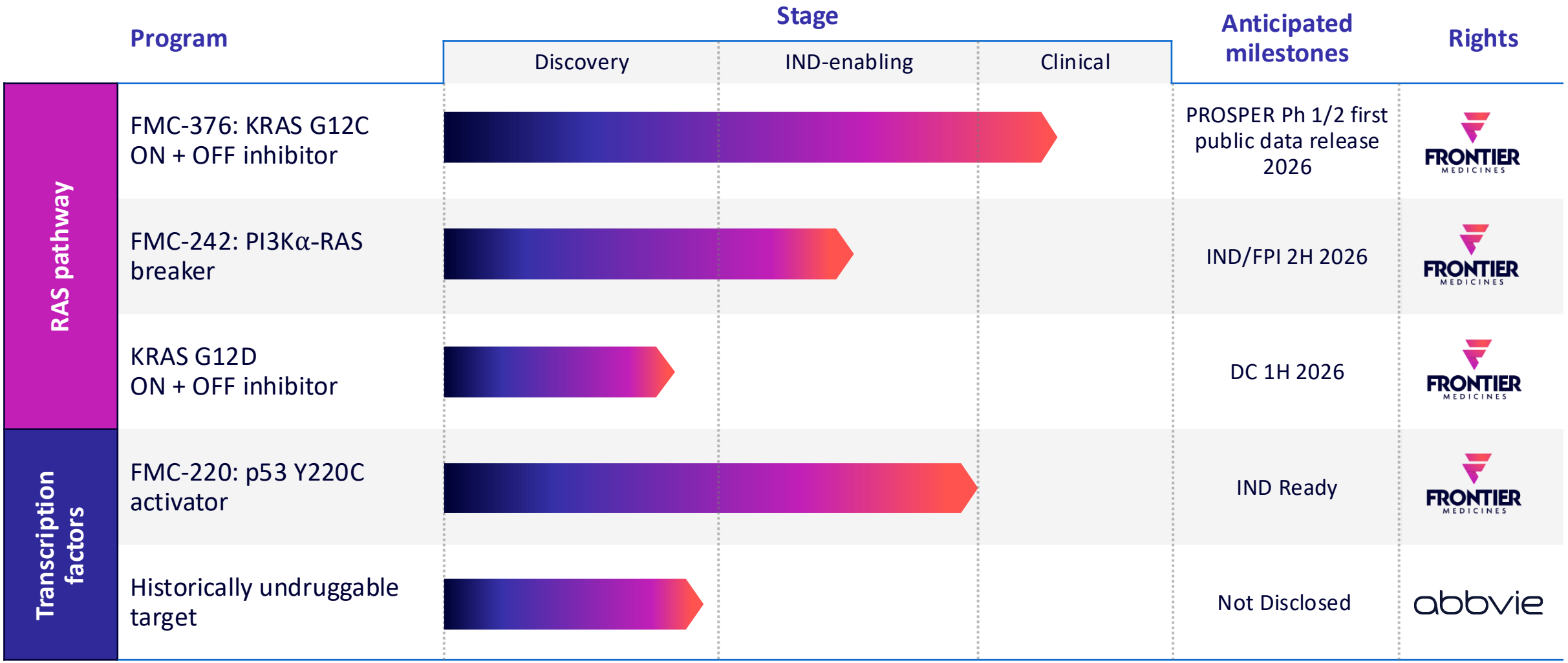
Clinical-stage precision pipeline: harnessing the Frontier™ Platform to deliver best-in-class covalent medicines



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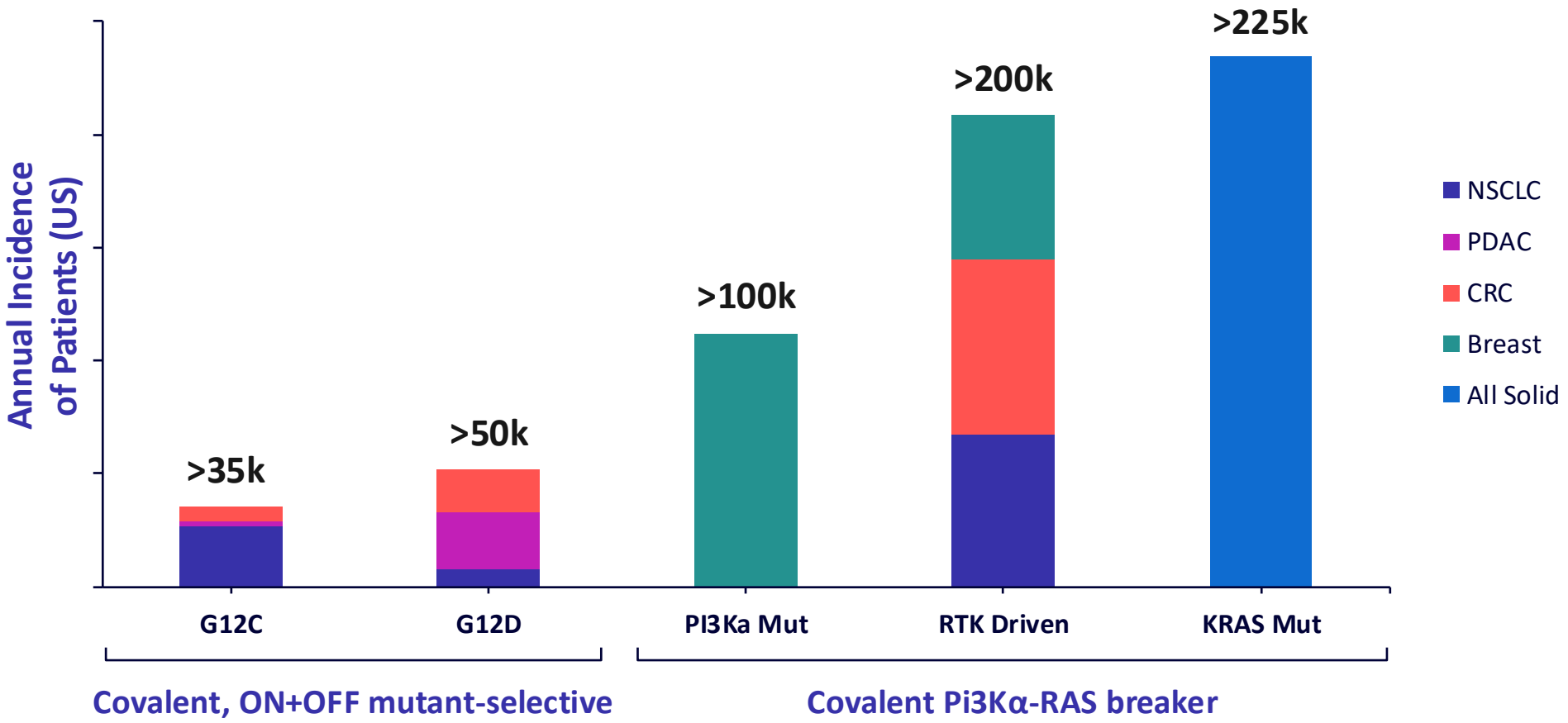
The Frontier™ Platform

Frontier's portfolio of RAS-pathway inhibitors present a vast commercial opportunity



Source: Cancer Facts & Figures 2025. Cancer.org. Adjusted for mutation rates.

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FMC-376
KRAS G12C ON+OFF Inhibitor

Designed to address resistance mechanisms of OFF state G12C inhibitors and provide significantly better tolerability to enable combination with pembro and other agents

For lung, pancreatic, and colorectal cancers

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The Frontier™ Platform

FMC-376

ON + OFF is the next generation of KRAS^{G12C} inhibitors in NSCLC

OFF only

Divarasib (Roche)
- 59%/15.3 mo ORR/PFS, ***no* prior G12Ci**
- AE: nausea (79%), vomiting (66%), diarrhea (62%)
- Combo with pembrolizumab

Calderasib (Merck)
- 38%/8.3 mo ORR/PFS, ***no* prior G12Ci**
- AE: pruritus (29%), diarrhea (21%), rash (15%)
- Combo with pembrolizumab

Adagrasib (BMS), Fulzerasib (GenFleet), Garsorasib (InventisBio), Sotorasib (Amgen), Olomorasib (Lilly)

- **All OFF inhibitors succumb to the same resistance mechanisms**
- **All OFF inhibitors cause increased liver toxicity in combo with pembro at optimal dose levels**

ON only

Elironrasib / RM-6291 (RVMD)
- 42%/6.2 mo ORR/PFS in **prior G12Ci**
- AE: diarrhea (31%), nausea (22%), QTc (22%)
- Combo with daraxonrasib

- **Corroborated the ON hypothesis by demonstrating efficacy in patients that have become resistant to OFF inhibitors**

ON + OFF

FMC-376 (Frontier)
- Ongoing, **including prior G12Ci**
- Combo with pembrolizumab

BBO-8520 (BBOT)
- Ongoing
- Combo with pembrolizumab

- **Potential to overcome resistance to OFF inhibitors due to ON + OFF activity**
- **Potential for low rates of liver toxicity in combo with pembro at optimal dose levels due to increased selectivity**

Source: Divarasib JCO (2025; single agent efficacy and safety). Calderasib: ESMO 2025; ASCO 2025; Sotorasib NDA; WCLC 2022; Adagrasib NDA; ESMO 2023; D3S-001: Cancer Discovery (2024); Olomorasib: ASCO 2024; JTO 2025; Fulzerasib: IASLC 2024; Elironrasib: AACR/NCI/EORTC 2025, November 2025 company presentation; BBO-8520 BBOT Company Press Release (2026); Garsorasib European J Can 2026

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FMC-376 overcomes drivers of KRAS^{G12C} inhibitor resistance in NSCLC and therefore is effective in KRAS G12Ci pretreated patients

Mechanisms of KRAS^{G12C} inhibitor resistance in NSCLC*	% patients	FMC-376 activity
Adaptive resistance†	50%	✓
KRAS G12C / RTK / PI3Kα / NF1 / p53 / KEAP1 or other amplification/mutations	37.5%	✓
Secondary K, H, or NRAS / RAF / MEK / MAPK mutations	12.5%	?

KRAS^{G12C} inhibitor efficacy has been limited by the presence of either:

- Adaptive/compensatory signaling (ON-state↑)
- Secondary mutations

FMC-376 overcomes the majority of innate and acquired resistance mechanisms due to the ability to inhibit both ON and OFF states of KRAS G12C *nearly equipotently*

* *Cancer Discov* (2025) 15 (7): 1325–1349; † Patients with no identified mutation

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FMC-376

Favorable safety & encouraging efficacy set up for potential best-in-class profile in NSCLC

- **Favorable safety/tolerability profile** across more than 40 patients and multiple doses tested
  - Low frequency of related liver and GI toxicities
  - Good potential to combine with pembro given low liver toxicities
  - Clinicians report patients feel much better on FMC-376 versus other KRAS G12C inhibitors
- **Encouraging preliminary efficacy** observed in heavily pretreated NSCLC patients at multiple dose levels
  - Including in KRAS G12Ci pretreated patients
- **Differentiated mechanism** of similar potency for both ON+OFF states overcomes majority of known resistance mechanisms to OFF state inhibitors
- **Deepening responses over time** potentially attributable to ON+OFF mechanism

Source: PROSPER DCO Jan 5, 2026

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FMC-376: Delivering a best-in-class option to patients

The FMC-376 difference:

Favorable safety/tolerability profile across multiple dose levels

Encouraging preliminary efficacy in heavily pretreated NSCLC patients, including those previously experienced on another KRAS G12Ci

Next: continue to build monotherapy data set in NSCLC **as well as explore combo w/ pembro**

Ph 1/2 PROSPER trial actively recruiting & public data release coming this year

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FMC-242
PI3Kα-RAS Breaker

Exquisitely selective, allosteric inhibitor of PI3Kα-RAS/RTK PPI that spares normal enzymatic activity

For lung, pancreatic, colorectal, breast, and other solid tumors

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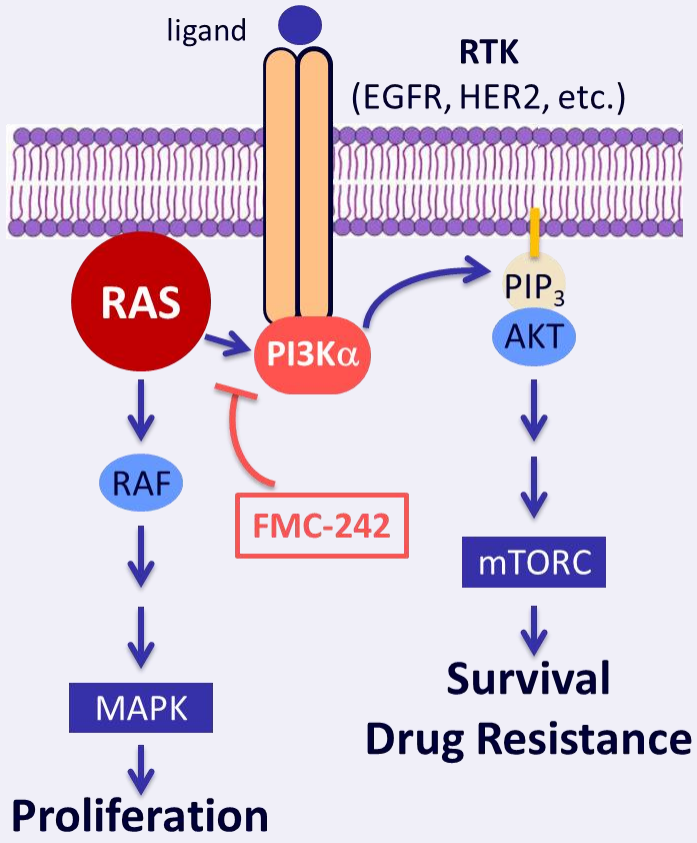
Selective inhibition of PI3Kα –RAS interaction provides broad therapeutic opportunities

PI3Kα is an essential cofactor in both KRAS and RTK driven cancers



Therapeutic Opportunities	Indications
Receptor Tyrosine Kinase (RTK) driven disease	50% CRC, 35% NSCLC, 20% BCa
KRAS mutant disease	14% of all cancers
PI3Ka mutant disease	~35% BCa

M. Rokita et.al. (2013) Oncotargets and Therapy 6: 967-976; J. Spano et.al. (2005) ESMO Annals of Onc 16 (2):189-194; A. Al Jassim (2025) J. Immunother Precis Onc 8 (3): 233-241; S. Ahn (2020) J Path and Tras Med 54(1): 34-44; I. Prior (2020) Can Res 80 (14): 2926-2974; K. Nakamura (2024) Can Med 13 (14): 1-9

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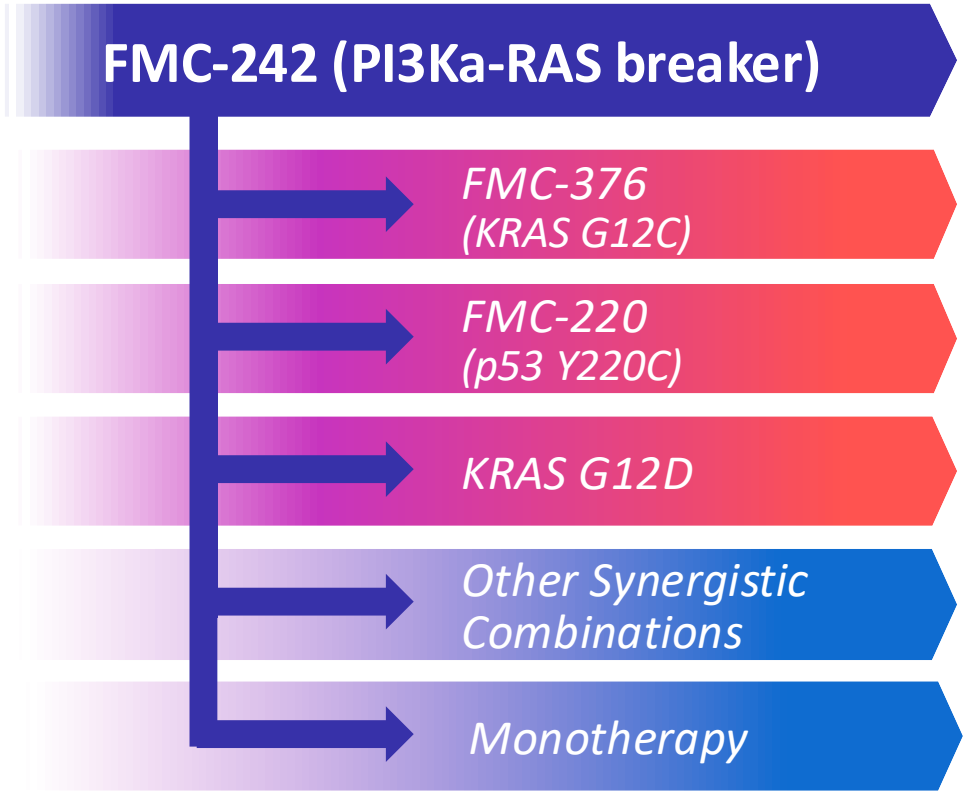
FMC-242 has the potential to become a foundational therapy targeting drug resistance in combination across many cancers



- **Durable pathway suppression** as the *ultimate pan-RAS inhibitor in combo* as well as PI3Ka inhibitor, including mutants, while sparing hyperglycemia
- **Synergistic combinations** w/ internal pipeline programs as well as with many other mechanisms and drugs (e.g. cetuximab, trastuzumab, osimertinib, others)
- **Monotherapy potential** in particular disease settings and lines of therapy

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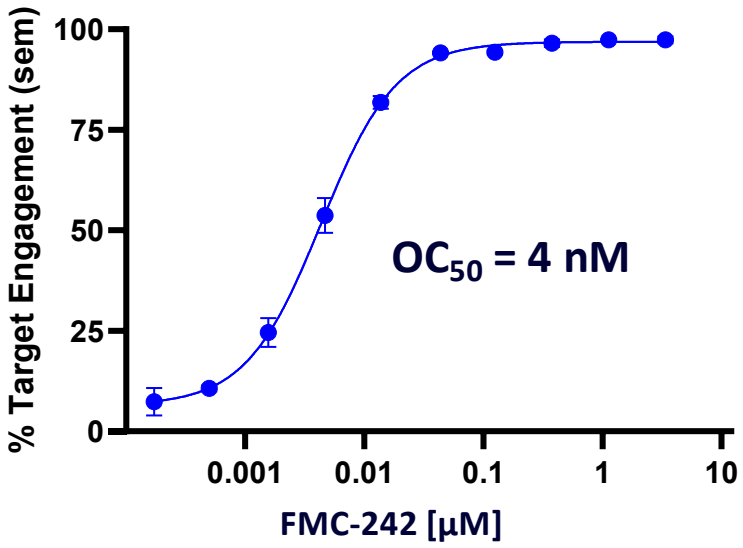
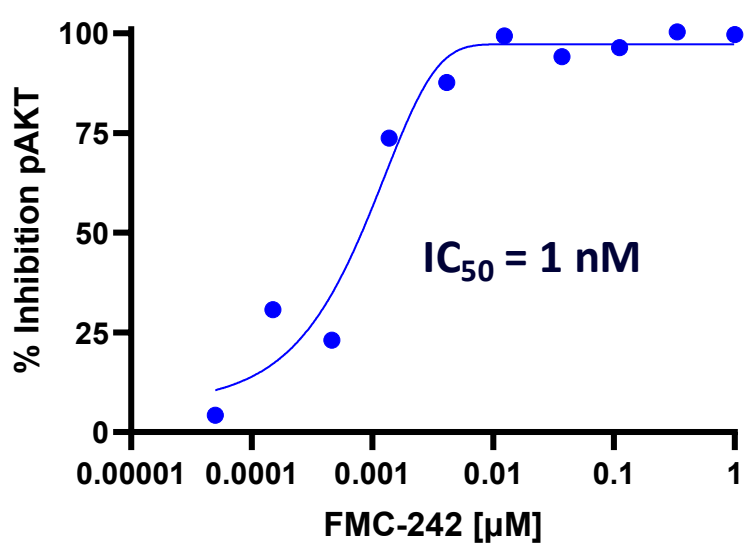
Covalent engagement of C242 potently inhibits AKT activation and tumor cell viability

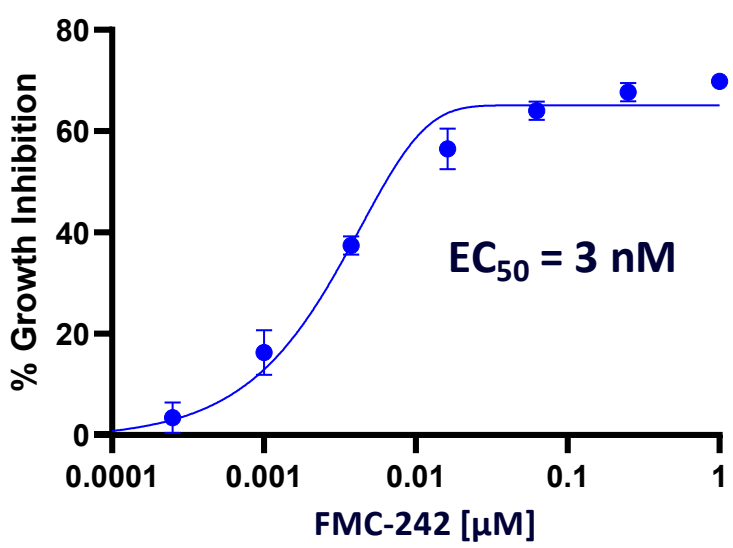
A. Target engagement



B. Inhibition of AKT activation



C. Inhibition of tumor cell viability



KYSE-410, Gastric ca. HER2, KRAS G12C, p53

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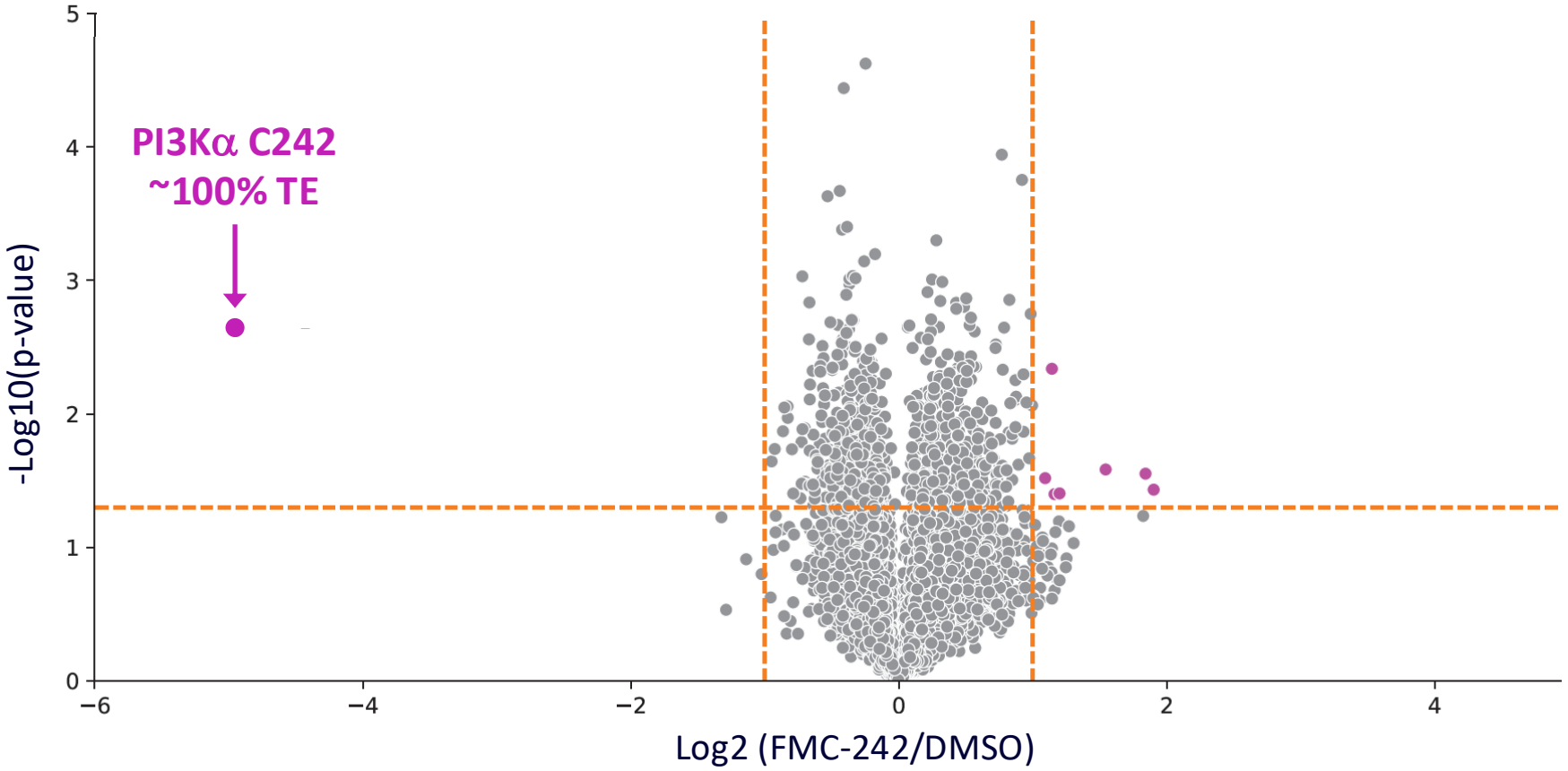
FMC-242 achieves extreme proteomic selectivity and complete target engagement of PI3Kα C242



Volcano plot depicting selectivity of FMC-242 after a 2 μM (465X the OC_{50}) treatment for 2hrs in KYSE-410 cells. Orange dashed lines represent significance thresholds of a 2X fold change and a p-value of 0.05. Each dot represents a quantified cysteine (n = 22,620)

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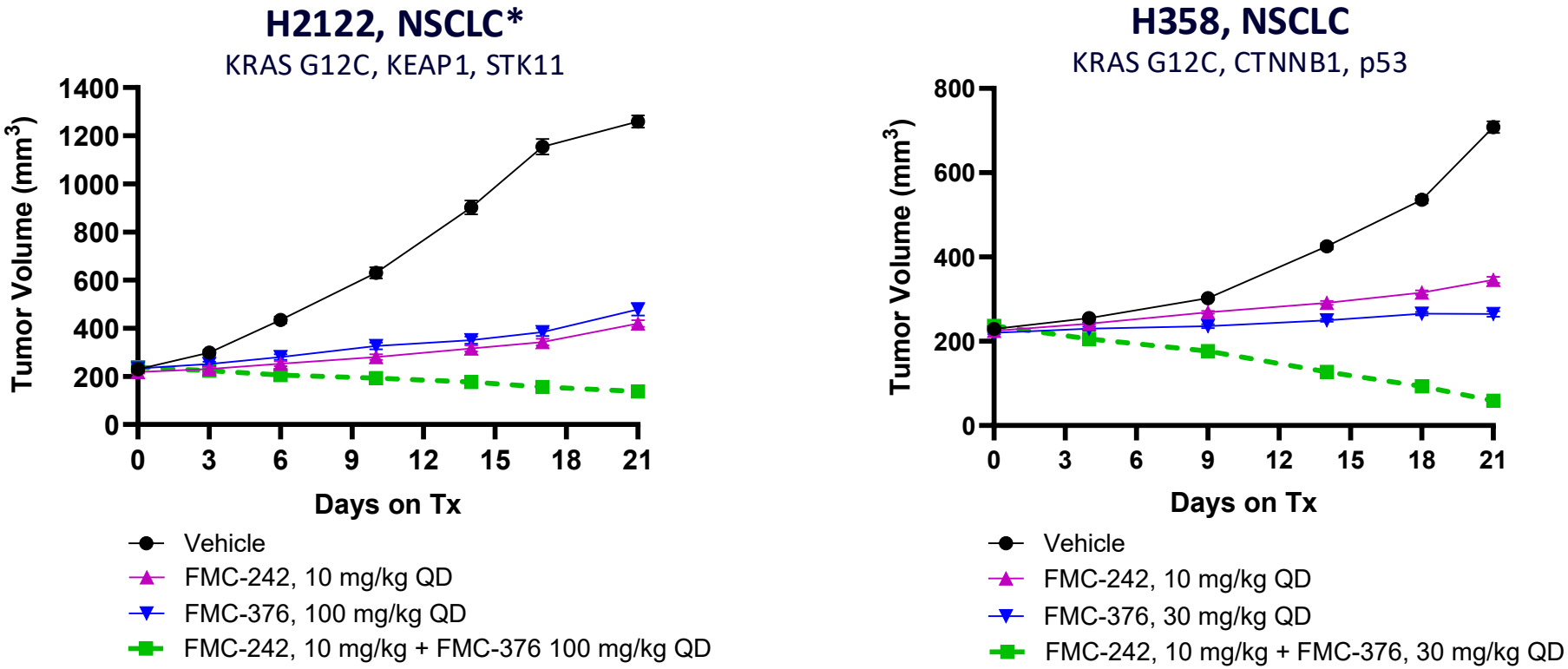
FMC-242 demonstrates synergy with FMC-376 (ON+OFF KRAS G12Ci) delivering potent tumor regressions in combination

FMC-242 + FMC-376 combination



*KRAS inhibitor resistant model

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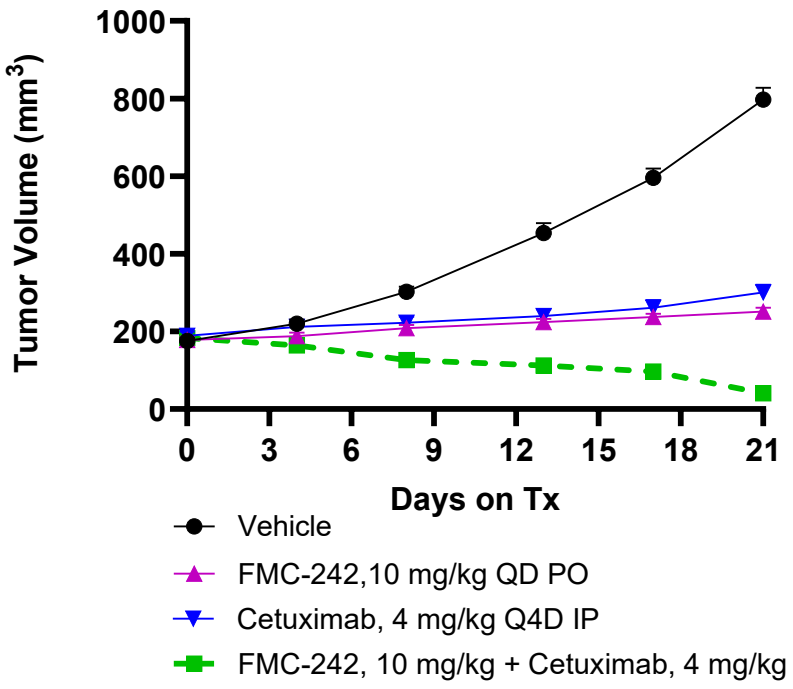
FMC-242 demonstrates synergy with EGFR and HER2 inhibitors delivering potent tumor regression in combination

Cetuximab

H1975, NSCLC

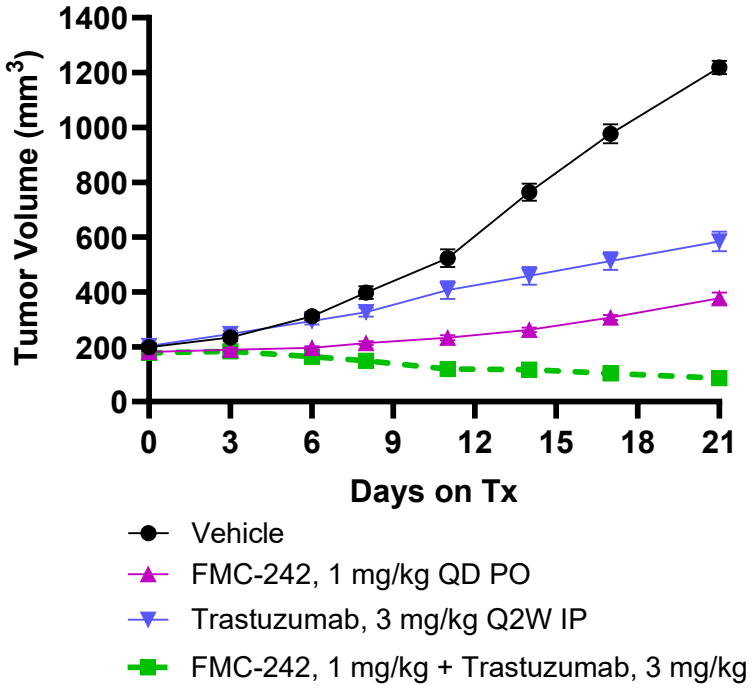
EGFR L858R, T790M



Trastuzumab

KYSE-410, Gastric

HER2, KRAS G12C, p53



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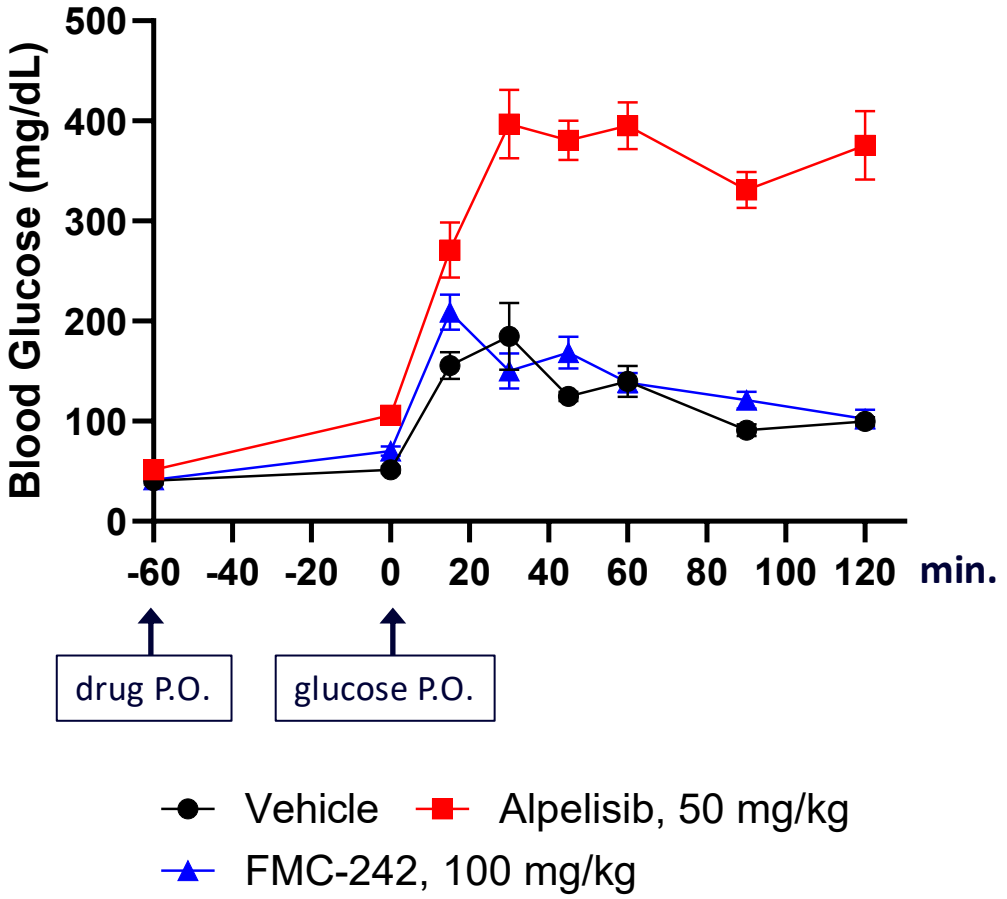
FMC-242 does not disrupt normal glucose metabolism at ≥ 30x the efficacious dose

Oral glucose tolerance text



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FMC-242: a highly selective, covalent allosteric inhibitor of PI3Kα-RAS PPI that spares normal functions

PI3Kα-RAS Breaker

IND/FPI 2H2026

Preclinical data shows

- **Unprecedented potency**
- **Exceptional target coverage**
- **Broad inhibition of HER2+, EGFR, RAS mutant tumor cell viability**
- **Tumor regressions**
- **CNS exposure**
- **Spares glucose metabolism**
- **Highly selective**

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Exciting set of catalysts and milestones for 2026

R&D catalysts

- Phase 1/2 data release for FMC-376
  - Including combo data with Pembro
- Initiate Phase 1/2 study for FMC-242
- Initiate Phase 1/2 study for FMC-220
- Advance KRAS G12D ON+OFF (covalent) program to DC and into IND-enabling studies
- Advance AbbVie collaboration, including transcription factor program to next stage

Strategic milestones

- Complete next financing for Frontier
- Execute multiple new deals, including around platform and new targets
- Complete Series-A financing of newco spinout, Vulcan Bio, a novel targeted degradation approach to address protein aggregate diseases, inflammatory conditions, and *even aging itself*

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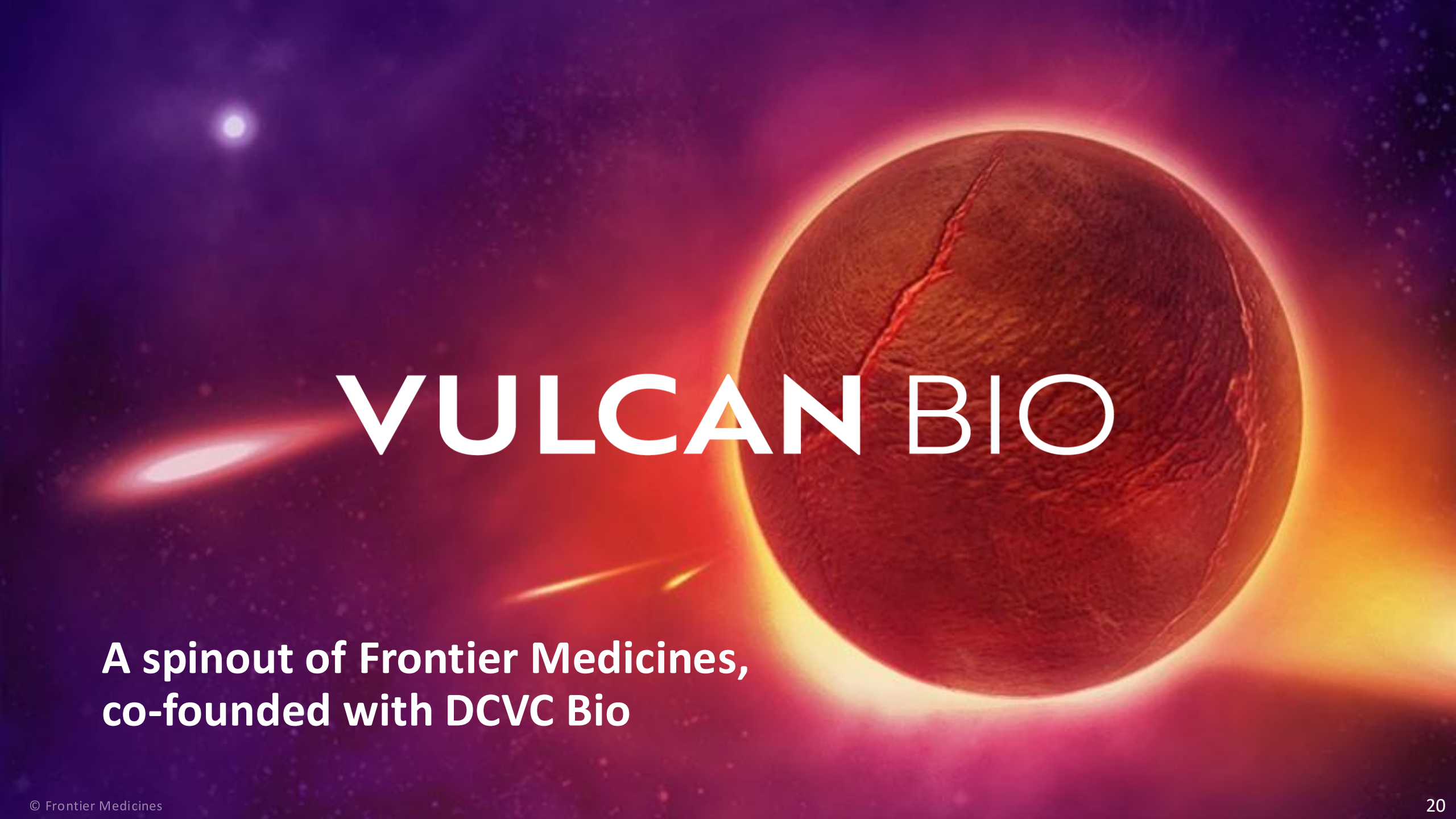

A spinout of Frontier Medicines, co-founded with DCVC Bio

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There are currently very few treatments that address the underlying cause of protein aggregate diseases

There are approximately 10M Americans suffering from protein aggregate diseases such as ALS, Huntington's, Alzheimer's and Parkinson's.

While limited treatments are available for some of these protein aggregate diseases, they treat symptoms and some slow progression as opposed to targeting the underlying drivers of the disease, which requires clearing pathogenic intracellular protein aggregates.

Vulcan Bio is applying the Frontier ™ Platform to create medicines based on a novel modality of degradation invented at Frontier called AutoTAC ™ to do exactly what is required.

At Vulcan Bio, we plan to change this.

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Thank you

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