AN2 Therapeutics

Developing treatments for rare, chronic, and serious infectious diseases with high unmet needs

AN2THERAPEUTICS.COM

November 2023

Disclaimer

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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: the timing, progress, and anticipated results from AN2's Phase 2/3 pivotal clinical trial; anticipated timing of the data readout of the Phase 2 portion of AN2's pivotal Phase 2/3 trial; timing of enrollment in the Phase 3 portion of AN2's pivotal Phase 2/3 trial; AN2's anticipated progress, business plans, business strategy and planned clinical trials; the potential clinical benefits and therapeutic potential of epetraborole to address unmet needs for patients with NTM lung disease and melioidosis; AN2's estimated cash runway, and planned usage and the timing of use of its capital resources; ability of AN2 to expand into other geographies; 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 progress enrollment in its Phase 2/3 pivotal clinical trial of epetraborole; the ability of AN2 to effectively and timely make amendments to the Phase 2/3 pivotal trial design pursuant to additional FDA feedback; timely enrollment of patients in its current and future clinical trials; AN2's ability to procure sufficient supply of its product candidate 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 candidate; the significant uncertainty associated with AN2's product candidate 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 current and future 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 reports to be filed with the SEC, including AN2's Report on Form 10-Q for the quarter ended September 30, 2023. These filings, when available, are available on the investor relations section of our website at investor.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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AN2 Therapeutics
(Co-founder & Board Chair)
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AN2 Therapeutics is a clinical-stage biopharmaceutical company developing treatments for rare, chronic, and serious infectious diseases with high unmet needs

- **Epetraborole (EBO): Pivotal Phase 2/3 antibiotic product candidate for non-tuberculous mycobacterial (NTM) lung disease**
  - **Large market opportunity given the high unmet need; Arikayce, the only approved therapy for NTM lung disease in TR setting only**
    - **Arikayce: 9-month 2023 WW net sales of $222M (+16%Y/Y)[1]**
  - **Ideal Target Product Profile**
    - Novel mechanism of action, broad spectrum antimycobacterial activity
    - Convenient, once-daily oral dosing
    - Superior profile compared to SoC combination regimen in preclinical NTM models
    - Multiple Phase 1 studies out to 28 days of dosing support well-tolerated dose and high probability of target attainment
  - **Enrolling patients in Phase 3 portion of pivotal trial expected to support U.S. and Japan regulatory approval for TR MAC lung disease**
    - QIDP, Fast Track, and orphan drug designations granted in U.S.
    - Phase 2 part fully enrolled with 80 patients; topline results expected summer 2024
  - **Potential to develop epetraborole to address additional geographies and NTM indications**
- **We expect our boron chemistry expertise to drive future pipeline of differentiated compounds**
- **$150.2M cash, cash equivalents and investments as of 9/30/2023 to fund operations through summer 2025[2]**

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TR= treatment refractory

[1] Insmed 2023 10-Q; [2] On August 15, 2023, the Company sold an aggregate of 7,777,778 shares of the Company's common stock at a purchase price of $9.00 per share under an underwritten offering. This resulted in aggregate gross proceeds to the Company of approximately $70M, before deducting underwriting discounts and commissions and offering expenses.

Epetraborole (EBO): NTM Lung Disease

IDWeek 2023: Three posters and two oral presentations that advance understanding of epetraborole in NTM lung disease

IDWeek October 2023

Oral presentation: Epetraborole: A novel antibiotic for NTM lung disease & melioidosis

Oral presentation: In vitro susceptibility of recent mycobacterium abscessus isolates to epetraborole and comparators by broth microdilution

Poster title: A phase 1, multicenter, open-label, parallel-group study to assess the safety and pharmacokinetics (PK) of oral epetraborole tablets in adult subjects with varying degrees of renal function

Poster title: A phase 1, open-label, single dose study to evaluate the pharmacokinetics (PK), safety, and tolerability of epetraborole tablets and the impact of alcohol dehydrogenase (ADH) genotype on the PK of epetraborole and metabolite M3 in healthy japanese adult subjects

Poster title: Epetraborole in vitro activity against Mycobacterium avium complex recent clinical isolates from Japan

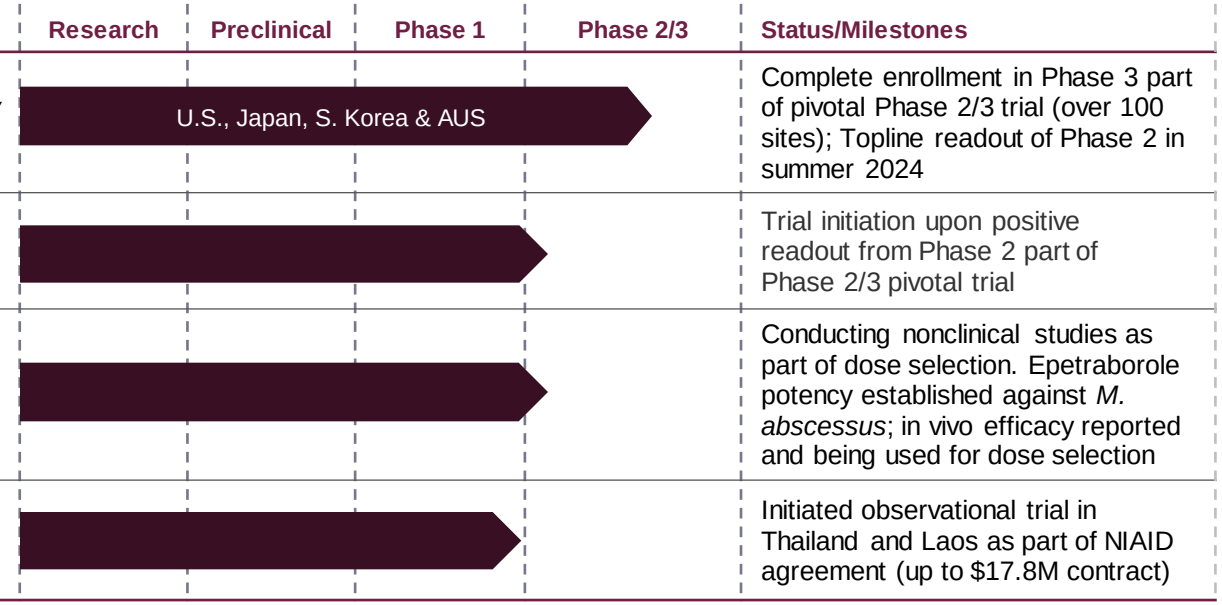
Pipeline targets high unmet needs in rare, chronic, and serious infectious diseases

Lead asset – epetraborole enrolling Phase 3 for TR MAC

Pipeline accelerates epetraborole's broader potential and taps into other high unmet needs

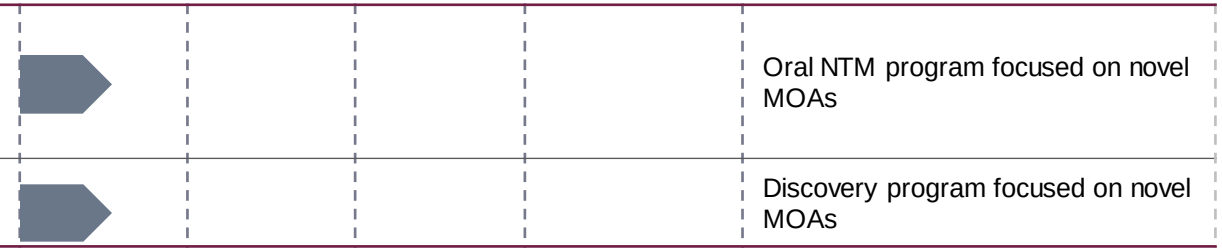
Boron chemistry approach enables targeting of novel biological targets

EPETRABOROLE



AN2-502998 (formerly AN15368)

Boron Chemistry Platform



* Global health programs

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NTM lung disease
a rare, chronic and progressive infectious disease

- **NTM is a group of >200 species of mycobacteria commonly found in water and soil; unlike tuberculosis, not transmitted person-to-person[1]**
- **Epetraborole is being developed for the most common type of NTM, *Mycobacterium avium* complex (MAC)**
  - MAC causes ~80%[2] of cases of NTM lung disease (complex currently includes 12 species, most common are *M. avium, M. intracellulare*, and *M. chimaera*)
- **Symptoms similar to those associated with other chronic respiratory diseases (e.g., cough, sputum production, fatigue)**
- **Causes chronic infection that progresses to fibrosis, permanent lung damage, and respiratory failure[1,2,3]**
  - 65+ age group most affected[4]
  - 5-year mortality rate between 10-48%[5]

1. Prevots DR, Marras TK. Epidemiology of human pulmonary infection with nontuberculous mycobacteria: a review. Clin Chest Med. 2015;36(1):13-34; www.bacterio.net/mycobacterium.
2. Nontuberculous Mycobacteria (NTM) Infections, Healthcare-Associated Infections, Centers for Disease Control webpage (last updated August 12, 2019).
3. Nontuberculous Mycobacteria Lung Disease, Rare Disease Database, National Organization for Rare Disorders webpage (last updated 2018).
4. Who Is At Risk? About NTM Fact Page, Insmed webpage.
5. Diel R, et al. High mortality in patients with Mycobacterium avium complex lung disease: a systematic review. BMC Infect Dis. 2018;18(1):206. Published 2018 May 3.

NTM lung disease underserved and growing market opportunity

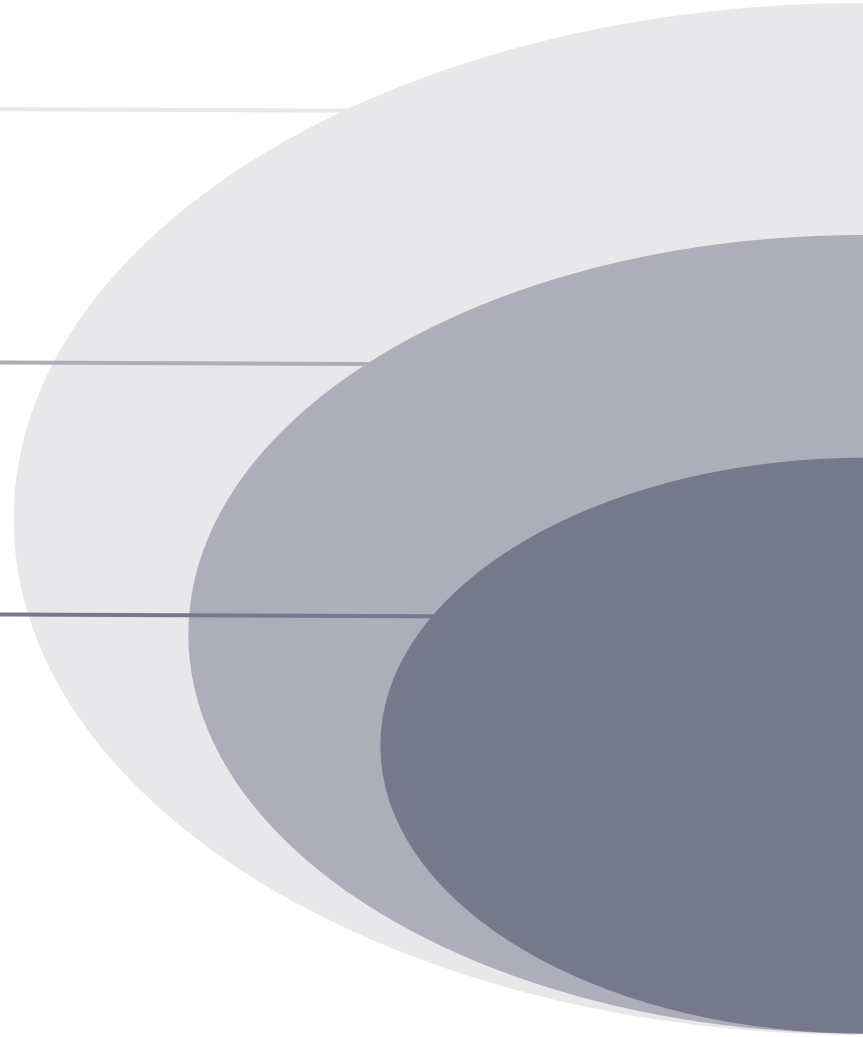
Initial indication targeting treatment-refractory MAC lung disease

~200,000 estimated patients with NTM lung disease in U.S.[1,2]

~55,000[1,2]
Diagnosed with NTM lung disease

~44,000[1]
Diagnosed with MAC lung disease

~15,000[1]
Diagnosed with treatment-refractory MAC lung disease*



**Treatment-refractory = Patients that remain culture positive despite ≥6 months of guideline-based antibiotic therapy*

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1. Internal analysis Q1'22, AN2 Therapeutics, Inc.
2. Strollo SE, et al. Ann Am Thorac Soc. 2015;12(10):1458-1464

Current treatment regimens for patients with NTM *Mycobacterium avium* complex (MAC) lung disease leave a significant unmet medical need

All NTM treatments, except Arikayce, are used off-label

Treatment-Naïve Patients

2020 ATS/ETS/ESCMID/IDSA Guidelines recommend triple oral combination therapy, 3 times weekly

Antimycobacterial agent	Efficacy	Safety Liabilities
Macrolide (e.g., azithromycin)	**~65% efficacy** based on culture conversion	QT prolongation, GI intolerability, increasing resistance
Ethambutol		Optic neuritis, liver tox, peripheral neuropathy
Rifamycin (e.g., rifampin)		Liver tox, drug-drug interactions

If NTM culture positive after 6 months of treatment

Treatment-Refractory Patients

Intensify guideline-based therapy (e.g., daily) and/or add new agents to combination

Antimycobacterial agent	Efficacy	Safety Liabilities
Amikacin liposome inhalation suspension (Arikayce)	**29% efficacy** based on culture conversion by month six (vs. 9% controls)	Respiratory toxicity, voice changes, ototoxicity
Unproven oral therapies • Clofazimine • Bedaquiline • Linezolid	N/A	• Many tolerability issues, including GI, QT prolongation, liver tox, drug-drug interactions, blue discoloration of skin • None FDA-approved

Duration of therapy is ≥ 12 months beyond culture conversion

Arikayce (Inhaled liposomal amikacin): first and only FDA-approved NTM lung disease drug

Arikayce is associated with a high discontinuation rate and increased adverse events versus SoC therapy alone

Arikayce Pivotal Study (CONVERT) Results

CONVERT Study Parameter	Arikayce	Control
Efficacy		
Culture-converted by month 6	**29%**	9%
Safety		
Withdrawn from study	**20%**	9%
Upper respiratory adverse events	**18%**	2%
Ototoxicity	**17%**	10%

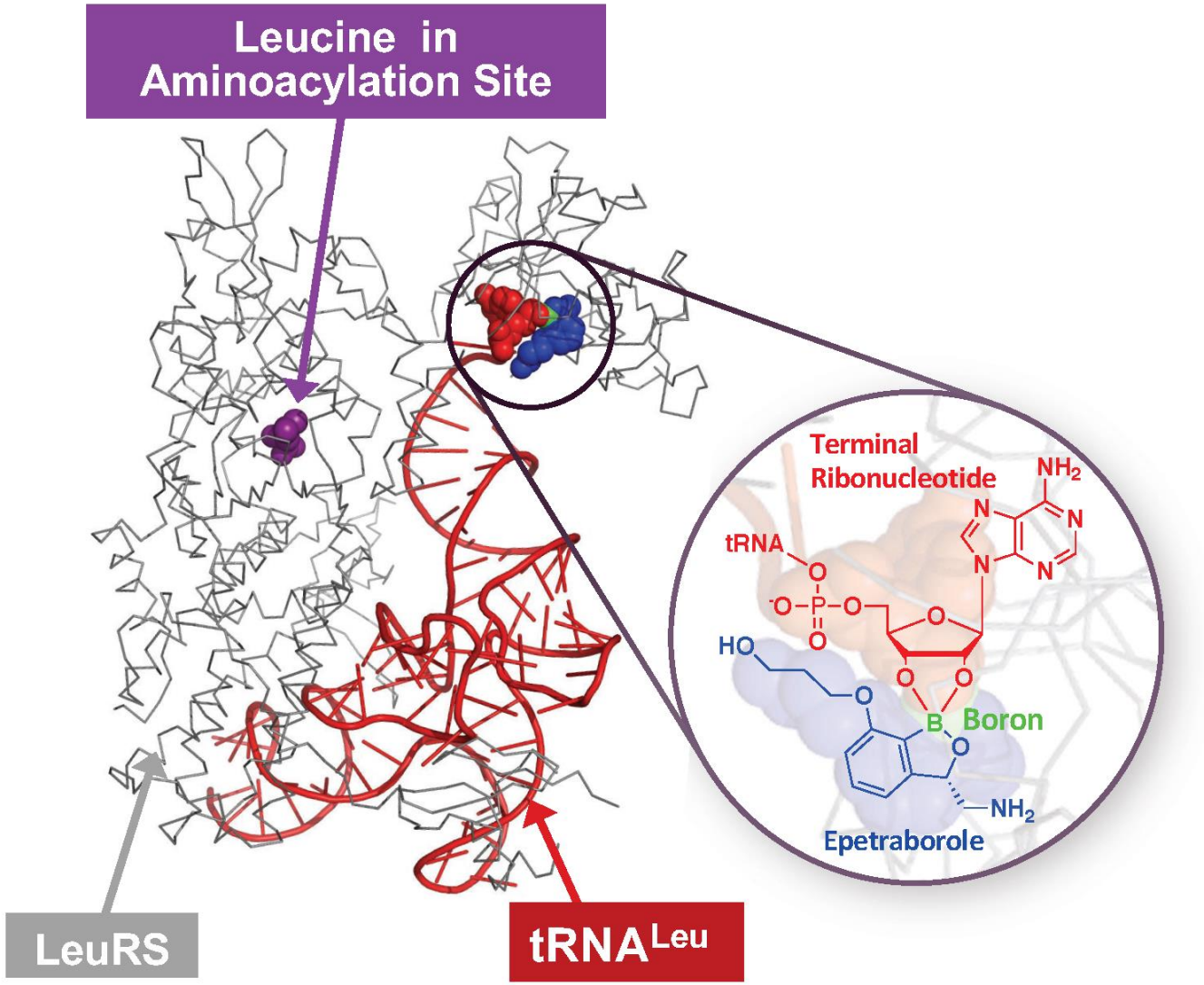
Arikayce Boxed Warnings

- Associated with an increased risk of respiratory conditions (hypersensitivity pneumonitis, bronchospasm, exacerbation of underlying lung disease and hemoptysis) that have led to hospitalizations in some cases

- Other common side effects: dysphonia, cough, ototoxicity, upper airway irritation, musculoskeletal pain, fatigue, diarrhea and nausea

Novel mechanism of action

EBO inhibits the protein synthesis enzyme leucyl-tRNA synthetase (LeuRS) by binding to the terminal adenosine ribose of $tRNA^{Leu}$ in the editing site



V. Hernandez et al. AAC (2013) 57: 1394

Broad antimicrobial activity

EBO in vitro antimicrobial activity against 161 clinical isolates of MAC from U.S. and Japan

	MIC (mg/L)		
	Epetraborole	**Clarithromycin**	**Amikacin***
MIC Range	0.25 - 16	0.125 - >64	2 - >64
MIC_{50}	2	1	16
MIC_{90}	4	4	32

- 98.8% of MAC isolates have EBO MIC ≤8 mg/L
- Antimicrobial activity of epetraborole, clarithromycin, and amikacin against 161 isolates of MAC including 73 *M. intracellulare* isolates, 75 *M. avium* isolates, 10 *M. chimaera* isolates, and 3 unspeciated *M. avium* complex isolates
- Clarithromycin is a generic macrolide antimicrobial used to treat patients with MAC lung disease and Arikayce is the only approved therapy for the treatment of MAC lung disease

EBO's novel MoA allows it to maintain activity against MAC isolates resistant to clarithromycin

MoA = Mechanism of Action

MIC = Minimum Inhibitory Concentration

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*Amikacin is the active component of Arikayce

IDWeek 2023: Poster title: Epetraborole In Vitro Activity Against Mycobacterium Avium Complex Recent Clinical Isolates from Japan

ID Week 2022: Poster Title: In Vitro Activities of Epetraborole, a Novel Bacterial Leucyl-tRNA Synthetase Inhibitor, Against *Mycobacterium avium* Complex Isolates

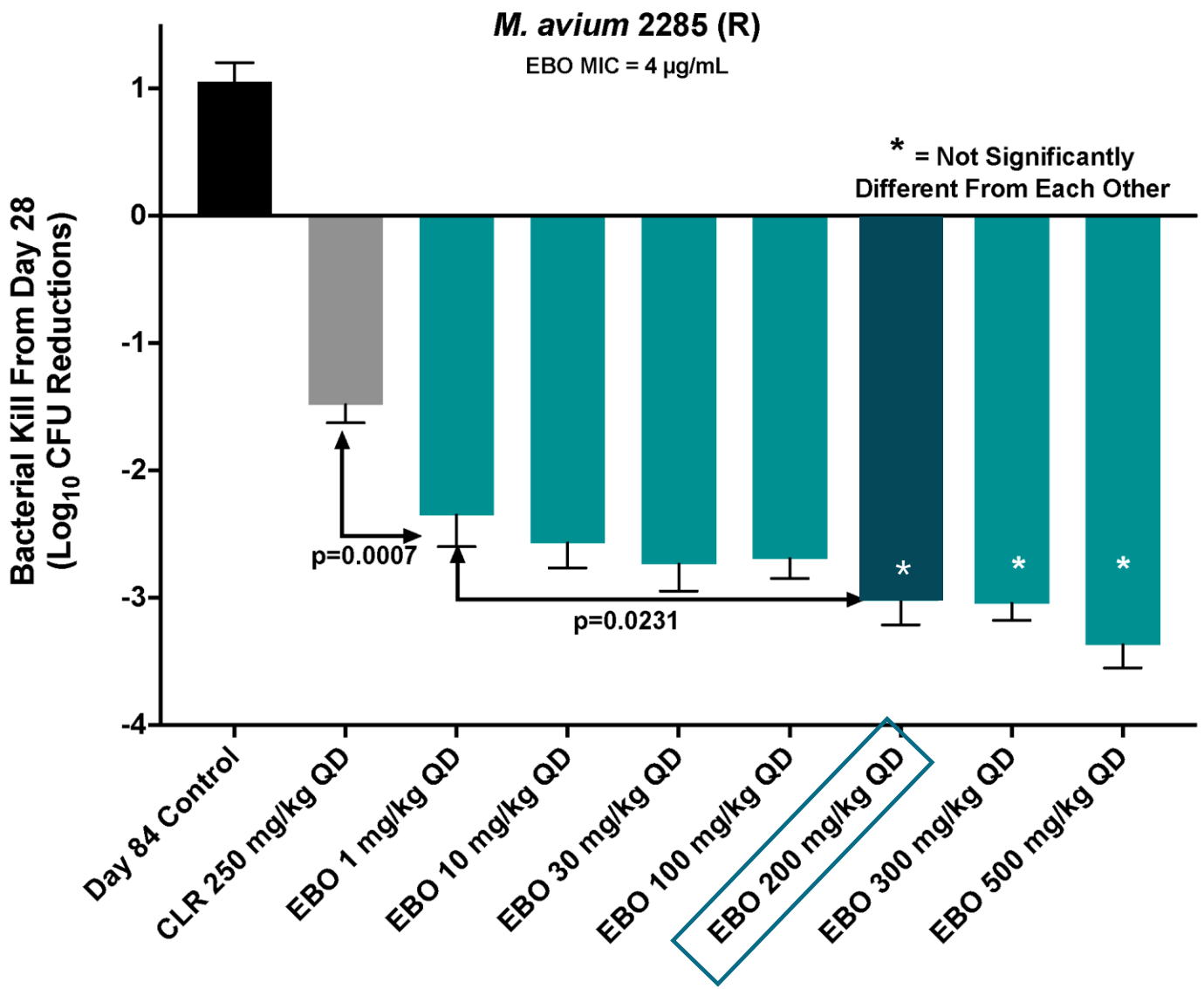
Epetraborole antibacterial activity in a chronic model of MAC lung disease in mice

Showed improved antibacterial activity of epetraborole at all doses compared to the daily humanized clarithromycin dose of 250 mg/kg

CFU = Colony Forming Units

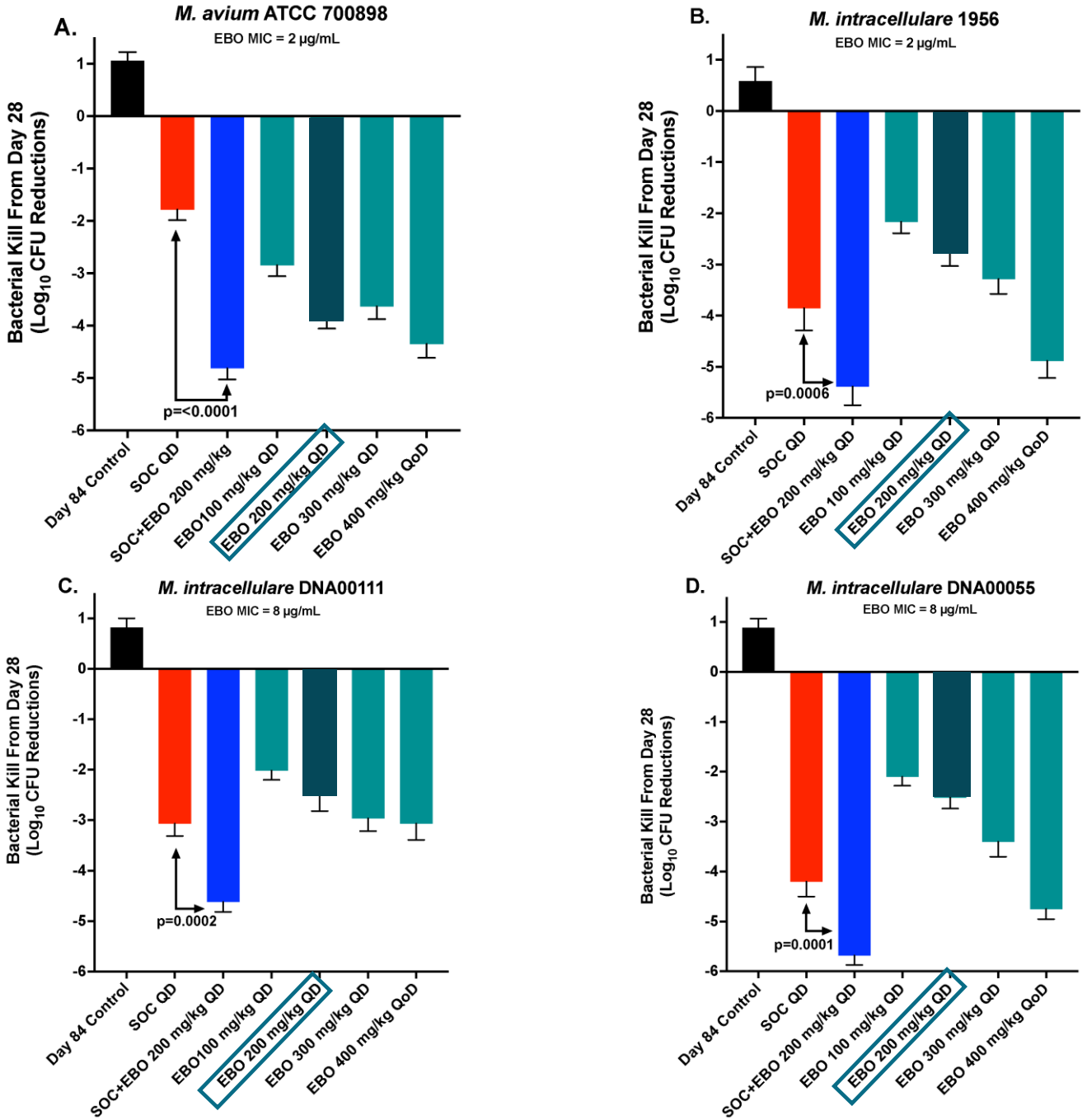
EBO=Epetraborole; CLR=Clarithromycin

Epetraborole (EBO) and Clarithromycin (CLR) antibacterial activity in a chronic model of MAC lung disease in mice against *M. avium* 2285 (R)



Epetraborole antibacterial activity in a chronic model of MAC lung disease in mice

Significant reductions in MAC CFU with EBO monotherapy; superior decreases with EBO + SoC regimen compared to SoC alone



CFU = Colony Forming Units

EBO=epetraborole

SOC=clarithromycin, ethambutol, rifabutin

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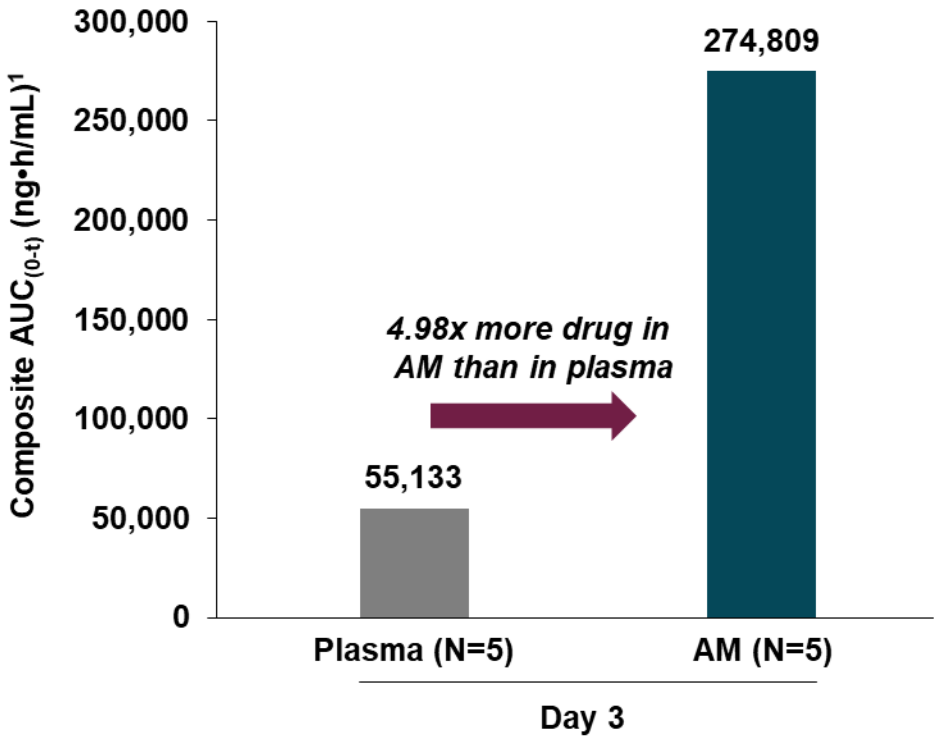
ID Week 2022: Poster Title: Epetraborole, a Novel Bacterial LeucyI-tRNA Synthetase Inhibitor, Demonstrates Potent Efficacy and Improves Efficacy of Standard of Care Regimen Against *Mycobacterium avium* complex in a Chronic Mouse Lung Infection Model

Favorable pharmacokinetics

Results from Phase 1 trial showed the concentration in lung macrophages (site of NTM infection) was 5x higher than in plasma



[1]AUC based on concentrations at 2,6, and 12-hour timepoints.
AM = alveolar macrophages

Results suggest therapeutically relevant doses of epetraborole may be achieved in macrophages at doses that are substantially lower than MTD in previous trials

MTD = Maximum Tolerated Dose

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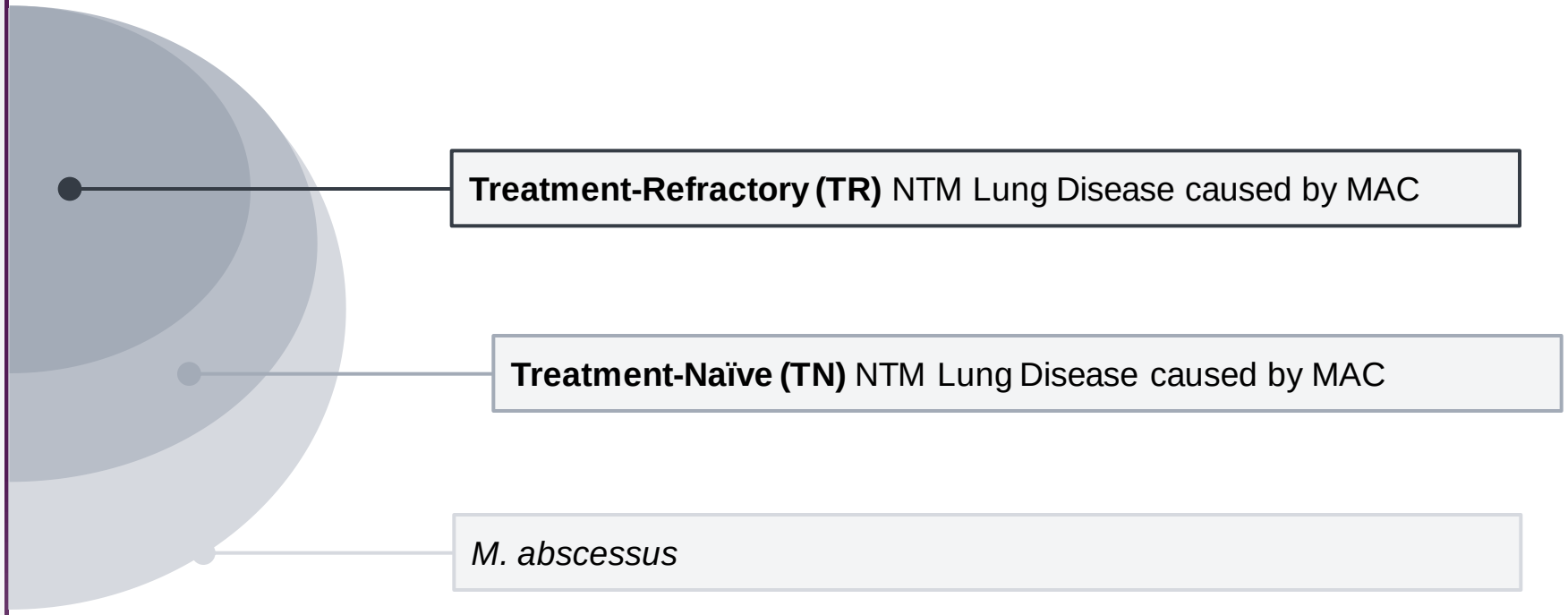
[1] Tenero *et al*. AAC 57:3334-3339 (2013)

Commercial strategy:

Establish treatment refractory market, rapidly expanding to treatment-naïve MAC and M. abscessus



- **TR MAC**
  - **Represents unmet medical need**
  - **Trial design and success precedented by two previous Insmed trials**
    - Both trials showed optimized background regiment (OBR) as 9% culture clearance and ability to be superior with add-on design
  - **TN MAC and *M. abscessus* also represent high unmet need indications that can follow after POC**

EBO-301: A Phase 2/3 pivotal clinical trial of epetraborole in treatment-refractory MAC lung disease

Phase 3 part underway

Phase 2 part fully enrolled

Over 100 Clinical Sites

Plan to use LPAD pathway in U.S.

Microbiological primary endpoint in Japan to support potential registration

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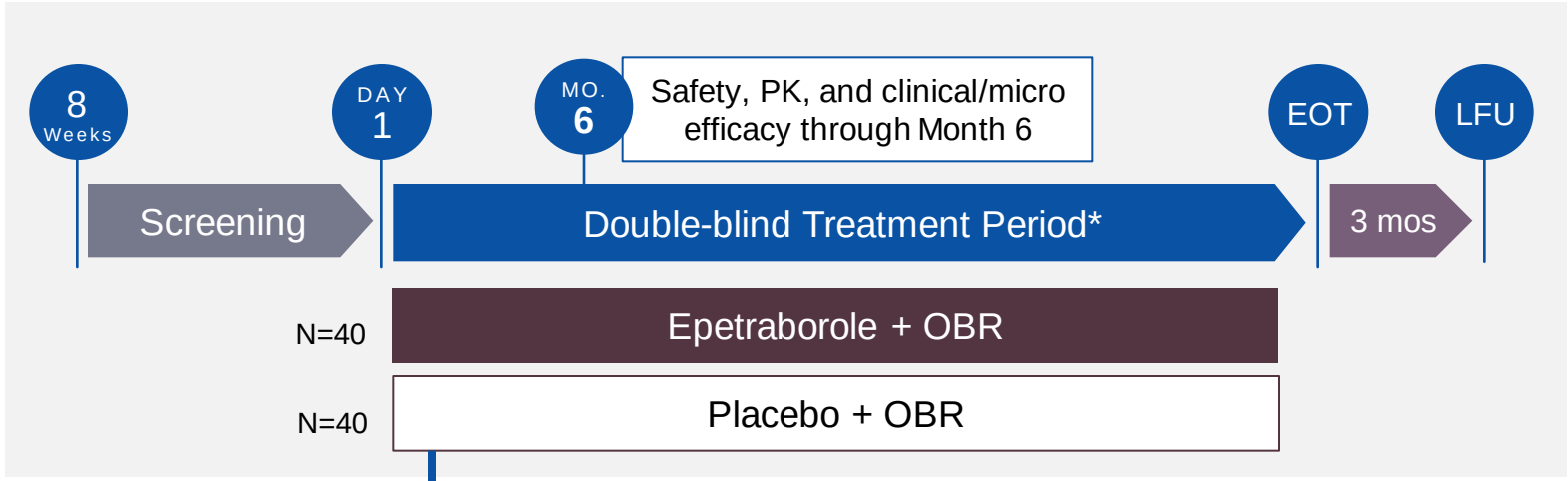
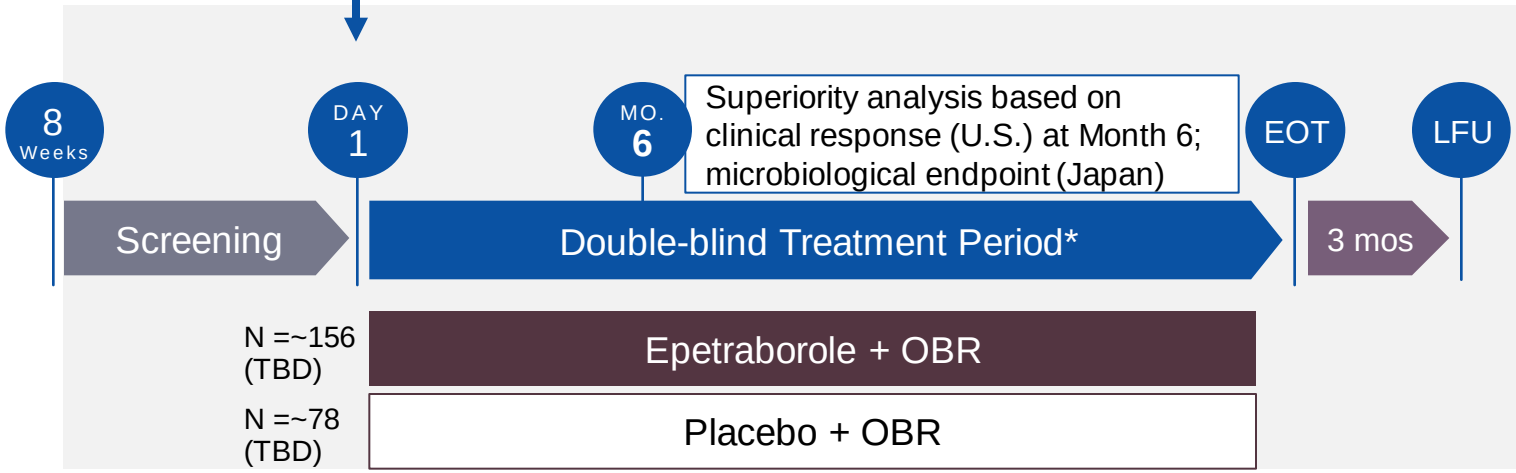
Phase 2 Part



Seamless enrollment,
No pause between Phase 2 and 3

Phase 3 Part

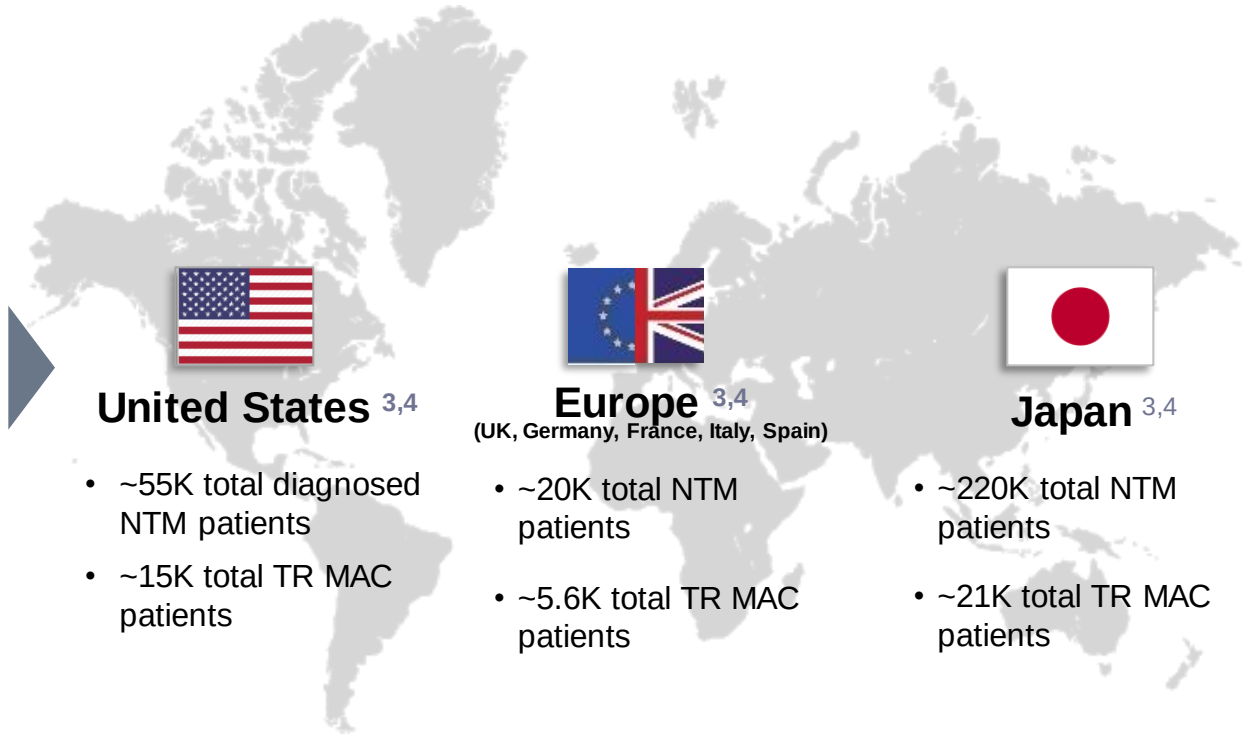


* Patients who culture convert will be treated for 12 months from 1st negative culture per treatment guidelines.
EOT = End-of-Therapy; LFU = Late Follow-up; LPAD = Limited population anti-infective drug pathway; OBR = Optimized Background Regimen; TBD = Final sample size to be confirmed based on Phase 2 Part data.

Significant market opportunity:

U.S. & Japan major markets

ARIKAYCE shows significant sales potential despite challenging profile



United States [3,4]

- ~55K total diagnosed NTM patients
- ~15K total TR MAC patients

Europe [3,4]
(UK, Germany, France, Italy, Spain)

- ~20K total NTM patients
- ~5.6K total TR MAC patients

Japan [3,4]

- ~220K total NTM patients
- ~21K total TR MAC patients

- **ARIKAYCE® 9-month 2023 WW net sales of $222M (+16%Y/Y)[1]**
  - **US $186M (full year 2022)[2]**
  - **Similar pricing in Europe and Japan**
- **Prevalence estimated to increase by ~8% per year in the U.S.**

1. Insmed 2023 10-Q
2. Insmed FY 2022 10-K
3. Internal analysis, AN2 Therapeutics, Inc.
4. Strollo SE, et al. Ann Am Thorac Soc. 2015;12(10):1458-1464

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Epetraborole

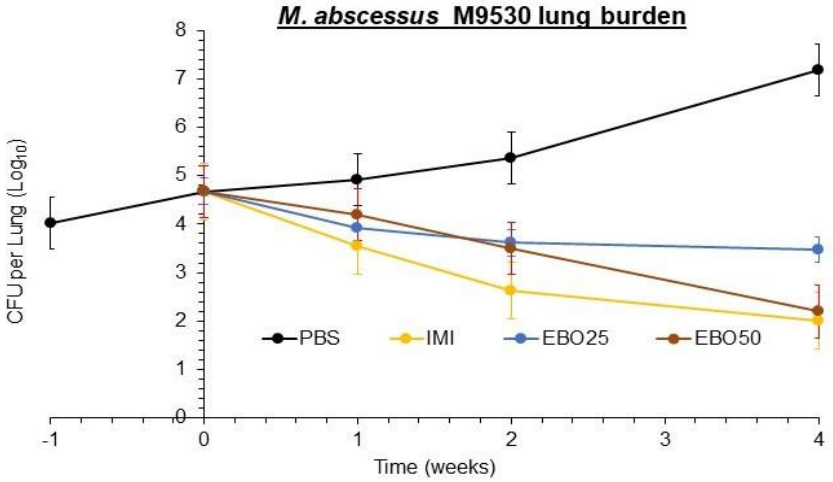
Potent In Vitro & In Vivo Activity vs. M. abscessus (Mab)

147 respiratory Mab isolates from U.S. & Europe

- **MIC range 0.03–0.25 µg/ml; MIC_{90} = 0.12 µg/ml**
- **Macrolide resistance, amikacin resistance, and morphology did not impact EBO activity**

Antimicrobial	MIC (µg/mL) MIC range	MIC_{50}	MIC_{90}
Epetraborole	**0.03 - 0.25**	**0.06**	**0.125**
Clarithromycin	≤0.25 - >32	>32	>32
Amikacin	4 - 64	16	64
Imipenem	≤1 - >32	8	32
Linezolid	≤0.5 - >16	16	>16
Moxifloxacin	≤0.5 - >4	4	>4
Cefoxitin	4 -128	32	64
Doxycycline	0.25 - >4	>4	>4
Tobramycin	4 - >8	>8	>8
Clofazimine	≤0.25 - 1	0.5	1
Minocycline	≤0.125 - >8	>8	>8
Tigecycline	0.25 -1	0.25	1
Rifabutin	0.5 - >4	>4	>4
Ethambutol	8 - >32	>32	>32

Similar CFU reductions vs. imipenem in a chronic model of Mab lung disease (immuno-compromised C3HeB/FeJ mice)



Unpublished data from Gyanu Lamichhane's Lab at Johns Hopkins University.

PBS = Phosphate-buffered saline (negative control);
IMI = Imipenem 100 mg/kg SC BID;
EBO25 = Epetraborole 25 mg/kg PO QD;
EBO50 = Epetraborole 50 mg/kg PO QD.

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CFU = Colony-forming units; Mab = *Mycobacterium abscessus*; MIC = Minimum inhibitory concentration.

Intellectual property:
≥12 years exclusivity

United States

- Composition of Matter (COM) patent expires June 2028
  - Without Hatch-Waxman extensions & pediatric exclusivity
- Up to 4-5 years of extensions
- Protection to ~**June 2033**

U.S. Regulatory Exclusivity:

- **12 years post-marketing**
  - Orphan Drug (7 years)
  - GAIN Act (QIDP) (5 years)

Europe

COM Patents Issued in 2014

- Europe provides 10 years of exclusivity from launch with centralized filing

Japan

- Similar mechanisms available in Japan

QIDP = Qualified Infectious Disease Product Designation

Attractive target product profile to address unmet needs in NTM with potential to become an important component of therapy

Planned Target Product Profile (TPP) Criteria[1]	EBO	ARIKAYCE®	SPR-720[2]	MNKD-101
Targeted for treatment refractory patients	✓	✓	X	✓
Broad-spectrum against mycobacterial isolates	✓	✓	✓	✓
Novel target with no observed cross-resistance	✓	X	✓	X
Oral route of administration	✓	X	✓	X
Potential for improved safety & tolerability for long duration	✓	X	?	?
Potential for predictable PK at site of infection	✓	X	X	X
Potential for reducing treatment duration	✓	✓	✓	✓

1. Wu ML, Aziz DB, Dartois V, Dick T. NTM drug discovery: status, gaps and the way forward. Drug Discovery Today. 2018;23(8):1502-1519
2. Spero Therapeutics
3. MannKind Corporation

TPP criteria and product profiles presented in this table are based on an in-house analysis of published data, drug product labeling, and have been combined from multiple sources presented in different studies. SPR-720 and MNKD-101 are product candidates in clinical development by third parties and are not approved therapies for patients.

Our global health commitment

AN2 Therapeutics

- AN2 leadership team is committed to applying our know-how to help solve some of the toughest infections in global health
- Intent is to fund these efforts primarily through non-dilutive funding from sources such as public and private agencies and foundations
- Current programs in melioidosis, malaria, tuberculosis and Chagas disease with the following partners

MORU Tropical Health Network
Bill & Melinda Gates foundation
Colorado State University
NIH National Institutes of Health
wellcome

Global health agreement partners:

NIH

Adjuvant Global Health Technology Fund
Adjuvant Capital

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