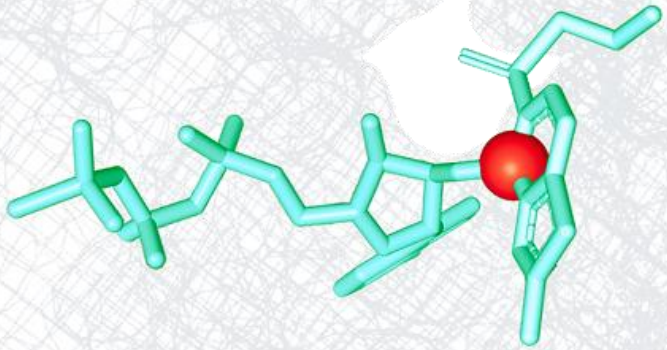
AN2Therapeutics

INVESTOR OVERVIEW



SEPTEMBER 2026

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “believe,” “estimate,” “predict,” “potential” or “continue,” or the negative of these terms or other similar expressions. Forward-looking statements expressed or implied in this presentation include, but are not limited to, statements regarding: the potential of the Company’s boron chemistry platform and advancement of the Company’s development programs; potential for epetraborole to treat polycythemia vera ; expectations regarding the Company’s clinical trials, including initiation, enrollment, conduct, sites, leadership and investigators, the timing of data and related announcements, and regulatory clearance to proceed; market size and sales potential; the predictivity of data; cash runway; the scope, duration, and enforceability of the Company's intellectual property rights and exclusivity position; and other statements that are not historical fact. These statements are based on AN2’s current estimates, expectations, plans, objectives and intentions, are not guarantees of future performance, and inherently involve significant risks and uncertainties.

Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, but are not limited to, risks and uncertainties related to: AN2’s ability to implement its plans for its internal boron chemistry platform and pipeline programs; timely enrollment of patients in AN2’s clinical trials and investigator-initiated clinical trials; inability to obtain regulatory clearance to conduct trials; AN2’s ability to procure sufficient supply of its product candidates for its clinical trials; the potential for results from clinical trials to differ from preclinical, early clinical, preliminary or expected results, or results from different patient populations; the ability of particular preclinical models in non-human primates to predict safety and efficacy in humans; significant adverse events, toxicities or other undesirable side effects associated with AN2’s product candidates; the significant uncertainty associated with AN2’s product candidates ever receiving any regulatory approvals; AN2’s ability to obtain, maintain or protect intellectual property rights related to its current and future product candidates; implementation of AN2’s strategic plans for its business and product candidates; the sufficiency of AN2’s capital resources and need for additional capital to achieve its goals; global macroeconomic conditions and global conflicts and other risks, including those described under the heading “Risk Factors” in AN2’s Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and other reports filed with the U.S. Securities and Exchange Commission (SEC). These filings, when made, are available on the investor relations section of AN2’s website at www.an2therapeutics.com and on the SEC’s website at www.sec.gov.

This presentation also contains estimates relating to market size and potential and timelines for clinical trials. These estimates involve a number of assumptions and limitations, and are subject to risks and uncertainties.

Forward-looking statements contained in this presentation are made as of this date, and AN2 undertakes no duty to update such information except as required under applicable law.

AN2 Therapeutics

Unlocking Boron's Promise for Patients

Clinical-stage pipeline

3 proof-of-concept studies initiating in 2026

Focused on acute needs

Polycythemia vera
novel oral

***M. abscessus* (NTM)**
no FDA-approved drugs

Chagas disease
no FDA approved drugs for adults

Near-term catalysts

Polycythemia vera
Startup activities underway for global study

M. Abscessus (NTM)
Enrollment ongoing

Chagas disease
Phase 2 initiation expected 4Q26

Boron-driven oncology innovation

Oncology
PI3Kα and ENPP1 programs

Bone disorders
Second compound expected 4Q26



AN2 BORON PLATFORM

Binding modes or targets not possible with carbon-based chemistry

Validated chemical space with multiple FDA-approved drugs

Pipeline

Product Name	Target/Mechanism	Research	Preclinical	Phase 1	Phase 2	Pivotal
Epetraborole (EBO)						
Polycythemia vera	Globin synthesis					
M. abscessus lung disease	LeuRS				IIT	
Melioidosis	LeuRS					
AN2-502998						
Chagas disease	CPSF3					
Research Programs						
Oncology	PI3Kα					
Oncology	ENPP1					
Bone disorders	ENPP1					
Tuberculosis	LeuRS					

Gates Foundation

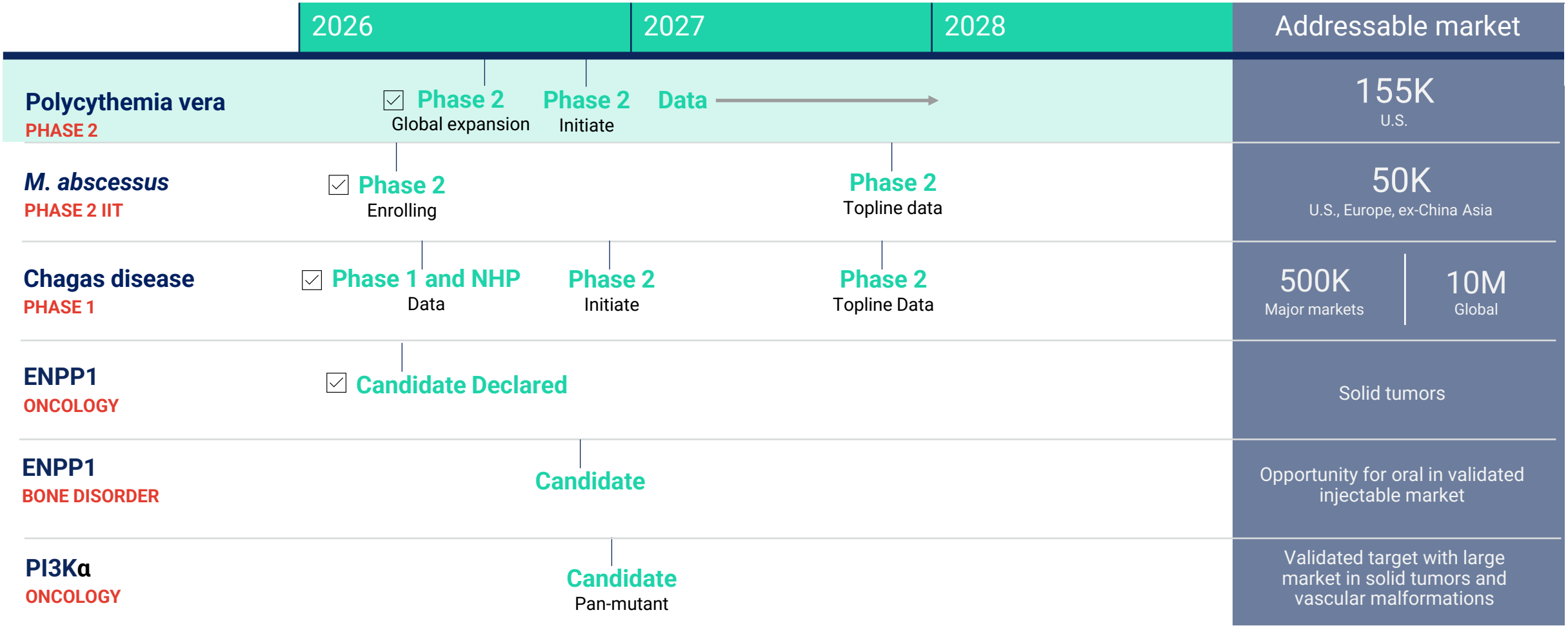
GSK

AN2Therapeutics

IIT= Investigator initiated trial Globin synthesis represents presumed MOA in PV

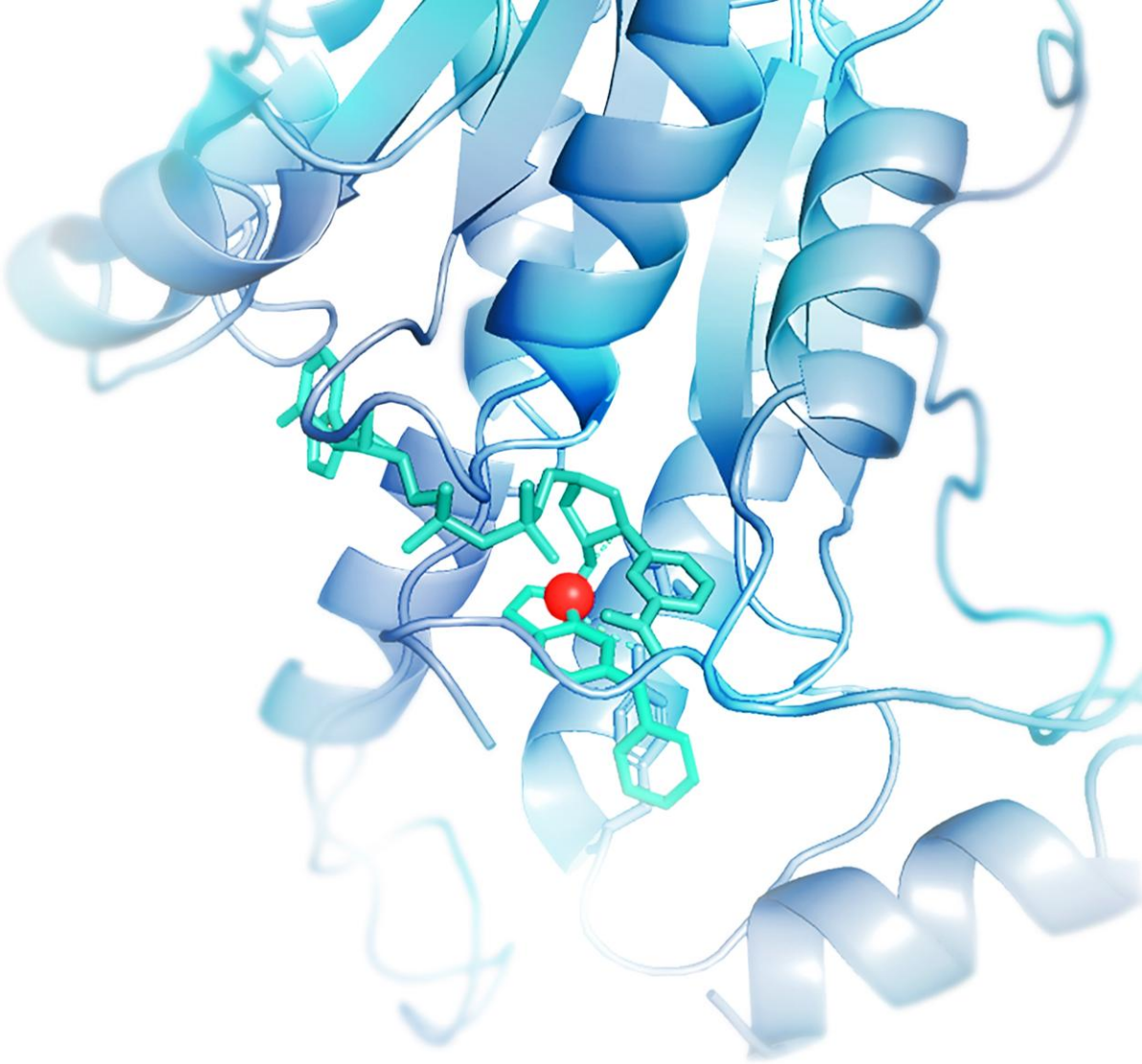
Advancing toward value-creating milestones over next two years

Leveraging proprietary boron chemistry platform to advance pipeline of potentially high-impact programs



POLYCYTHEMIA VERA

Oral epetraborole



AN2Therapeutics

Oral epetraborole potentially modulates red cell production via a novel MOA



Investigational Program Summary

Candidate	Status	Form	Market	Differentiation	Enabling data
Epetraborole	Phase 2	Oral	155,000 (U.S.)	Oral, red-cell targeting	Clinical and preclinical data

Potential once-daily oral administration

Data from prior preclinical and clinical studies in non-PV patients indicated consistent, dose-dependent, and reversible hematocrit reductions

Potential for red-cell selectivity, novel MOA, without additional cytotoxicity, pan-myelosuppression, or drug-drug interactions, with flexible titration

Near-term data readouts

- Periodic data throughout 2027
- Objective endpoints allow for Phase 2 data readouts during open-label phase (HCT, phlebotomy avoidance, tolerability)

A red-cell-driven disorder with unmet medical needs

Goals of Treatment

- ✓ Control hematocrit w/o phlebotomy dependence
- ✓ Alleviate symptoms
- ✓ Reduce thrombotic risks

without

- ✗ Cytopenias
- ✗ Thrombocytosis
- ✗ Anemia

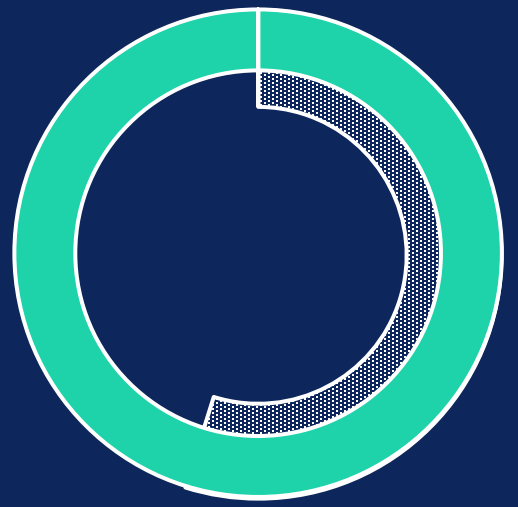
PV biology

- **Overproduction of red cells** caused by aberrant JAK signaling in the bone marrow
- Elevated red cell mass drives **persistent hematocrit elevation**, increased blood viscosity, PV-related symptoms, and heightened thrombotic risk

Treatments

- **Phlebotomy and low-dose aspirin**, yet seesaw effect often observed, requiring frequent intervention, with difficulty maintaining consistent hematocrit control
- **Cytoreductive therapies** (e.g., hydroxyurea, interferons) involve toxicities and broad myelosuppression and/or injectable administration (interferons, hepcidin-targeting agents)

U.S. Prevalence



Total cases: ~155,000

Uncontrolled HCT: ~75,000

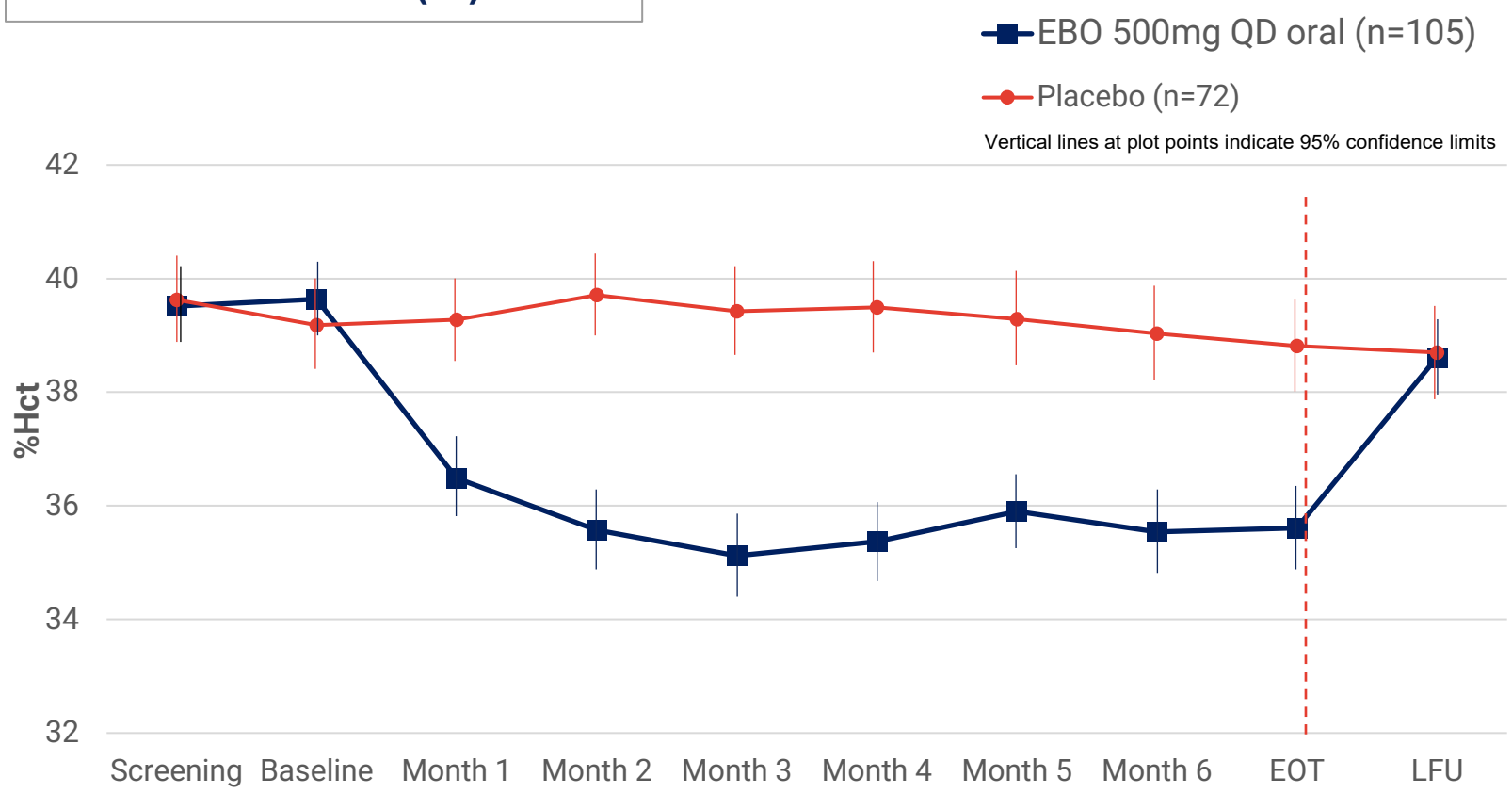
REVEAL Study – Grunwald et al., Clin Lymphoma Myeloma Leuk. 2019

Early and sustained hematocrit reductions in Phase 2/3 NTM study (n=177)

Hematocrit reductions observed throughout epetraborole treatment

Phase 2/3 NTM trial

Hematocrit (%)



Sustained, stable HCT reduction

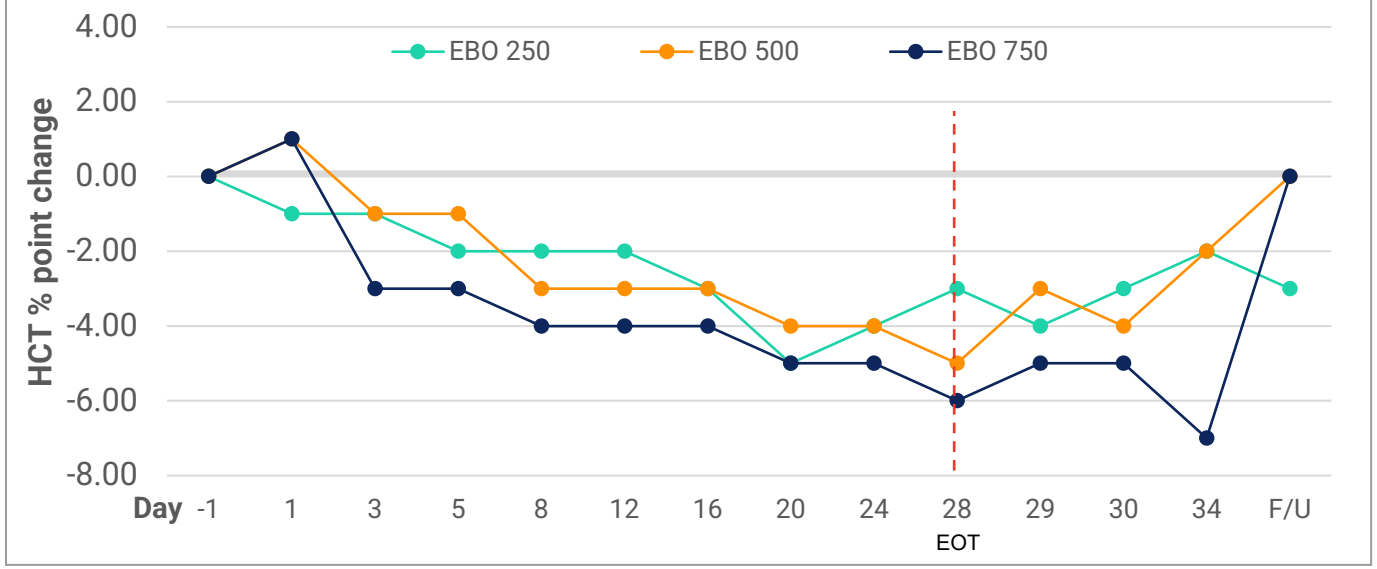
- HCT reductions were reversible upon treatment discontinuation, with no evidence of lasting marrow suppression
- Reductions in HCT occurred without broad myelosuppression or disruption of other hematologic lineages

Source: Company data on file

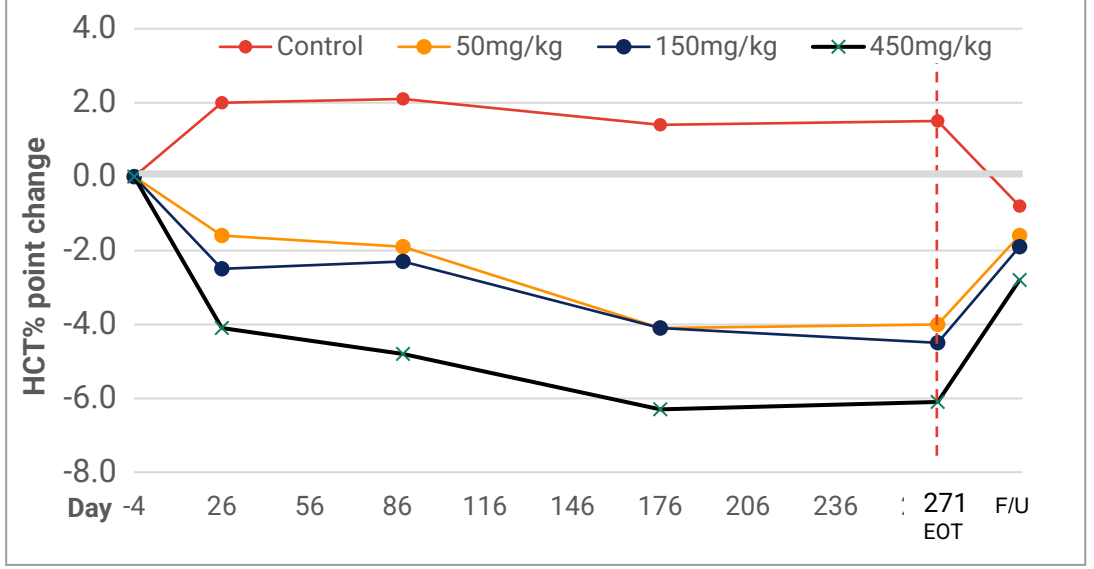
Trial replicated data in long-term NHP studies and healthy volunteers

Durable, reversible HCT reduction across epetraborole preclinical and clinical studies

Phase 1



Nonhuman primates



- Phase 1 data: absolute change from baseline
- Shows dose-related, stable, early HCT effect, with greater magnitude at higher dose level
- Stabilized during dosing and trended back toward baseline after discontinuation, consistent with a reversible pharmacologic effect

- Phase 1 followed NHP study, which showed similar trends in HCT reduction and reversibility, with stable effect observed over full 9 months of study

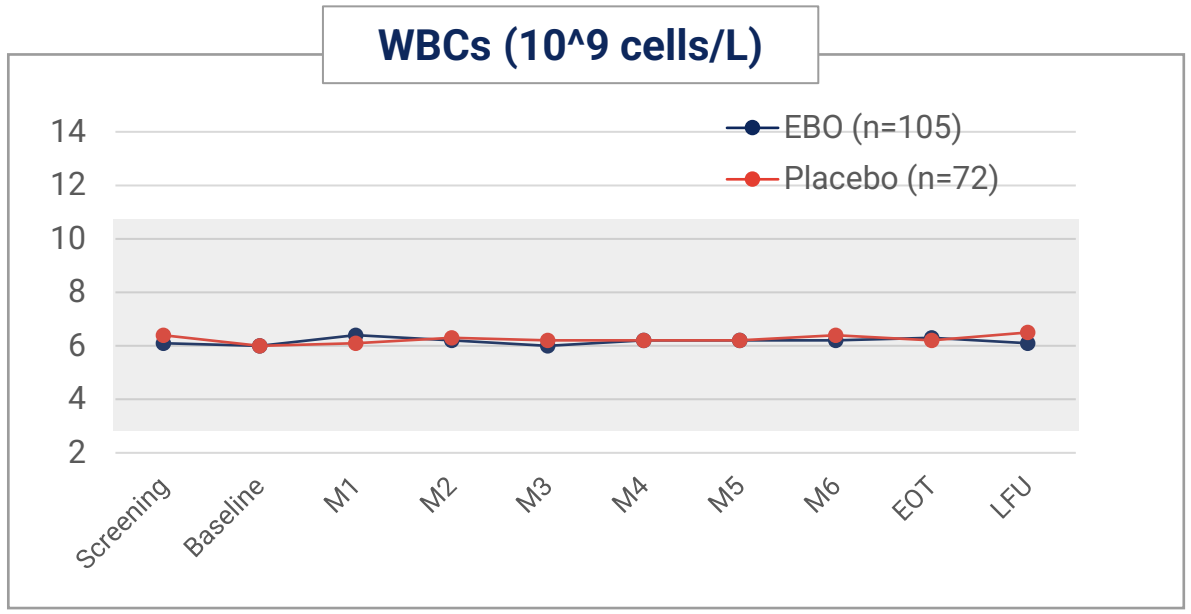
AN2Therapeutics

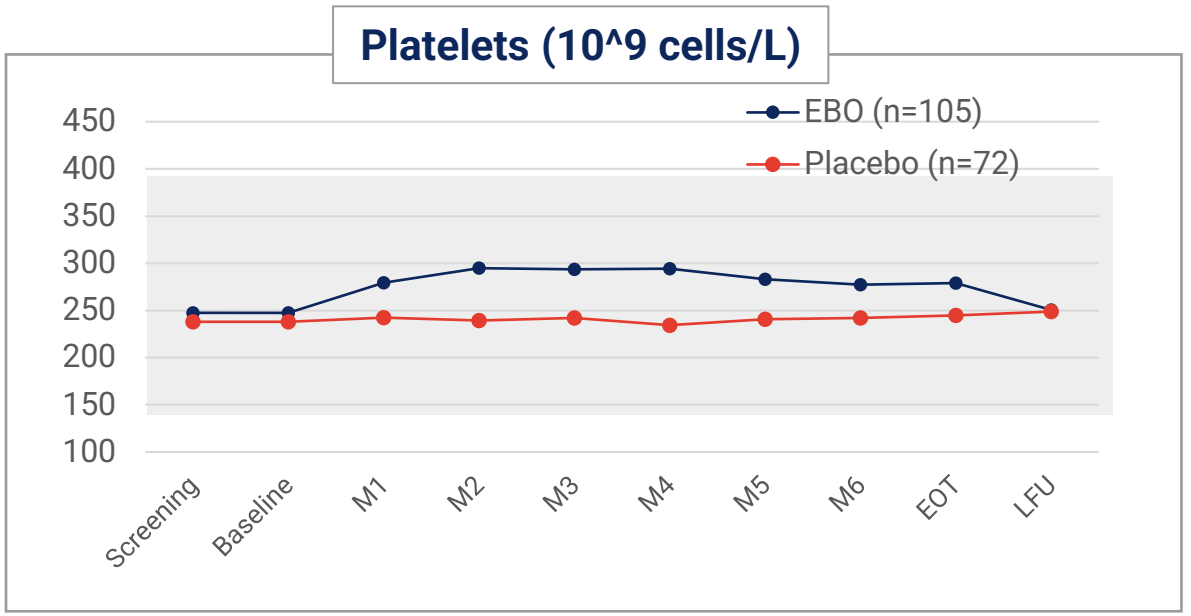
Source: Company data on file

Potential for selective red-cell effect and preserved WBCs and platelets

Data consistent with erythroid-lineage selectivity rather than generalized cytoreduction

In prior trials, platelet and WBC counts remained stable and within normal ranges, with no evidence of broad myelosuppression





Source: Company data on file

Normal range

Potential low-burden oral with targeted control of hematocrit levels

A well tolerated, red-cell selective option could offer additional flexibility to individualize hematocrit control

57% on hydroxyurea lack control after 3 months



HCT >45 HCT <45

48.5% of patients on cytoreductive therapy persist with HCT >45



HCT >45 HCT ≤ 45

Epetraborole target profile

Selectivity

Red-cell selective, targeted toward HCT control

Administration / titration

Oral, potential for simplified titration

Onset of hematologic effect

Weeks

Tolerability

Generally well tolerated in non-PV trials without notable DDI, renal, or liver effects

Potential clinical applications

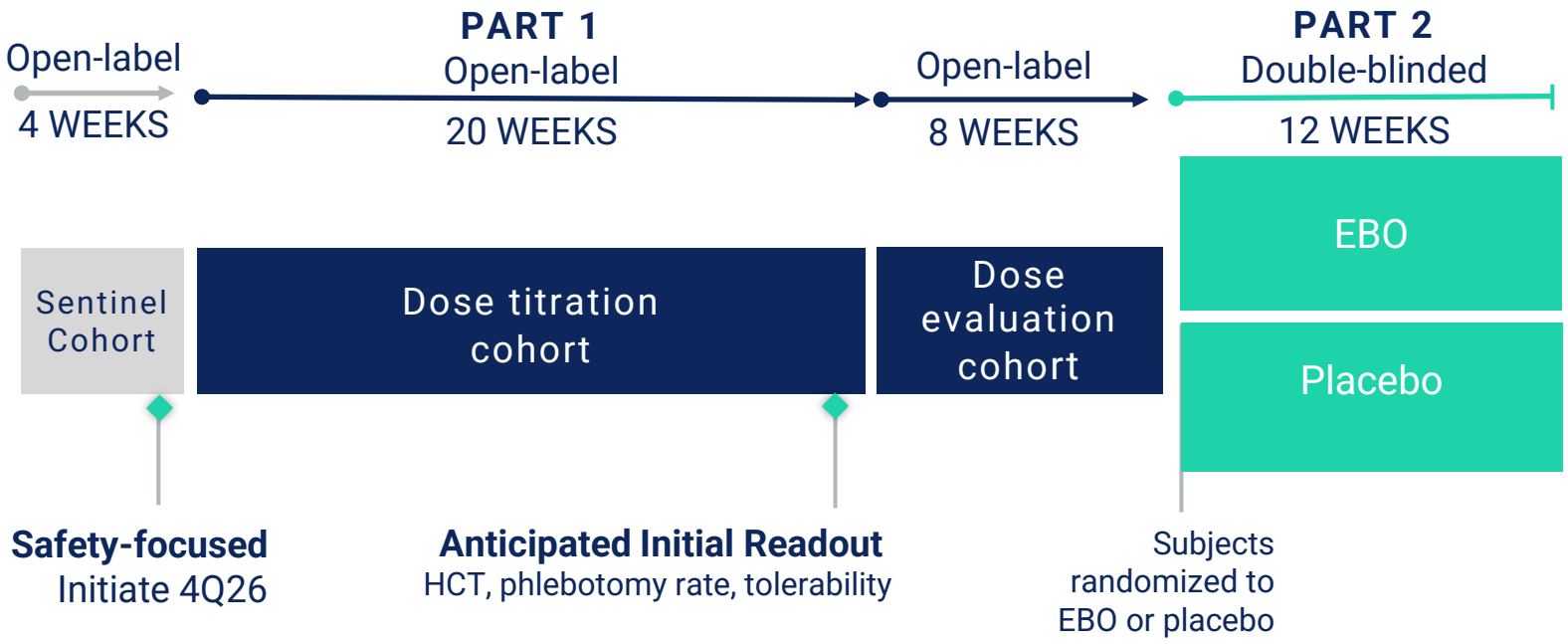
- Uncontrolled on phlebotomy +/- cytoreductive drugs
- New patients with normal WBC and platelets
- Combination use for additional HCT lowering without excessive cytoreduction
- Patients with phlebotomy burden as the main problem
- Patients who prefer oral therapies instead of injectables
- Patients experiencing or at risk for toxicities associated with broad cytoreduction
- Bridge or combination strategy for patients initiating interferons

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REVEAL Study – Grunwald et al., Clin Lymphoma Myeloma Leuk. 2019

Global Phase 2 design and early anticipated data readout

Study design consistent with prior PV programs, allows for early assessment of key efficacy measures



MAJOR OUTCOME MEASURES

1. Percent of patients maintaining "clinical success" defined as
   - had HCT control
   - did not undergo therapeutics phlebotomy after Week 4
   - completed the 12-week regimen
2. PBO-controlled changes in PROMIS, mMPN-SAF patient diary, and PGIC
3. Changes in standard hematological variables, plus EPO, WBV, serum hepcidin, serum iron, ferritin, TSAT, %HbA and % HbF
4. JAK2V617F allele burden will be measured to evaluate whether selective modulation of erythropoiesis influences clonal dynamics
5. Open-label extension (not shown) will collect longer-term response and durability data

Anticipated PV timeline

Subject to regulatory review and enrollment rates

3Q & 4Q26

U.S. IND & FPI

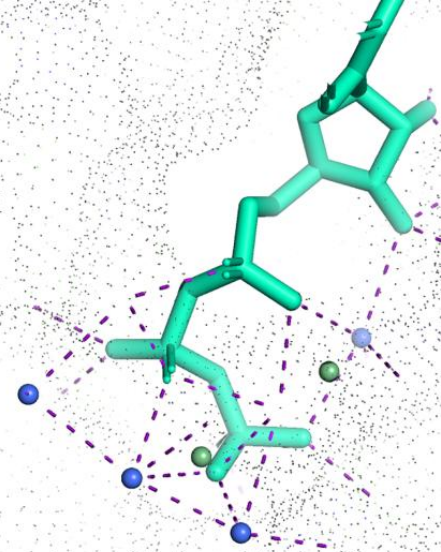
2027

Clinical data updates periodically throughout 2027



MYCOBACTERIUM ABSCESSUS COMPLEX LUNG DISEASE

Oral epetraborole

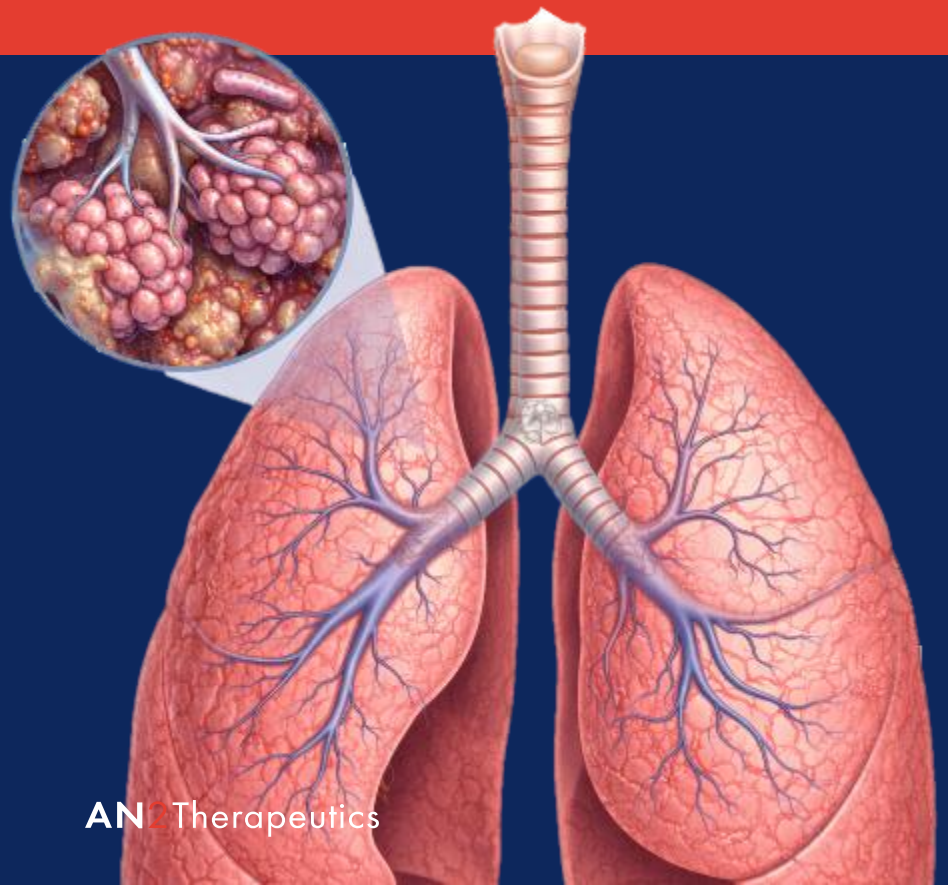


AN2Therapeutics

M. abscessus: chronic lung disease with no approved drugs

Investigational Program Summary

Candidate	Status	Form	Market	Current Therapies	Target Profile
Epetraborole	84-patient Phase 2 IIT initiated	Oral	50,000 (U.S., Europe, Japan)	Off-label only, IV, significant toxicities	Once-daily oral



Progressive, Irreversible Lung Damage

Persistent infection drives ongoing inflammation, declining lung function, and structural destruction

No FDA-approved Drugs

Off-label, 2 to 3 IV-only regimens with significant toxicities

20% 5-year mortality

Creates urgency to treat individual patients and an imperative to develop efficacious and tolerable anti-bacterials

Building on MAC experience with strong enabling data for *M. abscessus*

Differentiated Target Product Profile

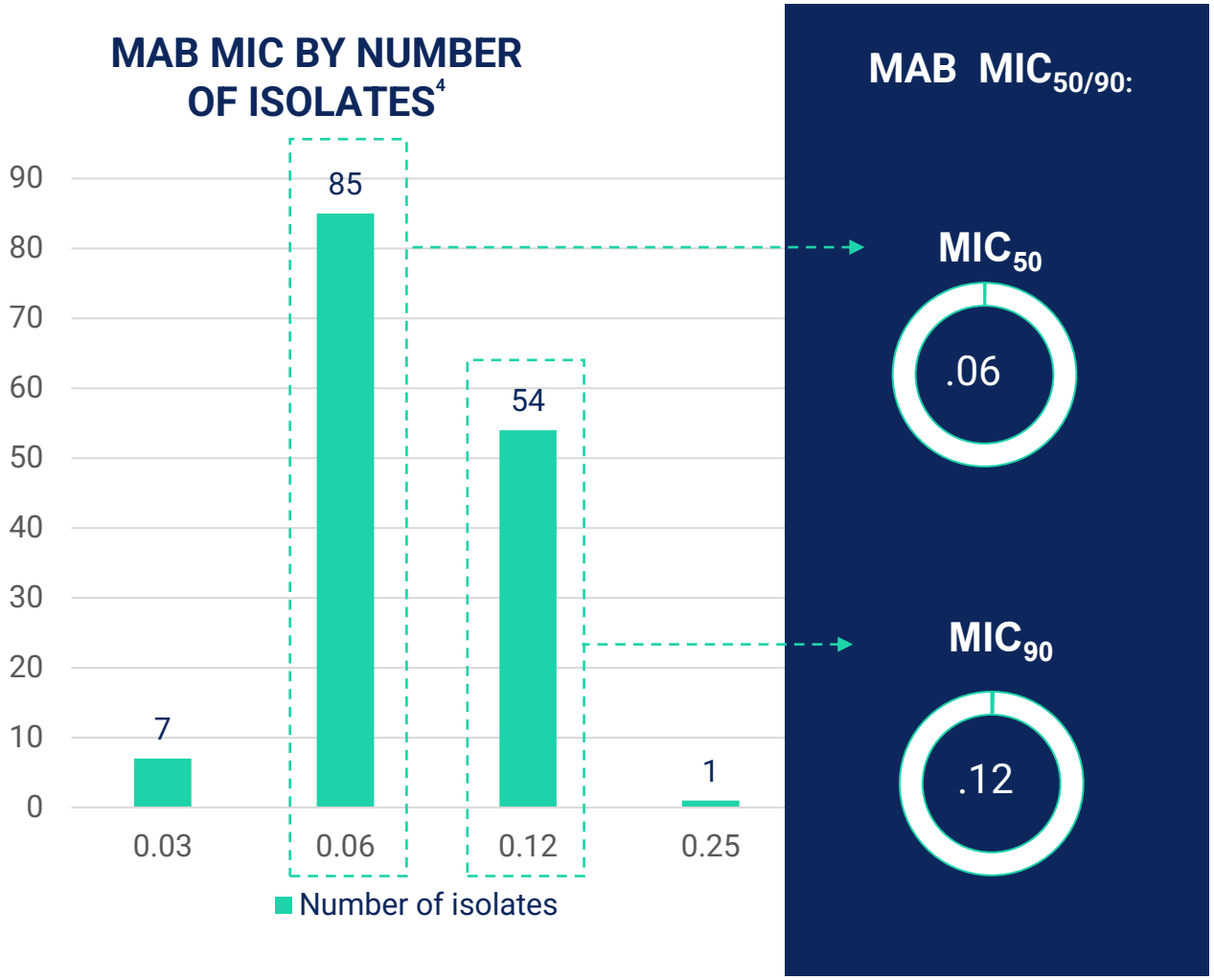
- Potential once-daily oral therapy would reduce treatment burden in an IV-heavy treatment landscape
  - Requirement for intravenous line placement
  - Inconvenience and expense of multiple visits for care
- Novel MOA suited for multidrug combination regimens
- Favorable hepatic safety results to date; CDAD not observed

Well-Controlled, Decision-Enabling Study Design

- 84-patient randomized, controlled IIT in MAB
- Includes microbiological and clinical endpoints to derisk FDA-recommended Phase 3 design
- Dose selection driven by PK/PD analysis and learnings from EBO-301 for TR-MAC lung disease

Prior MAC trial informs development strategy in MAB

Order of magnitude lower in vitro MICs in MAB support potential for PK/PD target attainment



Insights from prior MAC trial

- MIC in MAB orders of magnitude below MICs observed in EBO-301 TR-MAC population
- MAB MIC was not affected by subspecies, resistance to amikacin or clarithromycin, or by colony morphology
- Potency potentially overcomes lower drug exposure in extracellular bacteria
- Opportunity to study a less ill population (treatment-naïve), with shorter duration of disease
- More nodular bronchiectatic in MAB vs cavitary disease in MAC study
- No prior antibiotic therapy in treatment-naïve patients; lower risk of baseline-resistant pathogens

AN2Therapeutics

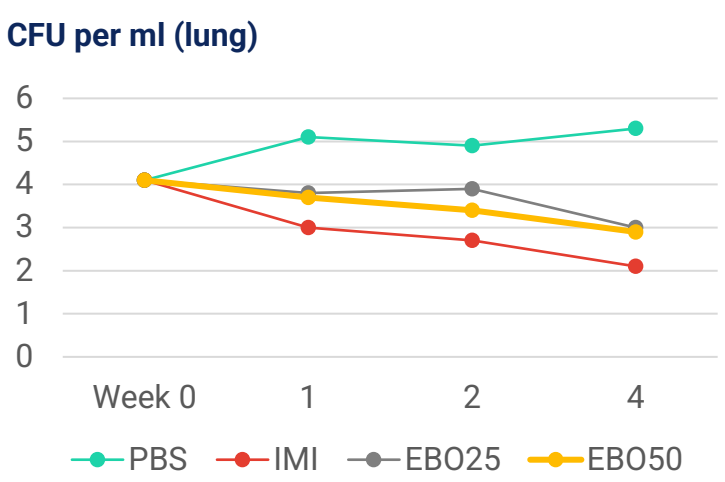
Nguyen MH, Calado Nogueira de Moura V, Keepers TR, van Ingen J, Daley CL. In vitro susceptibility of 147 international clinical *Mycobacterium abscessus* isolates to epetraborole and comparators by broth microdilution. *J Antimicrob Chemother*. 2025;80:713–716. doi:10.1093/jac/dkae461

Oral EBO matched gold-standard imipenem in preclinical mouse model

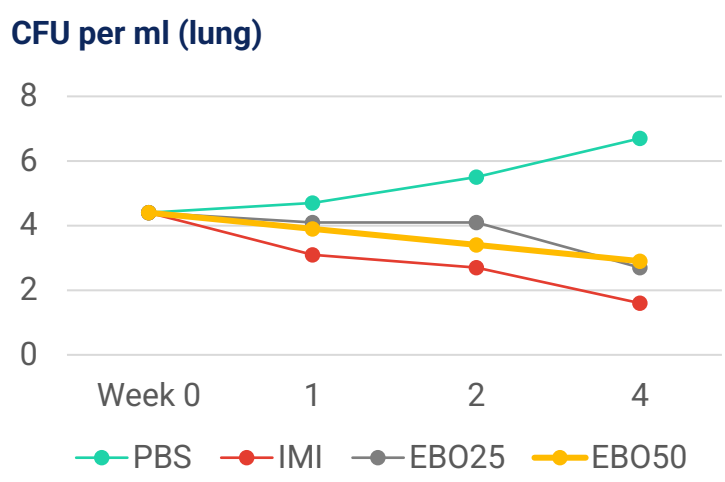
Off-label IV imipenem is current backbone therapy for MAB

Comparable activity to imipenem suggests LeuRS is a highly attractive target in MAB

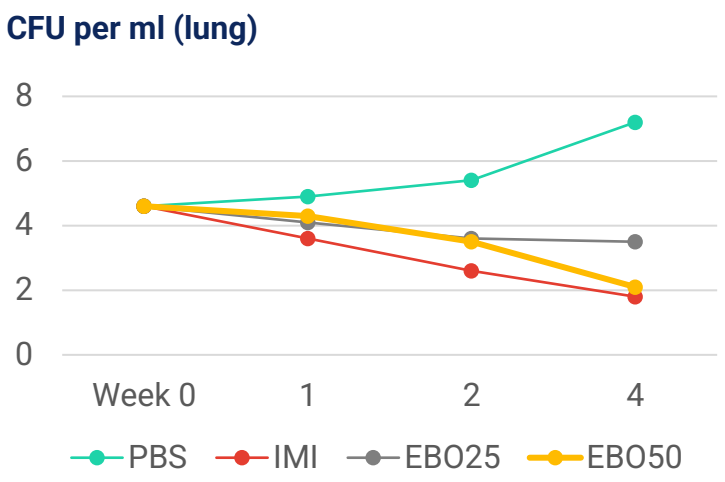
ATCC 19977



M9530



M9501



EBO 25: epetraborole 25O QD; EBO 50: epetraborole 500mg QD

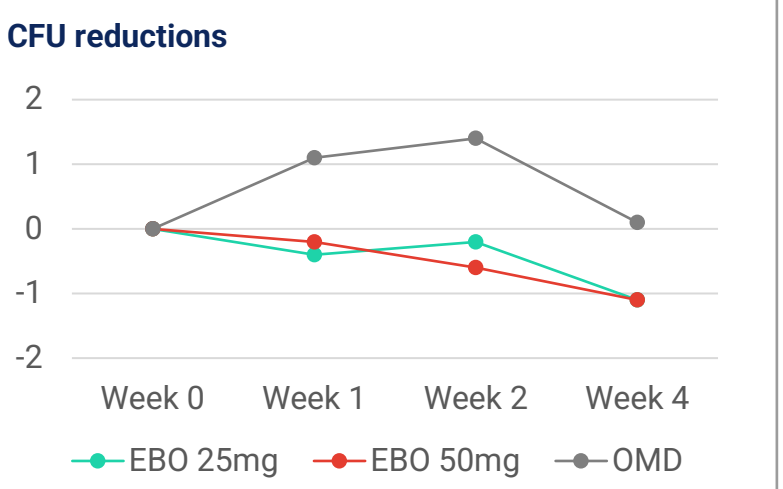
Rimal B, Lippincott CK, Panthi CM, Xie Y, Keepers TR, Alley MRK, Lamichhane G. Efficacy of epetraborole against Mycobacteroides abscessus in a mouse model of lung infection. Antimicrob Agents Chemother. 2024;68:e00648-24. doi:10.1128/aac.00648-24

Oral epetraborole demonstrated bactericidal activity in mouse model

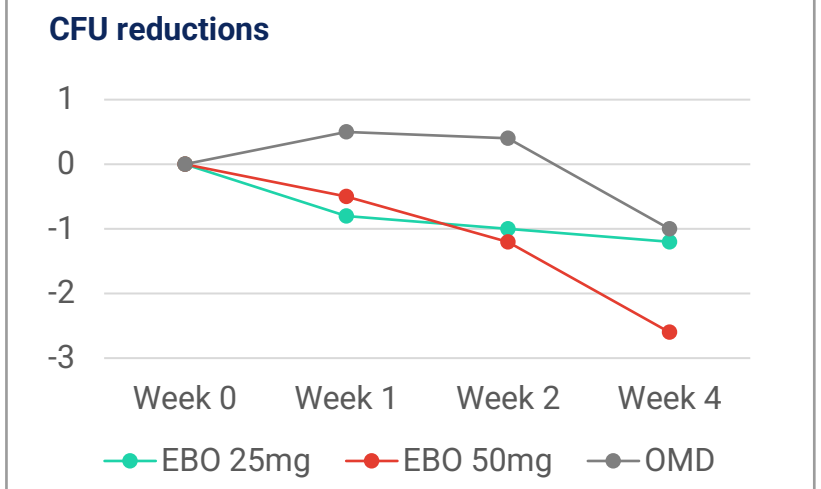
EBO shows bactericidal activity in an *in vivo* mouse model of MAB lung disease compared to omadacycline

The bacteriostatic profile of oral omadacycline in the same *in vivo* model translated into positive Phase 2 data in treatment-naïve MAB lung disease

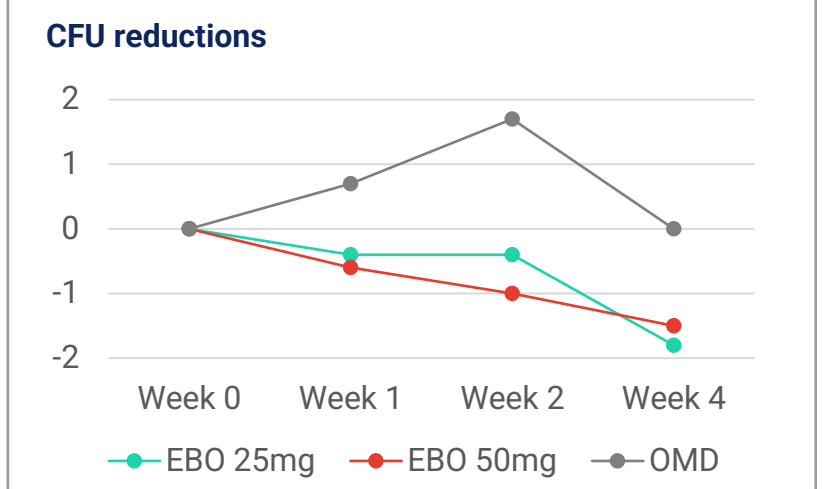
ATCC 19977



M9530



M9501



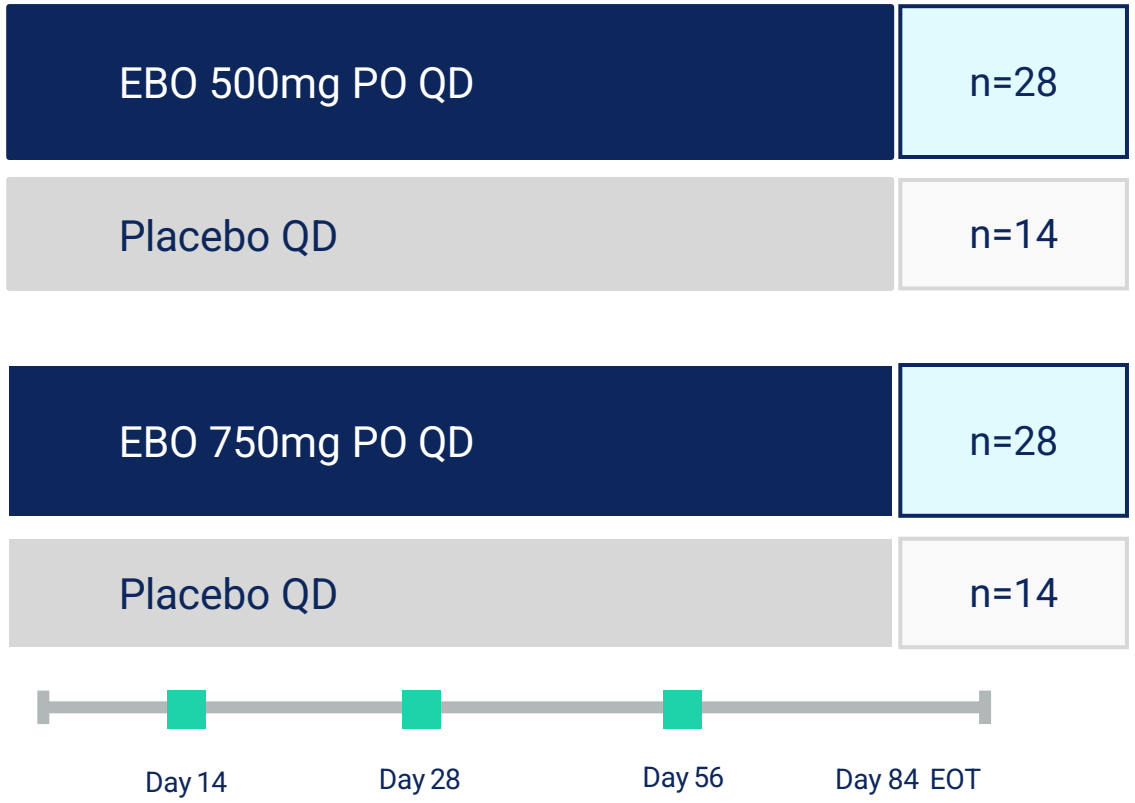
DeStefano M, Shoen C, Cynamon M, Alley MRK. Epetraborole, a potential oral agent for Mycobacterium abscessus lung disease. Poster presented at: NTM Conference at CSU; May 27–30, 2025; Fort Collins, CO. Poster No. 74; Nicklas DA, Maggioncalda EC, Story-Roller E, et al. Potency of omadacycline against *Mycobacteroides abscessus* clinical isolates in vitro and in a mouse model of pulmonary infection. *Antimicrob Agents Chemother.* 2022;66(1):e0170421. doi:10.1128/AAC.01704-21.

Phase 2 IIT study underway

EBO Regimen 1
(2:1)

vs.

EBO Regimen 2
(2:1)



STUDY OBJECTIVES

- Proof of concept in MAB lung disease
- Identify optimal dose and enable potential **Phase 3 registrational** trial

ENDPOINTS

- Sputum culture conversion
- Semi-quantitative count reduction
- Time to growth in culture
- Change in MICs
- PRO-based symptom improvement

STATISTICAL NOTES

- Placebo patient data will be combined for analysis, n=28

Anticipated MAB timeline

Subject to enrollment rates

January 2026

IIT IND

March 2026

Trial initiated

Late 2027

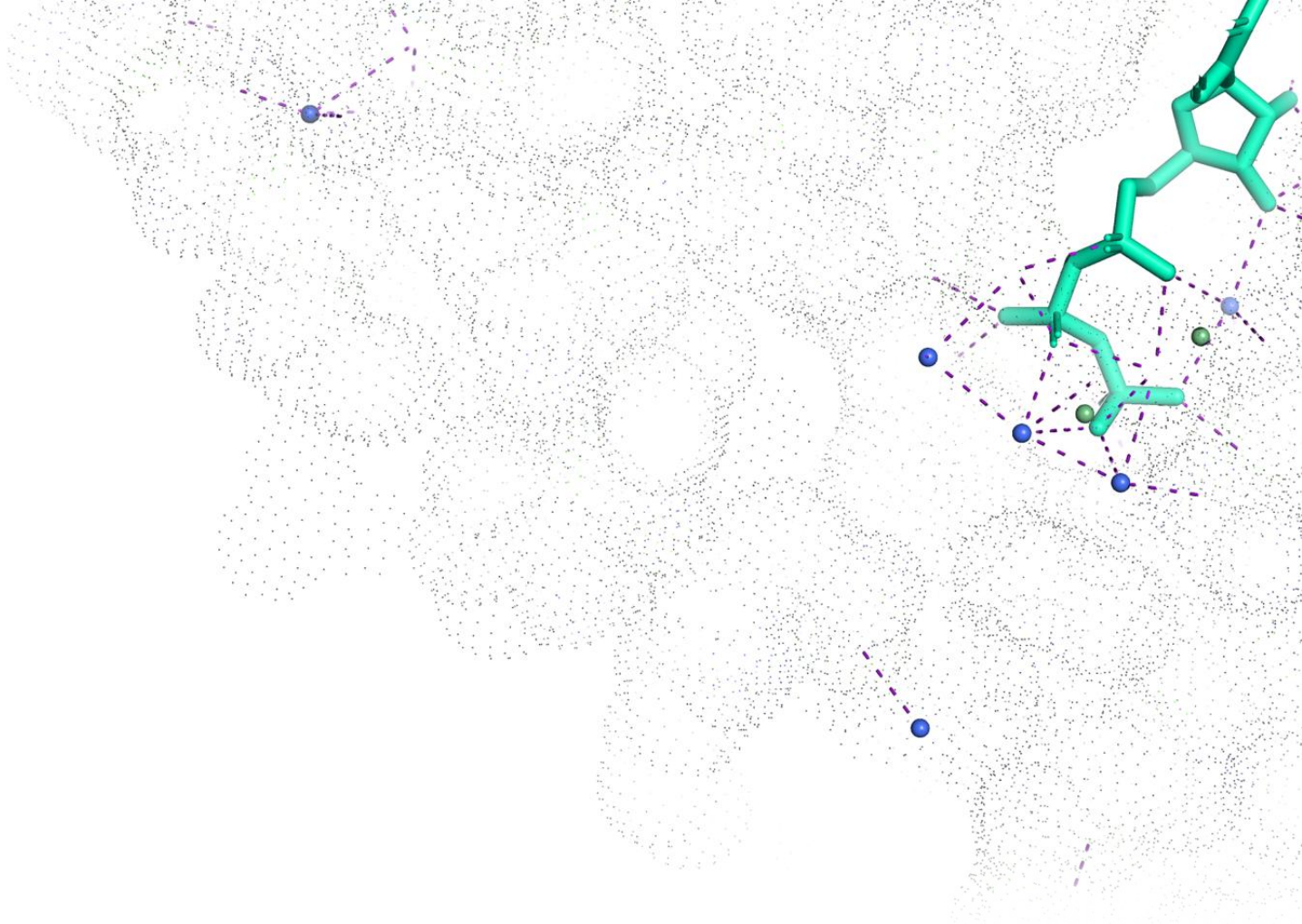
Topline data



CHAGAS DISEASE

(American trypanosomiasis)

Oral AN2-502998

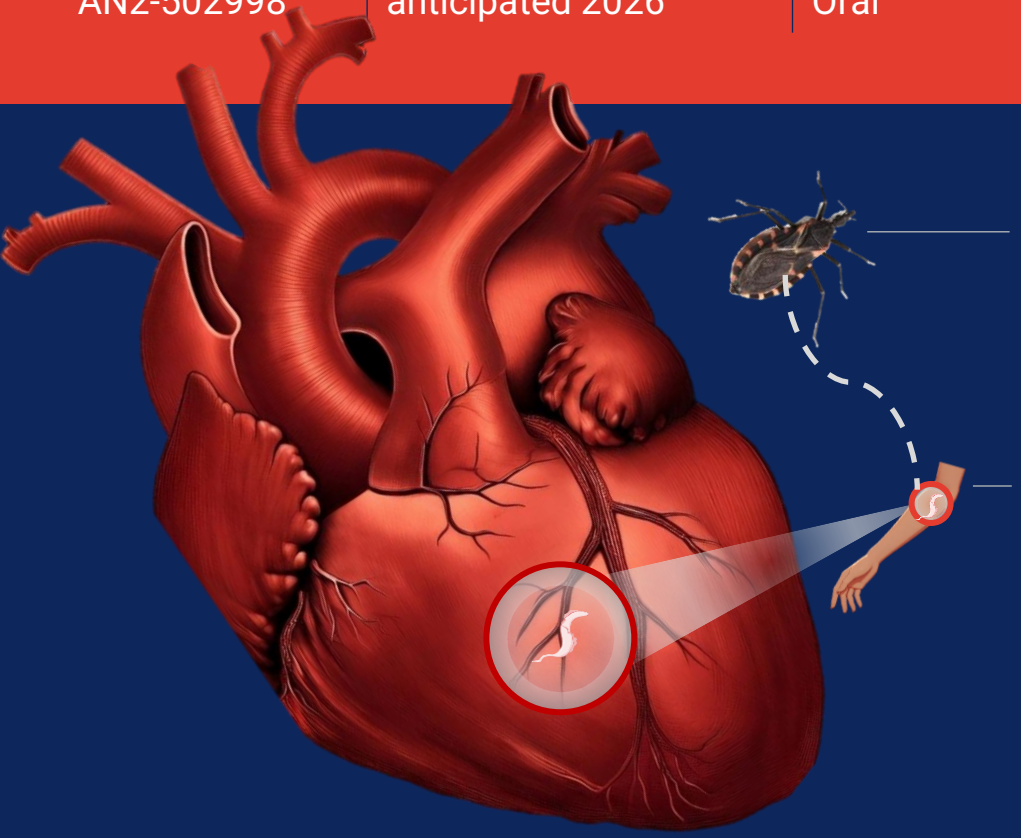


AN2Therapeutics

In Chagas disease, a silent parasite infects the heart, other critical organs

Investigational Program Summary

Candidate	Status	Form	Market	Current Therapies	Target Profile
AN2-502998	Phase 2 initiation anticipated 2026	Oral	300,000 (U.S.) 7-10M (Global)	No FDA-approved drugs for adults	Curative, oral



Main transmission by triatomine bugs (“kissing bugs”) that transfer *T. cruzi* parasite

T. cruzi parasite then lives and replicates in muscle tissue, including the heart

Persists within cardiac tissue and progressively damages myocardium over 10–30 years

30-40% of cases: arrhythmia, cardiac arrest, cardiomyopathy, heart failure, emboli, and other conditions

Additional organ systems vulnerable: GI (megacolon, megaesophagus), CNS

Other forms of transmission: mother to child, blood donation, organ transplant, food-borne

Expanding recognition of Chagas disease in the U.S.

IN THE NEWS

Chagas Disease, or deadly ”kissing bug” disease, has spread in the U.S. Here’s what to know

CBS NEWS | SEPTEMBER 9, 2025

Deadly ‘Kissing Bug’ Disease Chagas Has Spread in the U.S. – Here’s Which States Are Affected

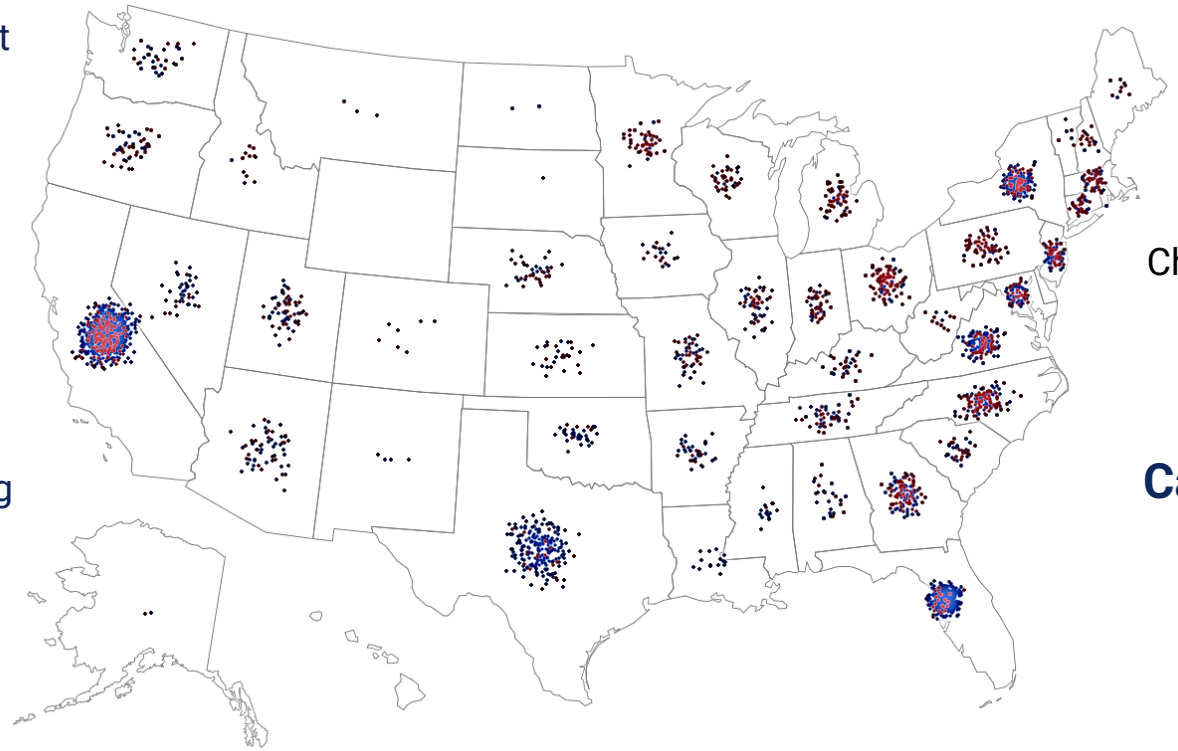
PEOPLE MAGAZINE | SEPTEMBER 6, 2025

‘Kissing bug’ disease is here to stay in the U.S., experts say. Here’s why it’s spreading

CNN | SEPTEMBER 16, 2025

“Chagas disease, long considered only a threat abroad, is established in California and the Southern U.S.”

LA TIMES | SEPTEMBER 1, 2025



United States

~300,000

No FDA-approved treatment

For adults with chronic Chagas disease, caused by *T. cruzi* infection

Canada, Japan, Europe

~200,000

Global

~7-10 million

Beatty NL, Hamer GL, Moreno-Peniche B, et al. Chagas Disease, an Endemic Disease in the United States. Emerging Infectious Diseases. 2025;31(9):1691-1697. doi:10.3201/eid3109.241700; Higuita N et al. Chagas disease in the United States: a call for increased investment and collaborative research. The Lancet Regional Health – Americas, Volume 34, 100768. June 2024; Manne-Goehler, J. et al. Access to care for Chagas disease in the United States: A health systems analysis. Am J Trop Med Hyg. 2015; 93:108-113 https://asm.org/articles/2021/april/chagas-disease-in-the-u-s-what-we-know-about-the-k; Cousin, E et al. Global, regional, and national burden of Chagas disease, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023. Lancet Infectious Diseases, v26. 3:284–301

Large U.S. patient population without an approved treatment

Standard of Care in U.S.

Benznidazole **or** **Nifurtimox**

- Pediatric only in USA/FDA; most cases are in adults
- Long treatment duration (40-120 days)
- Significant tolerability and safety issues in adults: ~80% TEAE rate, ~15% discontinuation
- Potential genotoxicity, carcinogenicity, embryo-fetal toxicity, and skin hypersensitivity

AN2-502998 Potential Product Profile

- Potential cure
- Oral treatment
- Favorable nonclinical data to date



Aldasoro E, et al, 2018. What to expect and when: benznidazole toxicity in chronic Chagas' disease treatment. J Antimicrob Chemother 73: 1060–1067; Lascano F, et al Review of pharmacological options for the treatment of Chagas disease. Br J Clin Pharmacol 2022;88:383–402; Molina I, et al, 2015. Toxic profile of benznidazole in patients with chronic Chagas disease: risk factors and comparison of the product from two different manufacturers. AAC. 59: 6125–6131; Viotti R, et al, 2014. Towards a paradigm shift in the treatment of chronic Chagas disease. Antimicrob Agents Chemother 58:635–639. doi: 10.1128/AAC.01662-13; Molina I, et al. Randomized Trial of Posaconazole and Benznidazole for Chronic Chagas' Disease. N Engl J Med 2014;370:1899–908; Bosch-Nicolau P, et al. Efficacy of three benznidazole dosing strategies for adults living with chronic Chagas disease (MULTIBENZ) Lancet Infect Dis 2024; FDA Labels: BENZNIDAZOLE tablets, for oral use (fda.gov) & LAMPIT (nifurtimox) tablets label (fda.gov)

A novel antiparasitic targeting CPSF3

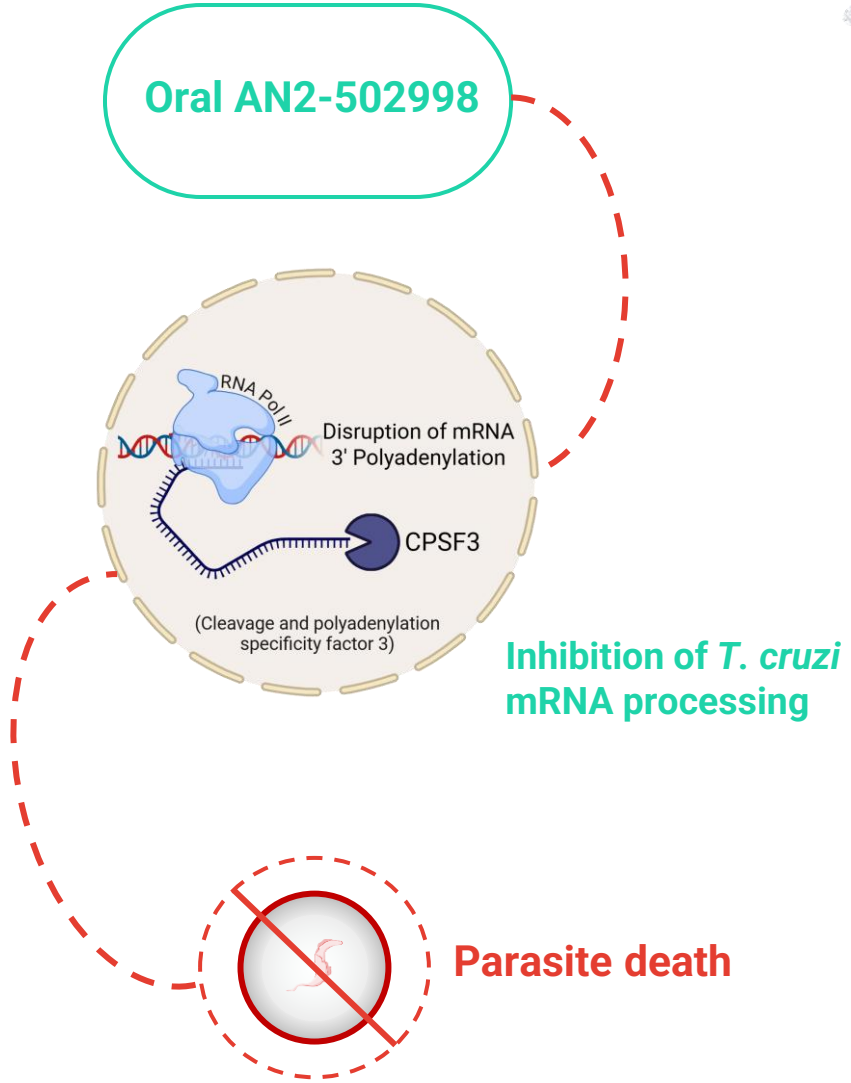
AN2-502998's presumed mechanism of action: inhibition of CPSF3 in the *T. cruzi* parasite. CPSF3 target is essential in *T. cruzi* parasite mRNA processing. Inhibition of *T. cruzi* CPSF3 leads to parasite death.[1]

- **CPSF3 is a validated target for trypanosome disease**

  Target clinically validated with EMA-approved acoziborole, which demonstrated ~95% cure rate in Ph 2/3 study for related trypanosome parasitic disease (HAT)

- **AN2-502998 is an oral, small molecule benzoxaborole**

  Same chemical class as 2 FDA-approved drugs (crisaborole and tavaborole), EMA-approved drug



AN2-502998 is formerly known as AN15368; Padilla, A.M., et al. Discovery of an orally active benzoxaborole prodrug effective in the treatment of Chagas disease in non-human primates. Nat Microbiol 7, 1536–1546 (2022); Betu Kumeso VK, et al. Efficacy and safety of acoziborole in patients with human African trypanosomiasis caused by Trypanosoma brucei gambiense: a multicentre, open-label, single-arm, phase 2/3 trial. Lancet Infect Dis. 2023 Apr;23(4):463-470.

Phase 1 FIH and NHP efficacy with 28-day treatment support advancement to Phase 2

NHP EFFICACY STUDY

100%

PARASITE ELIMINATION

with **28-days** of AN2-502998 treatment

- NHPs with naturally acquired infections
- Durable parasitic elimination at target exposures attainable in humans

PHASE 1 FIH STUDY*



AN2-502998 generally well tolerated at exposure levels consistent with NHP efficacy thresholds



SAD: 6 dose levels

MAD: 3 dose levels

WELL TOLERATED

Generally well tolerated at all dose levels
No dose-limiting toxicities observed in healthy adults

EXPOSURES CONSISTENT WITH NHP EFFICACY

Exposures achieved across all dose levels including at or above the NHP 1-month cure (anticipated efficacious exposure range)

NHP=Nonhuman primate; SAD=single ascending dose; MAD=multiple ascending dose; *NCT07024589

Efficacy evaluation in NHPs with naturally-acquired *T. cruzi* infection potential translation to human efficacy

NHPs in Native Transmission Environments

Natural habitat with endemic vectors

Genetically heterogeneous *T. cruzi* parasites

Only compound to have demonstrated curative activity in NHPs with long-term, naturally acquired infection of diverse *T. cruzi* genetic types

- **Higher translational potential**: Demonstrates activity in a biologically complex model that closely reflects human infection
- **Strain breadth addressed**: Activity observed against genetically heterogeneous, naturally circulating parasite populations
- **Authentic immune context**: Efficacy evaluated in the presence of naturally evolved host–parasite immune dynamics

Has aligned with human clinical outcomes: NHP study data would have predicted human clinical trial results:

- Benznidazole: Human efficacy matched NHP efficacy in retrospective NHP study
- E1224 (ravuconazole): Failed in humans, despite efficacy in mouse models. Failed in retrospective NHP study

Padilla, A.M., et al. Discovery of an orally active benzoxaborole prodrug effective in the treatment of Chagas disease in non-human primates. Nat Microbiol 7, 1536–1546 (2022); Torrico F, et al. E1224 Study Group. Treatment of adult chronic indeterminate Chagas disease with benznidazole and three E1224 dosing regimens. Lancet Infect Dis. 2018 Apr;18(4):419-430; Bosch-Nicolau, P et al. Efficacy of three benznidazole dosing strategies for adults living with chronic Chagas disease (MULTIBENZ), Lancet Infect Dis. 2024 Apr;24(4):386-394; Molina I, et al. 2014. Randomized trial of posaconazole and benznidazole for chronic Chagas' disease. N Engl J Med 370:1899–1908. doi: 10.1056/NEJMoa13131224; Tarleton RL. Avoiding Clinical Trial Failures in Neglected Tropical Diseases: The Example of Chagas Disease. Clin Infect Dis 2022;76:1516–20

Favorable infrastructure potentially enables fast, targeted patient access in the U.S. if approved

1
Defined and scalable patient population

- Low-cost diagnostics available, enables scalable test-and-treat strategy with precedent in silent diseases such as HCV, HIV, and latent TB
- Localized communities with elevated disease awareness support targeted education and screening

2
Favorable coverage and access dynamics

- Pricing research based on health economics supports framework similar to HCV for curative profile
- Large covered-lives footprint across U.S. payers supports broad patient access

3
Long-term exclusivity & PRV eligibility

- Exclusivity potential into mid-2040s with pending, granted, and filed cases
- PRV upon approval – Chagas disease designated neglected tropical disease

A market poised for transformation – comparable to Hep C Story

Chagas disease exhibits similar structural attributes that historically unlocked Hepatitis C market with Harvoni and Sovaldi: silent, slowly proliferating, irreversible critical-organ damage, high mortality

	HEPATITIS C	CHAGAS
Early symptoms	**Both asymptomatic**	
Disease duration	**Both progress silently over decades**	
Historic Tx (pre-DAA)	**Toxic, inconsistent efficacy**	
Therapeutic opportunity	**Oral cure**	
Primary organ	Liver	Heart
Progression	Fibrosis → cirrhosis	Cardiomyopathy → CHF, AA, death
Infected → serious disease	15-30%	20-30%
Prevalence	3M (U.S.)	300,000 (U.S.)

Illustrative therapeutic analogy; diseases differ in prevalence and biology.

Anticipated timeline for Chagas

Subject to regulatory review and enrollment duration

2Q 2026

Phase 1 & NHP data

2026

Phase 2 initiate

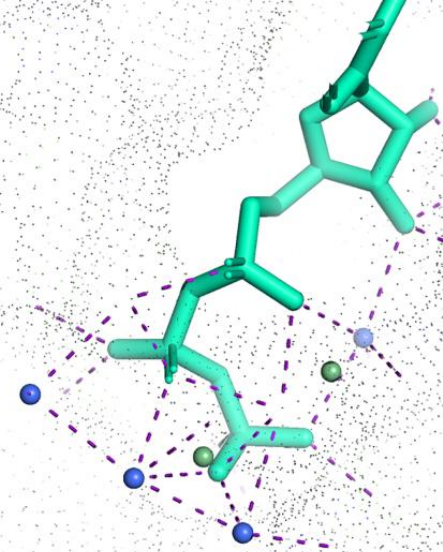
2H 2027

Phase 2 topline data



ONCOLOGY PROGRAMS

Research



AN2Therapeutics

Two high-potential lead targets enabled by boron chemistry

PI3Kα (CANDIDATE EXPECTED 2026)

Targeting third-generation design with true pan-mutant coverage, high selectivity over wild type

- Large market (17% of all solid tumors; 35% of breast cancer) with multiple potential combo partners
- 1st and 2nd generation compounds provide clinical validation but deficiencies in toxicities (first gen) and helical coverage (second gen)
- Lilly-Loxo/Petra deal (2020); Lilly-Scorpion deal (2025)
- AN2 lead op data show pan-mutant coverage (H1047, E542, E545) with ~7- to 50-fold selectivity over WT; a true 3rd generation best-of-class profile
- Boron platform offers unique chemistry and IP advantages including FTO in crowded field

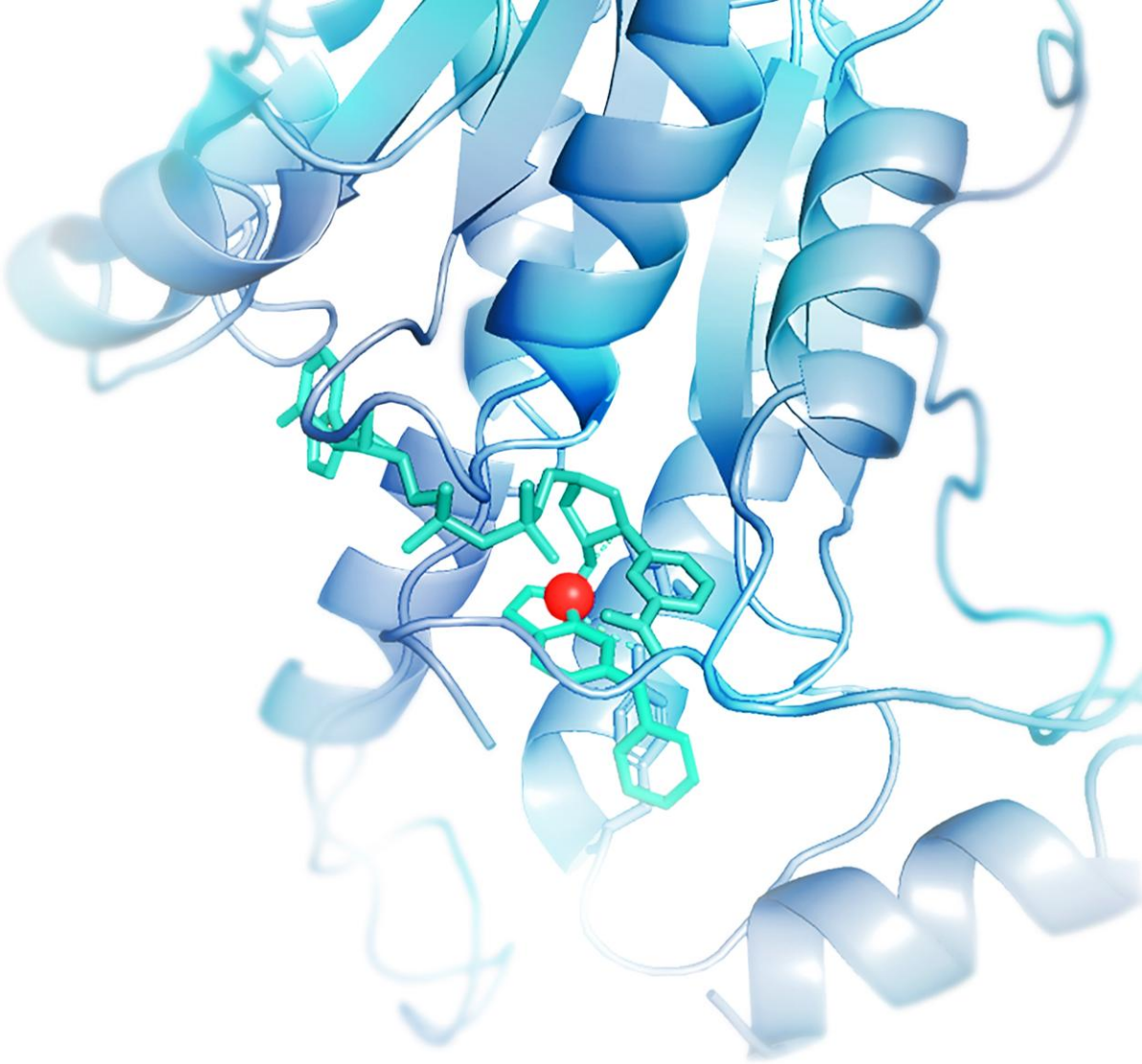
ENPP1 (CANDIDATE DECLARED FOR SOLID TUMORS)

Alleviate immune suppression to enhance efficacy of checkpoint inhibitors and DNA-damaging agents

- Activates immune system's on/off switch that turns "cold" tumors "hot" and blocks tumor metastasis
  - Early clinical validation emerging
- Large market opportunity as combination partner with checkpoint inhibitors, DNA damaging agents (PARP, chemo, ADC, radiation)
- Lead op data shows best-in-class potential

ONCOLOGY

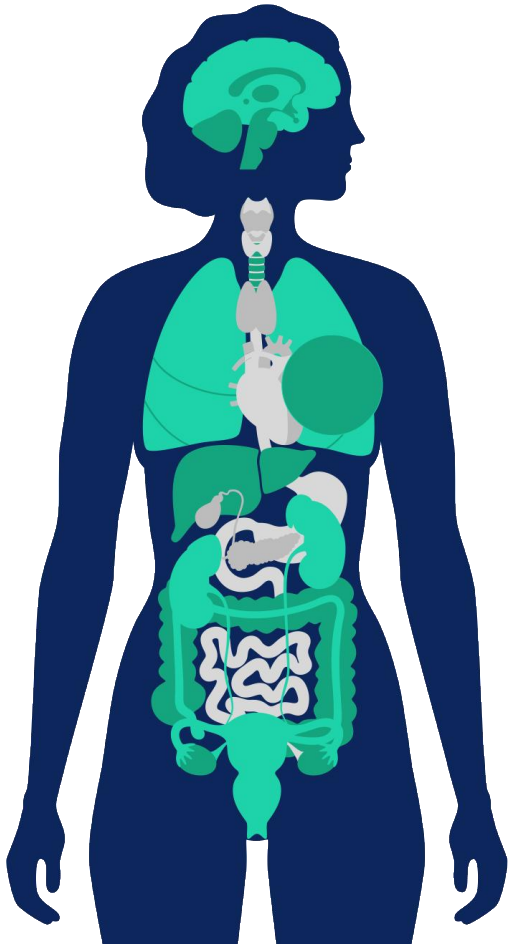
PI3Kα



AN2Therapeutics

Opportunity for 3rd gen pan-mutant PI3Kα with WT-sparing selectivity

TISSUES AFFECTED BY PI3Kα MUTATIONS



PI3Kα is part of a key signaling pathway that controls how cells manage metabolism and survival

Mutations in the PIK3CA gene can lead to uncontrolled cell growth and cancer metastasis

PI3Kα is the second most frequently mutated gene in cancer

Large market (17% of all solid tumors; 35% of breast cancer) with multiple potential combo partners

First- and second-generation therapies showed solid-tumor efficacy but lack selectivity over WT, leading to tolerability and efficacy issues limiting PFS across mutants

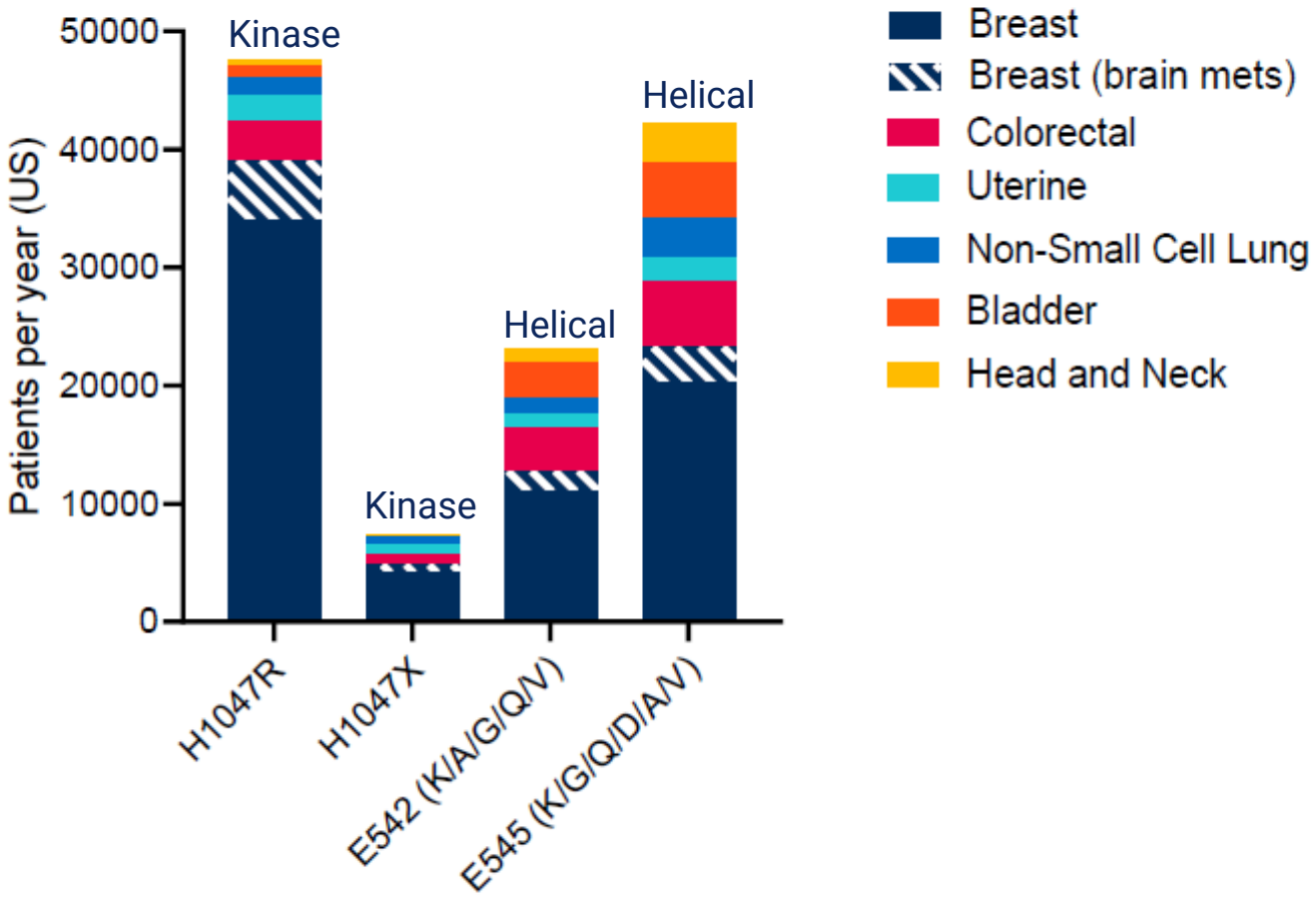
3rd generation pan-mutant, selective compounds are highly attractive targets, but chemistry has thus far proven challenging, which is where we believe boron creates a unique opportunity for a best-in-class profile

PI3Kα mutations are a large market opportunity; selectivity over WT proven to reduce SAEs and lead to longer mPFS

Targetable PI3Kα driver mutations take two major forms: **kinase** and **helical**

Highly prevalent in cancer patients

17% of all cancers	25% of endometrial cancer
35% of breast cancer	20% of colorectal cancer



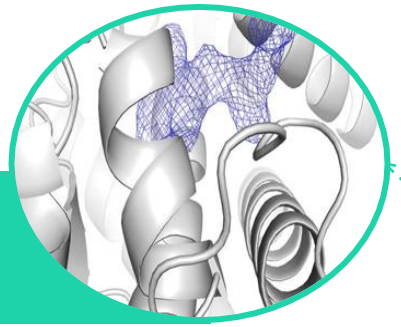
M.S. Lawrence, P. Stojanov, C.H. Mermel, *et al.* Discovery and saturation analysis of cancer genes across 21 tumour types Nature, 505 (7484) (2014), pp. 495-501
Voutsadakis et al., Clin Colorectal Cancer, 20(3), 2021, 201-215
Murali, R. et al., British Journal of Cancer, 110, 2014, 12-18, Oda et al., *Cancer Res,* 2005)

Helical selectivity, ~50% of mutations, will define next-gen compounds

	1st generation Alpelisib/Inavolisib ON MARKET	2nd generation RLY2608, STX-478 CLINICAL STAGE	3rd generation AN2 OPPORTUNITY
PAN-MUTANT/WILD-TYPE SPARING	No	Kinase dominant; diminished helical performance over WT	**True pan-mutant coverage** High selectivity across kinase (H1047) and helical (E545, E542)
HYPERGLYCEMIA	Grade 3	Minimal grade 3; grades 2 and 1 common	Improved efficacy by addressing dose limiting toxicities

Sammons et. Al., Updated efficacy of mutant-selective PI3Kα inhibitor RLY-2608 in combination with fulvestrant in patients with PIK3CA-mutant HR+/HER2- advanced breast cancer: ReDiscover trial; 2. Juric et. Al., A Phase 1/2 Trial of LY4064809 (STX-478), a Pan-Mutant-Selective PI3Kα Inhibitor in PIK3CA-Mutant Advanced Breast Cancer (ABC) and Other Solid Tumors: Updated Results from the PIKALO-1 Study

AN2 boron-based mutant-selective inhibitors designed to bind covalently to an allosteric site of PI3Kα



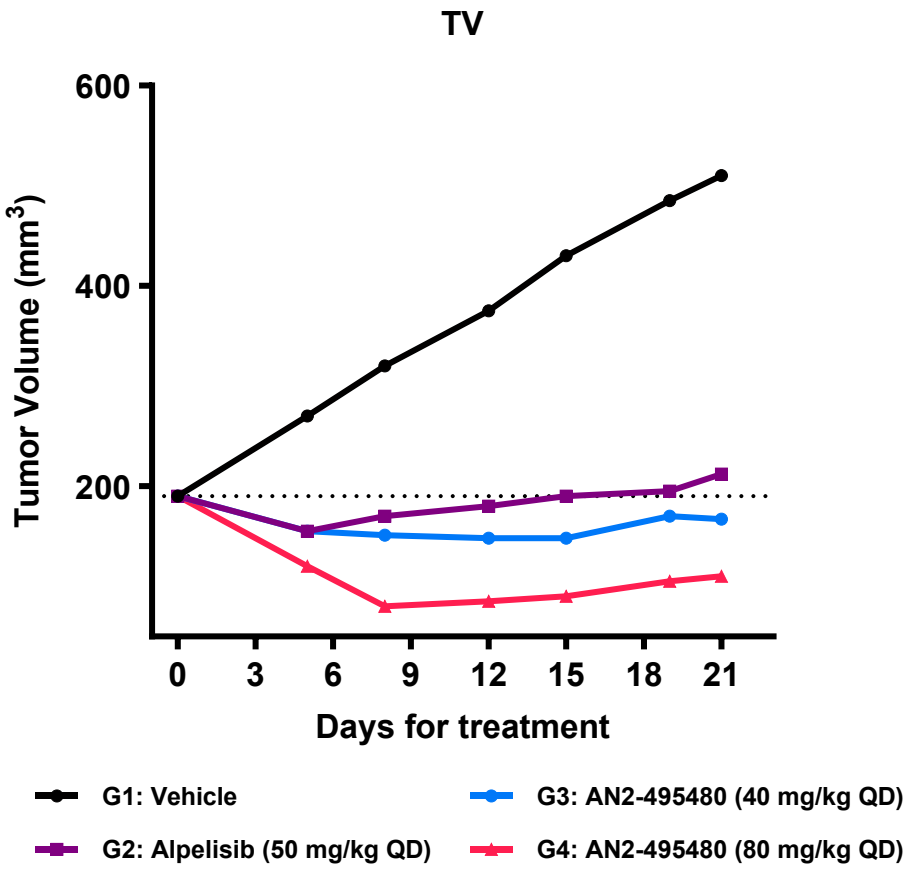
Covalent Allosteric Inhibitor
Best multi-mutant inhibitor
AN2 THERAPEUTICS

ATP-site (non-WT sparing)
GENENTECH + NOVARTIS

Kinase Allosteric Site 1
ONKURE

Kinase Allosteric Site 2
RELAY + SCORPION

In vivo efficacy superior to alpelisib without glucose disregulation



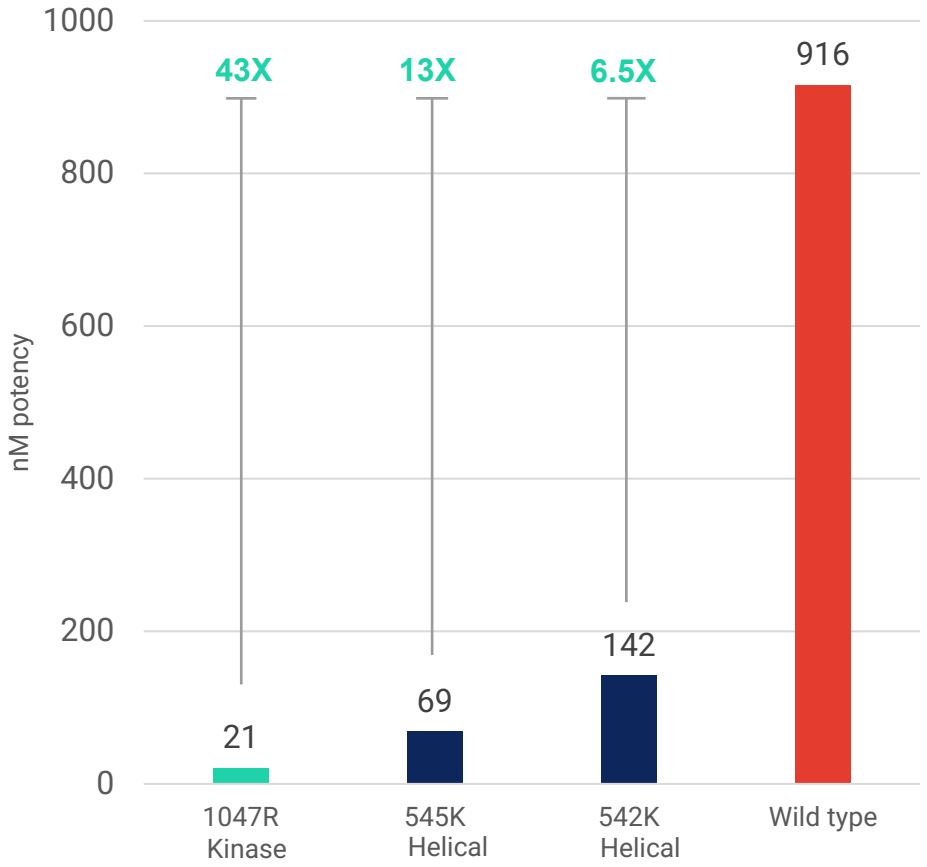
- Superior mouse efficacy in xenograft model against H1047R vs. apelisib
- 27X selective for H1047R mutant over WT
- No effects on glucose regulation

All competitor data generated by AN2 for IND-related purposes.

AN2 boron heterocycles – opportunity for best-in-class molecules

AN2-495877

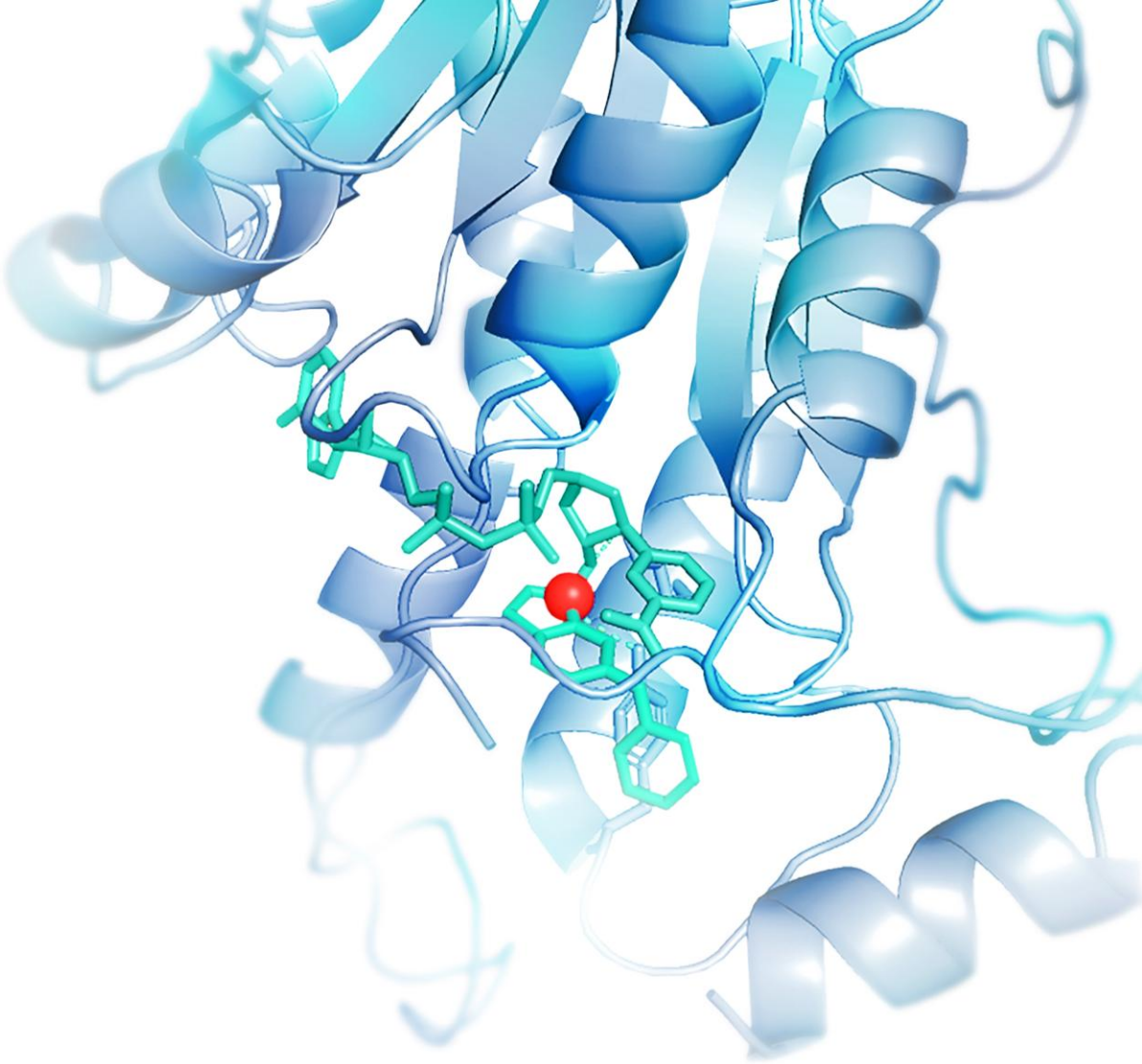
KINASE AND HELICAL SELECTIVITY



- Novel covalent binding to PI3Kα allosteric site with potentially differentiated on/off rate and kinetics
- Pan-mutant potency targeting 5-100 fold selectivity over WT covering most important mutants
- In vivo efficacy in murine models superior to alpelisib
- Tumor regression observed in vivo without hyperglycemia or hyperinsulinemia
- Strong IP/FTO from differentiated boron structures

ONCOLOGY

ENPP1

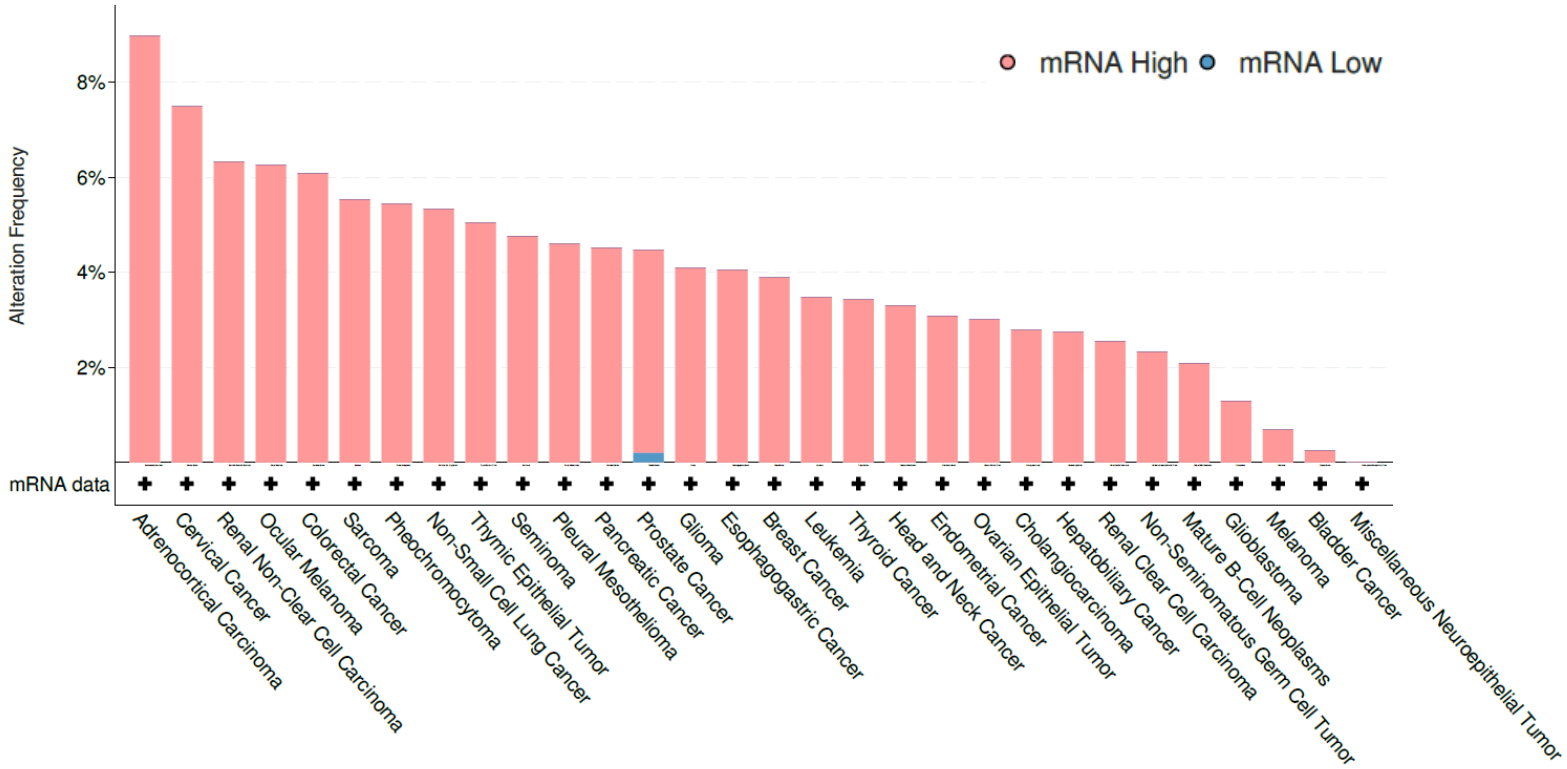


AN2Therapeutics

ENPP1 is highly expressed across various solid tumor types

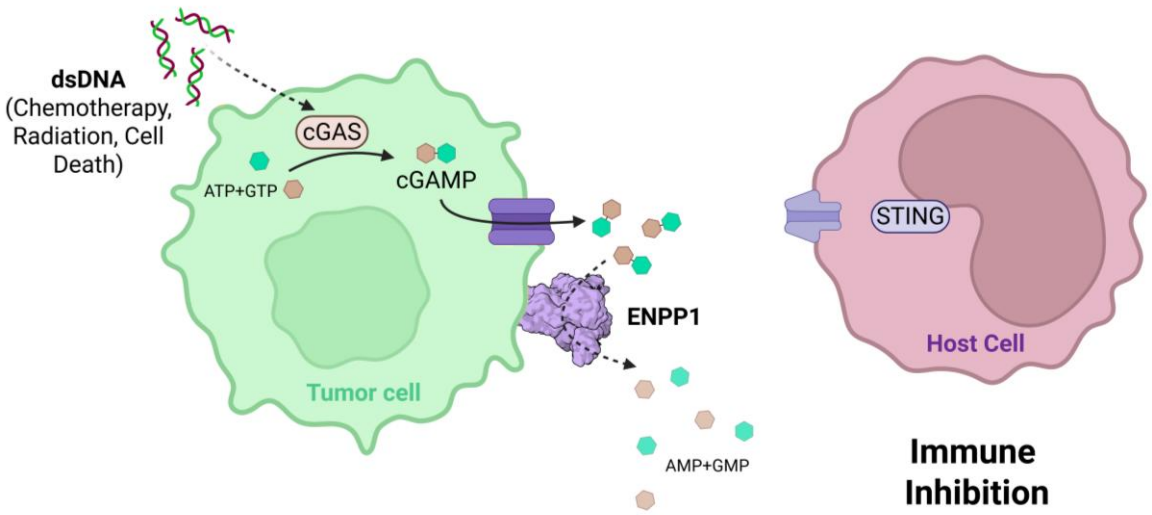
High incidence of ENPP1 overexpression in colon, lung, pancreas and breast

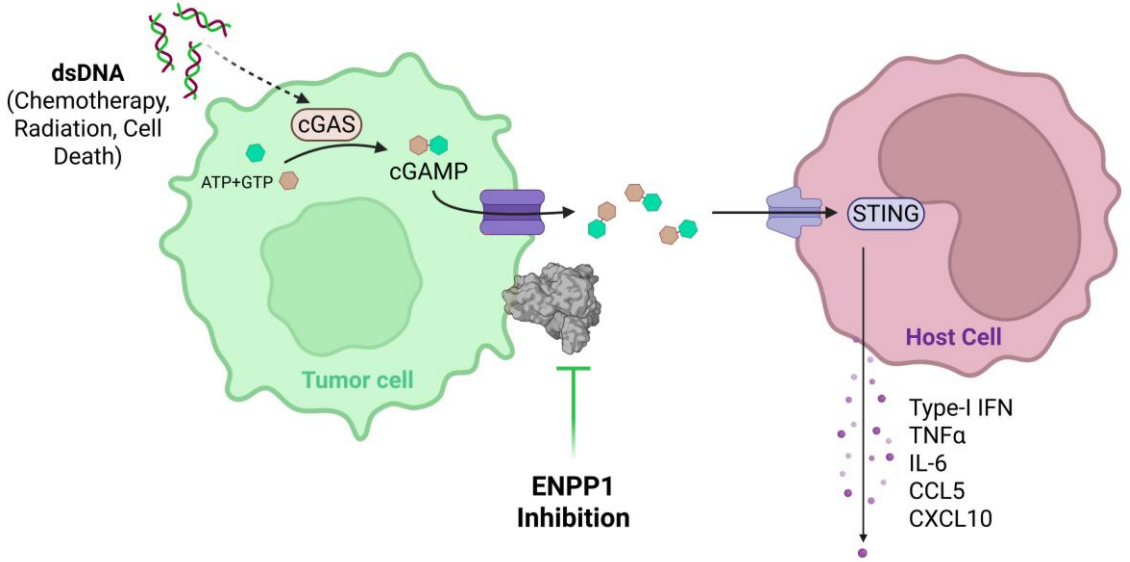
6% Colon	5% Lung
5% Pancreas	4% Breast



cBioportal; TCGA dataset

Tumors evade the immune system via increased ENPP1 expression





High ENPP1 immune inhibition

1. **ENPP1** sits on the outer membrane of the cancer cell lying in wait for the cGAMP messenger
2. **As cGAMP** exits the cancer cell, ENPP1 hydrolyzes and degrades it, thereby preventing its message from reaching the immune system
3. **Tumors** with high ENPP1 expression thus evade the immune system by remaining invisible or “cold”

ENPP1 inhibition immune activation

1. **Damaged** cancer cells alert the immune system via cGAMP dinucleotide chemical messenger
2. **cGAMP** activates an innate immune response against the cancer cells through the release of chemokines into the tumor microenvironment turning a “cold” tumor “hot”
3. **T cells** follow the chemokines into the now “hot” tumor microenvironment allowing for immune-mediated cancer cell killing

ENPP1 inhibitors ≠ STING agonists: different enzymes, different biology

	STING agonists	ENPP1 inhibitors
MECHANISM	Directly force STING into its active conformation, producing a rapid, global inflammatory burst	Block ENPP1, preserving endogenous cGAMP and enabling *natural, sustained* STING activation
ACTION	A pharmacologic “push” that overrides cellular control of the pathway	A physiological “release of the brake,” re-establishing immune reactivity and tumor-localized signaling
DELIVERY	Typically intratumoral due to poor bioavailability and systemic toxicity; limited to accessible lesions	Oral systemic delivery with demonstrated safety; ideal for metastatic or deep-seated tumors
SAFETY	High risk of cytokine-driven systemic inflammation and flu-like toxicities; narrow therapeutic window	Controlled, localized immune activation with lower cytokine risk and wider therapeutic window
EFFICACY	Transient immune activation; limited monotherapy activity; inconsistent tumor responses	Sustained innate activation supports durable antitumor immunity and effective combination strategies

High ENPP1 expression leads to worse outcomes

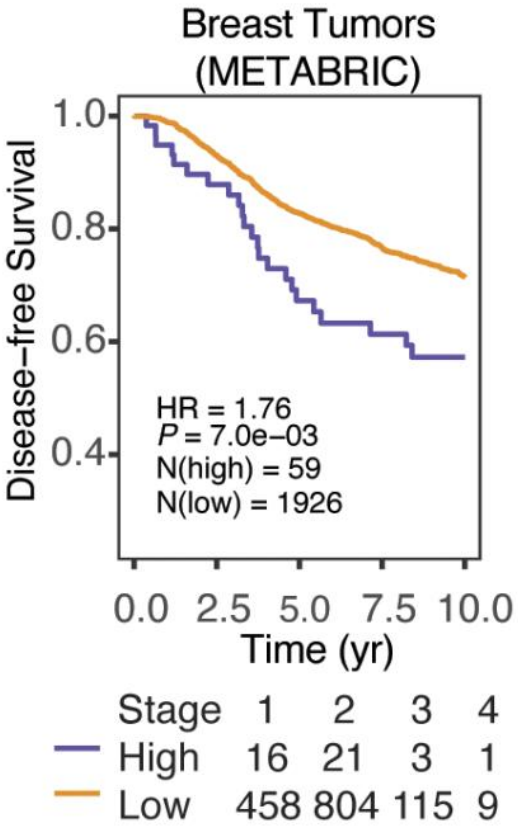
PUBLICATION

PNAS IMMUNOLOGY AND INFLAMMATION

ENPP1 is an innate immune checkpoint of the anticancer cGAMP-STING pathway in breast cancer

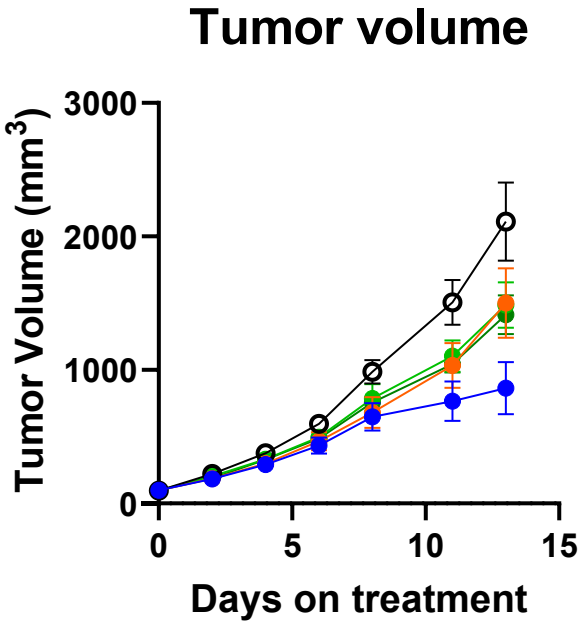
RESEARCH ARTICLE | DECEMBER 20, 2023

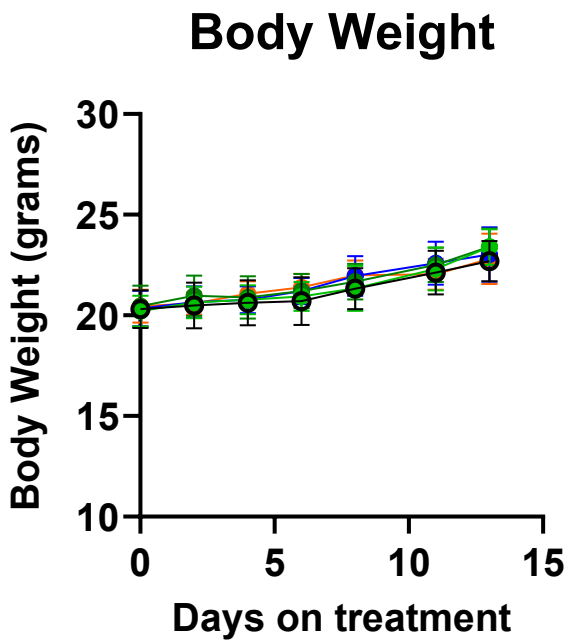
- Phase 1a dose escalation completed
- All dose levels safe and well tolerated
  - >17 months on therapy at 800mg BID (ongoing)
  - No grade 3 TRAEs, SAEs or DLTs
- Immune activation with significant improvement in PFS (p=0.001) in subjects with tumor ENPP1 and cGAS-positive phenotype
  - 75% disease control
- Phase 2 in CRC initiated in February 2025



Clinical candidate AN2-503321: Potential for single-agent efficacy compared to PD-1 and CTLA4 checkpoint inhibitors in EMT6 (breast cancer) model

AN2-503321 was well-tolerated and showed TGI at two highest doses tested, comparable to the inhibition observed with Anti-PD-1 antibody alone

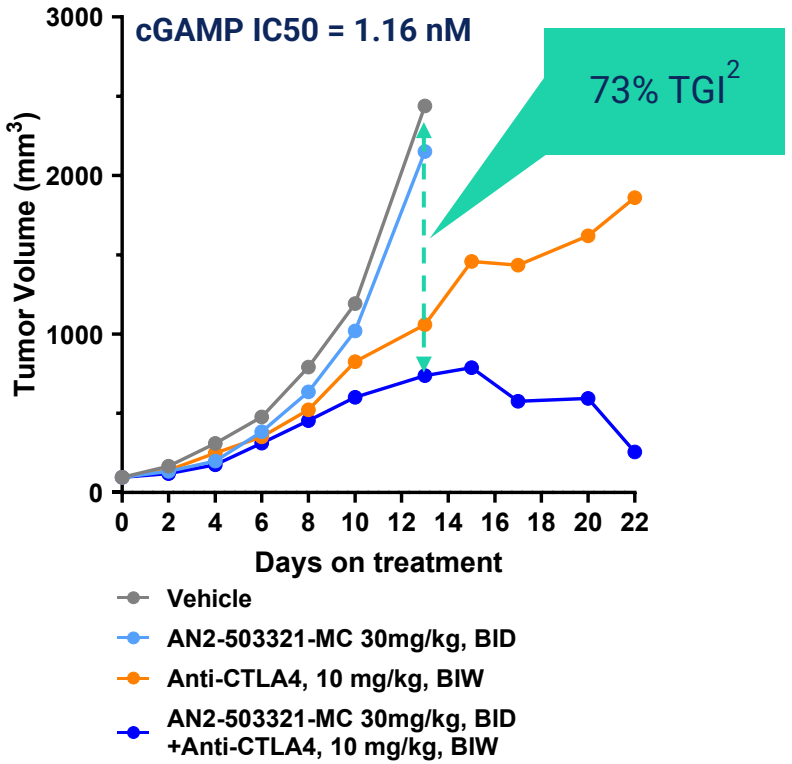




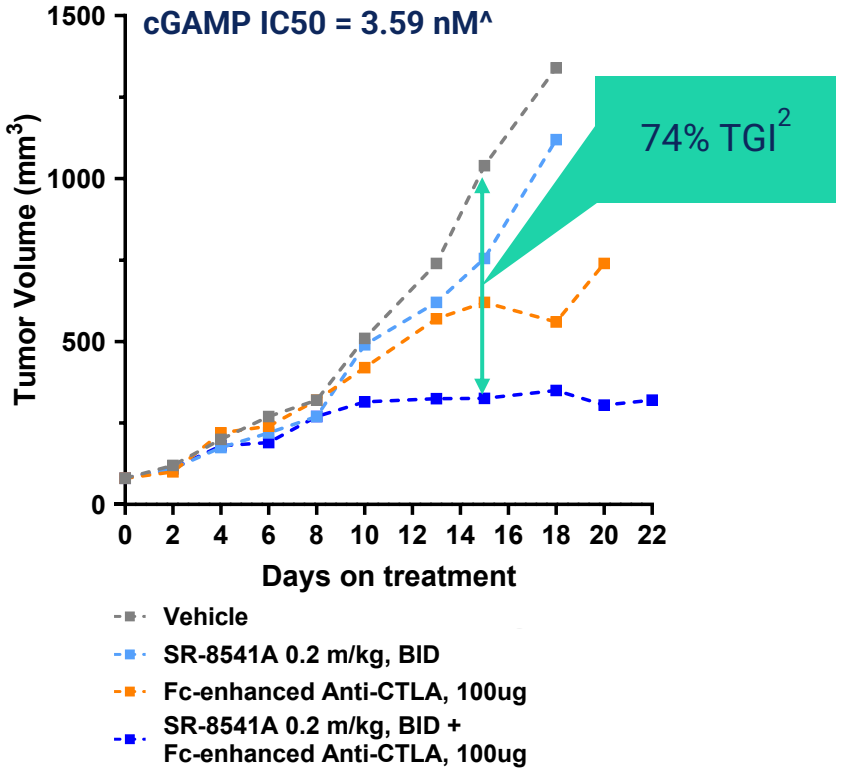
Treatment Group	TGI
Vehicle	-
AN2-503321 10 mg/kg BID, PO	31.1%
AN2-503321 30 mg/kg BID, PO	34.7%
Anti-PD-1 10 mg/kg BIW, IP	30.4%
Anti-CTLA4 10 mg/kg BIW, IP	61.9%

AN2-503321 and Stingray SR-8541A in CT26 (colorectal cancer) model

AN2-503321 EFFICACY DATA

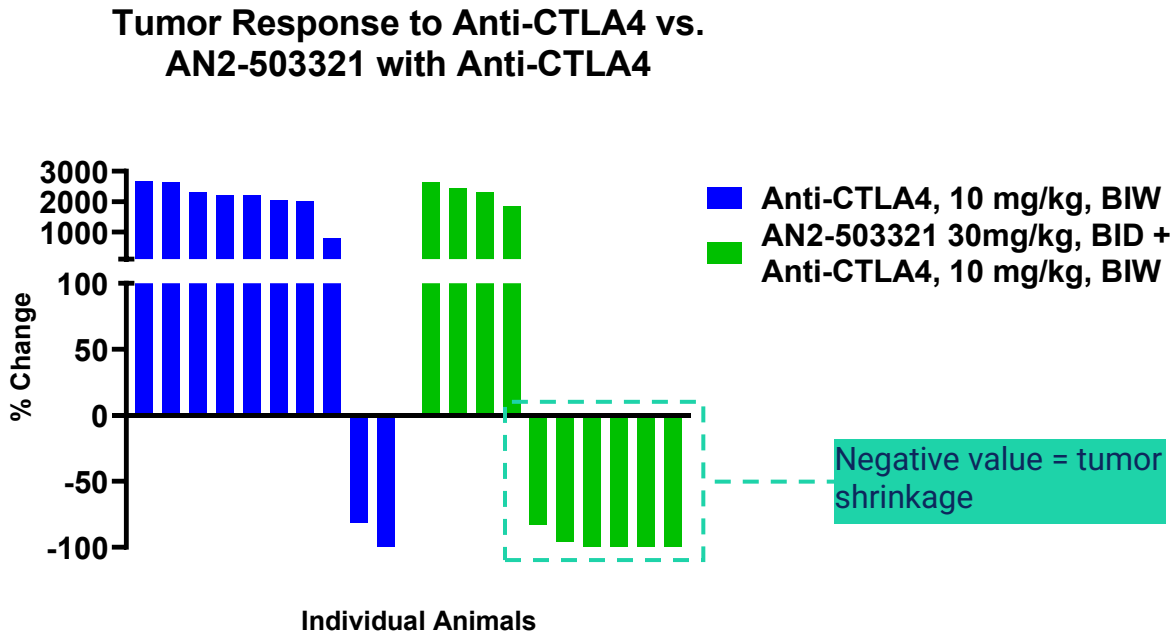


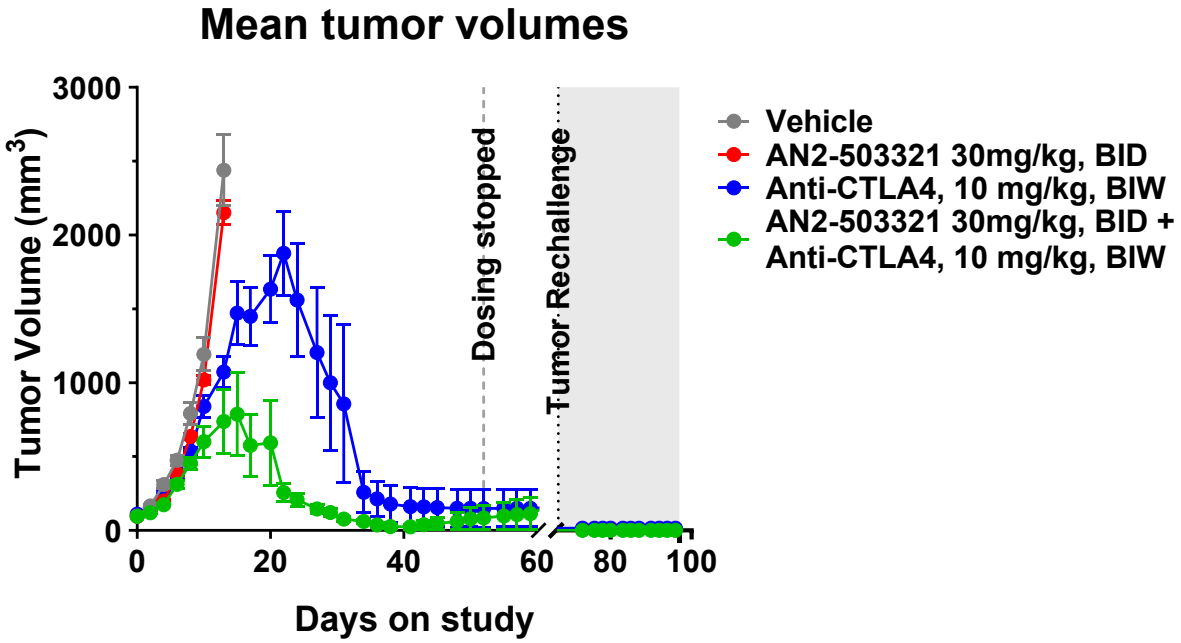
SR-8541A EFFICACY DATA – EXTRAPOLATED[1]



Extrapolated data from published SR-8541A CT-26 efficacy data. ^Published data; TGI calculated on Day 13 for AN2-503321 and Day 15 for SR-8541A, prior to the termination of any mice on study; Weston A. et al., Can Res, 2024 AACR, Weston A. et al., J of Imm of Can, 2023 SITC, Weston A. et al., J of Imm of Can, 2024 SITC

AN2-503321: promising results in colorectal model





AN2-503321 produced 3x complete responses

- 6/10 Complete response (CR) for AN2-503321 + anti-CTLA4 combo
- 2/10 CR for anti-CTLA4

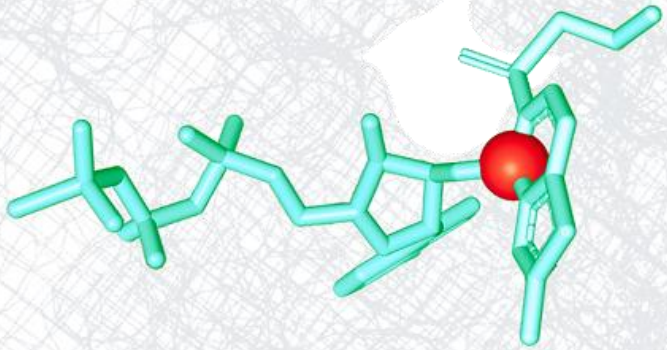
Responses durable upon rechallenge

- Durable response with no regrowth of CRs following cessation of dosing
- Resistance to cancer cell rechallenge is consistent with treatment-induced anti-tumor immunity

Company data on file

AN2Therapeutics

Unlocking Boron's Promise for Patients



Menlo Park, CA | IR@an2therapeutics.com