Investor Overview

AN2THERAPEUTICS.COM

December 2024

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this presentation include, but are not limited to, statements regarding: anticipated milestones, catalysts, value-creation opportunities, and inflection points, and potential of the Company's boron chemistry platform and pipeline programs; cash runway, cash burn reduction and ability to achieve catalysts/inflection points within cash runway; design, initiation, and timing of the Company's clinical trials and results, market opportunity and medical needs; expectations regarding data analysis from the EBO-301 Phase 2/3 trial in treatment-refractory MAC lung disease and potential clinical benefit, including the potential to reinitiate Phase 3 development; regulatory meetings and pathway and alignment with FDA guidance; 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: potential disruptions 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 existing and future clinical trials; AN2's ability to procure sufficient supply of its product candidates for its existing and future clinical trials; the potential for results from clinical trials to differ from preclinical, early clinical, preliminary or expected results; 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; continued funding by the National Institute of Allergy and Infectious Disease (NIAID) of AN2's development program for melioidosis; 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 and Quarterly Reports on Form 10-Q, and AN2's 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. 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.

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TRADEMARKS

This presentation contains trademarks, service marks, trade names

Conviction with Epetraborole



- Epetraborole showed potential for clinical improvement in two PROs: QOL-B and MACrO₂ using continuous score method
- QOL-B is primary endpoint for Arikayce pivotal ENCORE study
- FDA EOP-2 planned for 1H25
- Potential to reinitiate Phase 3 pivotal study in TR-MAC

Near-Term Catalysts Disciplined Capital Spend



Proven Boron Based Discovery Platform



- Founded by AN2 team originally from Anacor
- Established record of platform productivity
 - Novel targets
 - 2 FDA approved drugs, 1 pending
 - Anacor sold to Pfizer for \$5.2B
- Opportunity to identify novel targets beyond in oncology and ID

• EBO: EOP2 meeting 1H25

- Chagas: Phase 1 complete in 2025, upside in ID with ~300K patients in US
- Melioidosis: Start Ph 2 2H25
- 50% reduction in expenditures with restructuring initiatives extends cash runway through 2027

Validated Boron-Based Drug Discovery is Uniquely Suited to Deliver Novel Drug Candidates that Have Potential to be First in Class





Ability to interact with novel biological targets not achieved by traditional carbon chemistry

Drug-like design features can be optimized (oral, exposures, distribution, etc.); excellent selectivity and safety profile

Demonstrated track record Generated 2 boron-based FDAapproved drugs (Anacor Pharma) and 1 pending

Broad Pipeline of Boron-Based Chemistry Product Candidates



Anticipated Near, Medium, and Long-Term Catalysts with the Potential to Drive Significant Shareholder Value

Advancing key programs in infectious diseases and oncology with high unmet need

Near-Term



NTM Lung Disease

- Phase 2 clinical data appears aligned with FDA Guidance for primary endpoint. EOP2 meeting planned 1H25 to discuss potential pivotal trial
- EBO demonstrated nominal statistically significant clinical benefit in QOL-B respiratory domain (secondary endpoint) and MACrO₂ (post hoc)
- Microbiological assessment ongoing
- Generally well-tolerated; 2 (5%) EBO discontinuations due to TEAEs in Phase 2

Melioidosis

- Phase 2 initiation 2H25; topline data YE26; 100% funded by US Government to date
- ✓ PRV, stockpiling and regional sales to HMIC

\$1B+ Opportunity



Chagas Disease

- High unmet need with no approved therapies for chronic disease: ~300k patients in US and ~7M patients worldwide
- Only compound to date that cured infection in nonhuman primates
- Initiating Phase 1 trial mid-2025; projected Phase 2 POC data in 2027

Long-Term



Oncology and ID

- Leverage broad utility of AN2's boron drug discovery platform to expand into other therapeutic areas, starting with oncology
- Plan to deliver up to 3 development compounds in 2025

\$500M-\$1B Opportunity (US Only)

Restructuring initiatives extends cash runway through 2027

Epetraborole in NTM Lung Disease

Substantial Market Opportunity in NTM for Oral EBO Once-a-Day dosing

Key takeaways

- Chronic, progressive infection; life threatening in some patients whose disease becomes refractory to available therapies
- Coughing, chest tightness, fatigue leads to social isolation and quality of life impact
- Only one FDA-approved therapy in treatment-refractory MAC, inhaled therapy
 - Approved with surrogate endpoint of sputum culture conversion: 29% vs 8.9%; confirmatory trial to show clinical benefit ongoing
 - Discontinuations in trial: 33.5% vs 8% (treatment vs. placebo)
- Other regimens rely on off-label uses with significant safety and tolerability issues

Estimated U.S. diagnosed patient population



In August, Announced Phase 2 Top-line Results in TR-MAC (NTM)



Phase 2 portion: *PRO validation*

- Seamless Phase 2/3 design
- Phase 3 enrolled 97 patients, all completed 6-months of treatment – data anticipated mid-2025
- No evidence of induced resistance to epetraborole

Primary endpoints	Outcome
Validation of MACrO ₂ patient-reported outcome tool (responder outcomes)	Psychometric analysis supports validation
Percentage of patients achieving clinical response (responder outcomes)	Meaningful improvements favoring EBO 39.5% vs. 25% (p=0.186)
Adverse event profile	Generally well tolerated

Notable secondary endpoints	Outcome
Sputum culture conversion	5:4 favoring EBO
QOL-B least squares mean	+6.9 points favoring EBO (p=0.036)

EBO-301 Enrolled a Severely Refractory Population

Key points

- High rates of difficult-to-treat cavitary and fibrocavitary disease
- Nearly a decade of disease duration
- Significant population refractory or resistant to Arikayce / amikacin
- High levels of multi-drug resistance
- Microbial complexity and complex lung anatomy present challenges to successful bacterial eradication
- Suggests that sputum culture conversion may not be appropriate secondary endpoint for oral therapies in TR-MAC

Characteristic	EBO Ph 2 (n=80)	CONVERT (n=336)*
Non-cavitary NB (%)	47.5%	86.6%
Cavitary (C-NB and FC) (%)	52.5%	13.4%
Disease duration (years)	9.3	3.0-4.0
ALIS usage @ baseline	18.8%	0
Macrolide resistant @ baseline	32.2%	21.8%
Amikacin resistant @ baseline	61.7%	0

* Caution should be exercised when comparing data across independent studies

PRO outcomes from Phase 2 EBO-301 trial appear aligned with FDA Guidance¹



LSM= Least squares mean ¹ Nontuberculous Mycobacterial Pulmonary Disease Caused by Mycobacterium avium Complex: Developing Drugs for Treatment, Guidance for Industry, September 2023 ² Insmed Investor Presentation, October 2024

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³ Measures of patient improvement for QOL-B are shown by positive changes in the score measured from baseline

⁴ Measures of patient improvement for MACrO2 are shown by negative changes in the score measured from baseline.

Clear and Improving Clinical Response as Measured by QOL-B

QOL-B (respiratory) clinical response (least squares mean)



Key insights

- Increased score represents clinical improvement
- Same endpoint selected as primary in Arikayce TN-MAC pivotal trial, after alignment between Insmed and FDA
- Nominal statistical significance*
- Prespecified secondary endpoint
- Analysis suggests validated PRO in TR-MAC, subject to FDA review

*Statistical significance shown; considered "nominal" because QOL-B was not the prespecified primary endpoint in Phase 2 and no adjustment for multiplicity was performed

MACrO2 Analysis as Continuous Score Reinforces Outcomes Observed in QOL-B Respiratory Domain

MACrO₂ clinical response

(least squares mean)



Key insights

- Score reduction indicates clinical improvement
- Post-hoc analysis
- Nominal statistical significance*
- Analysis suggests validated MACrO2 continuous measure in TR-MAC, subject to FDA alignment
- Reinforces evidence of EBO's potential clinical effect and supports EBO's potential to meet a clinical primary endpoint in Phase 3

*Statistical significance shown; considered "nominal" because continuous MACrO₂ score was not a prespecified endpoint in Phase 2 and was conducted as a post-hoc analysis

	EBO + OBR N=39	Placebo + OBR N=41
TEAEs	37 (94.9%)	35 (85.4%)
Mild	20 (51.3%)	19 (46.3%)
Moderate	14 (35.9%)	14 (34.1%)
Severe	3 (7.7%)	2 (4.9%)
Life threatening	0	0
Death	0	0
SAEs	2 (5.1%)	5 (12.2%)
Drug discontinuation due to TEAE	2 (5%)	3 (7.3%)

Key insights

- Low discontinuations (5% EBO)
- GI events (41% vs 22%) generally mild and not treatment limiting; diarrhea, nausea, vomiting infrequent
- Hemoglobin effect consistent with preclinical and Phase 1b data; anemia observed in 15/39 epetraborole patients; initial decline, followed by stabilization and recovery post-treatment
- No anemia SAEs
- No study withdrawal due to anemia
- Safety profile supports further development





PRO outcomes from Phase 2 EBO-301 trial appear aligned with FDA Guidance for primary endpoint in Phase 3 trial

- Planning for FDA meeting in 1H25
- 97 Patients enrolled in truncated Phase 3 have completed 6 months (primary endpoint)
- Plan to maintain the blind on Phase 3 data while we discuss Phase 2 data with FDA and align on a statistical analysis plan for Phase 3 data
- Phase 3 data read out expected mid-2025, subject to timing of discussions with FDA



EBO-301 Phase 2 is the first trial to potentially **demonstrate PRO-based clinical POC** in treatment-refractory MAC patients



Better understanding of microbial complexity in TR-MAC patient population should help inform selection of appropriate secondary endpoint for oral therapy

Recent Enabling Data in *M. abscessus* Paves Way for Phase 2 Development







No FDA-approved treatments for NTM lung disease caused by *M. abscessus*



Off-label treatments have a high rate of drug resistance or tolerability limitations

SOC agent, Imipenem, is parenteral only. EBO had cidal activity similar to imipenem in mouse efficacy model

Antimicrobial Agents and Chemotherapy July 2024

M. abscessus burden in lungs of mice infected with isolates ATCC 19977 (A), M9501 (B), and M9530 (C). Time point -1 represented 24 h after infection with M. abscessus via the aerosol route. Time point 0 represents 1 wee infection and the day of treatment initiation. Time points weeks 1,2, and 4 represent the end of 1, 2, and 4 weeks of treatment with once-daily 1x PBS (PBS), twice daily 100 mg/kg subcutaneous imipenem (IMI), once-daily k after 25 mg/kg oral EBO (EBO25), or once-daily 50 mg/kg oral EBO (EBO50). Mean Mab burden in the lungs and standard error are shown (per group per time point, n = 5 at weeks -1, 0, +1, and +2, n=1- at week +4)

Epetraborole in Melioidosis



Melioidosis - Under-Reported, High Unmet Medical Need Disease

Caused by the Gram-negative bacterium Burkholderia pseudomallei

- Third most common cause of death from an infectious disease in SE Asia after HIV/AIDS & TB
- Incidence (estimated): 165,000 cases/year
- Potential emerging pathogen in U.S.

High Mortality - New approaches needed to address significant unmet clinical need

- Mortality: 89,000/year
- ~50% mortality 90-day all cause in AN2 observational trial recently conducted using IV standard of care treatment in hospital settings



100% Funded to date by the US Government (non-dilutive)

- Category B biothreat target (second highest behind anthrax, plague, smallpox)
- Military force protection
- US civilian population
- NIH funded: \$18M contract

Synergistic with EBO

Market potential

- Priority Review Voucher potential (\$100-150M)
- Government(s) stockpiling (\$50-100M peak sales)
- Treatment sales (e.g., Thailand, India, China, Brazil)

Potential to Reduce Mortality in Patients vs. SOC Alone



PLoS Negl Trop Dis 17: e0011795

- EBO showed cidal activity against multiple isolates (10) in an acute pulmonary murine infection model of melioidosis when subcutaneous (SC) dosing was delayed 12-hours after infection (conducted to date)
- MIC₉₀ of 1 µg/mL against 242 recent clinical isolates from NE Thailand
- EBO plus ceftazidime (CAZ) exhibits improved activity vs EBO or CAZ alone in a macrophage and murine models of infection (PLoS Negl. Trop Dis 17: e0011795)
- EBO has an additive effect to CAZ in macrophages and murine infection models (PLoS Negl. Trop Dis 17: e0011795)

Goal to Significantly Reduce Mortality in Melioidosis Treated Patients

Planned timeline



AN2-502998 in Chagas Disease



What is Chagas Disease?



Caused by the parasite *Trypanosoma cruzi* (*T. cruzi*)

Parasite lives in heart, GI, and other muscle tissue for decades



Causes arrhythmia, cardiac arrest, cardiomyopathy, heart failure, emboli, megaesophagus, megacolon, and other conditions

- No approved treatments in the U.S. for adults with chronic Chagas disease
 - Two therapeutics used off label have genotoxicity warnings in labels¹
- Available diagnostics, including a low-cost rapid test
 - Usually spreads through contact with triatomine bugs ("kissing bugs")
 - Other transmission routes: congenital, blood-borne, organ-derived, oral
 - Significant morbidity and mortality if untreated



Chagas Disease: Endemic in Latin America, Growing US Prevalence



Sources:

Global: WHO Chagas Fact Sheet (4 April 2024); dndi.org/diseases/chagas/facts

USA: Irish A, Whitman JD, Clark EH, Marcus R, Bern C. Updated Estimates and Mapping for Prevalence of Chagas Disease among Adults, United States. Emerg Infect Dis. 2022 Jul;28(7):1313-1320. doi: 10.3201/eid2807.212221;

Manne-Goehler J, Umeh CA, Montgomery SP, Wirtz VJ. Estimating the burden of chagas disease in the United States. PLoS Negl Trop Dis 2016; 10:e0005033 Europe & UK: Basile L, et al, Working Group on Chagas Disease Collective. Chagas disease in European countries: the challenge of a surveillance system. Euro Surveill. 2011;16(37):pii=19968. https://doi.org/10.2807/ese.16.37.19968-en

Chagas Disease: Growing Prevalence in the U.S.



Growing impact in the U.S.: ~300K infected



T. cruzi & 'kissing bug' vector present in ~27 US states

CDC estimates that 5.5%–7.5% of confirmed infections in blood donors are related to locally acquired infection

Estimated peak sales potential \$500M - \$1B



Confirmed' and 'Indeterminate' Chagas Disease Among Blood Donors in the United States (2007-2019). Source: AABB Chagas Biovigilance Network. https://www.aabb.org/docs/default-source/default-document-library/resources/chagas-graph-builder.html

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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

AN2-502998: Late Preclinical Drug Candidate with Curative Potential for Chronic **Chagas Disease**

Oral, small molecule benzoxaborole

- Novel target (CPSF3) is essential part of complex involved in RNA processing¹
- Chemical class with 2 FDA-approved drugs (crisaborole and tavaborole)
- Target proof-of-concept through related benzoxaborole: acoziborole, human African trypanosomiasis drug candidate with 95% cure rate in Ph 2/3 study²

In vitro potency against a spectrum of genetically diverse strains of T. cruzi¹

- Kills both actively dividing and dormant intracellular T. cruzi faster than benznidazole
- Cures *T. cruzi* infection in mouse models¹



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active benzoxaborole prodrug effective in the treatment of Chagas disease in non-human primates. Nat Microbiol 7, 1536–1546 (2022) 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 Di

AN2-502998 Cured Chronic T. cruzi Infection in NHP Model



AN2-502998: only compound to date to cure nonhuman primates (NHPs) with long-term, naturally acquired infection of diverse *T. cruzi* genetic types¹



NHPs naturally acquire *T. cruzi*-infection and develop chronic disease comparable to chronic Chagas disease in humans



T. cruzi-infected NHP study data mirror human clinical trial results for benznidazole and E1224 (Eisai) up to 1-year post-treatment period ^{2,3,4}

For benznidazole, E1224, and posaconazole, mouse models did not predict the clinical trial failure, hence the importance of this NHP model to de-risk nonclinical efficacy

#AN2-502998 was dosed at 30 mg/kg x 60 days in rhesus macaques1; half followed for >4 years

- * Benznidazole (15 mg/kg BID x 60 days) and E1224 (20 mg/kg x 60 days) NHP study was in cynomolgus macaques
- ^Parasites screened by blood PCR and hemoculture for 52 weeks
- 1 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: a proof-of-concept, randomised, placebo-controlled trial. 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): an international, randomised, double-blind, phase 2b trial. Lancet Infect Dis. 2024 Apr;24(4):386-394.

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4. 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



U NOVARTIS

Plan to enter Phase 1 **Mid-2025** Phase 2 planned protease inhibitor

Failed in clinic E1224 (ravuconazole)

Eisai



Failed in clinic posaconazole

Chagas Disease: Potential for Ph 2 POC Within Projected Runway

Planned timeline



Research Pipeline

Boron-Based Chemistry: Novel Oncology Targets



Potential for development in difficult to treat tumors:

- Pancreatic cancer
- Glioblastoma
- Metastatic tumors

Broad potential application

- Single agent efficacy has been observed in third-party studies in various tumor types
- Combination opportunities including tissue agnostic immunotherapy checkpoint inhibitors

Boron-Based Chemistry: Novel ID Targets



Novel oral NTM drugs

- Novel insights from ongoing clinical dev. work
- Experts in Mycobacterium drug R&D
 - GSK656, discovery led by Anacor scientists
- Complemented by nondilutive work in mycobacterium TB
 - Funded by BMGF
- Boron library identification of novel MOAs

Novel antiparasitic

- Lack of competitive R&D activity opportunity to target high unmet needs
- Examples
 - Tarsus: blephitis, rosacea
 - AN2: Chagas disease
- Limited/no competition
- Other high-value market opportunities creating opportunity for AN2

Leadership



Team With Significant Experience in Bringing Medicines to Market

SENIOR MANAGEMENT



Eric Easom, MBA, MEng Co-Founder, President & CEO ANACOR 2 Pfizer Lilly









Lucy Day **Chief Financial Officer** ANACOR Pfizer Centaur

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