Forward-looking Statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, the design, initiation, timing and submission to the U.S. Food and Drug Administration (FDA) of a New Drug Application (NDA) for tebipenem HBr and the potential approval of tebipenem HBr by the FDA; future commercialization, the potential number of patients who could be treated by tebipenem HBr and market demand for tebipenem HBr generally; expected broad access across payer channels for tebipenem HBr; the expected pricing of tebipenem HBr and the anticipated shift from intravenous to oral administration; the initiation, timing, progress and results of the Company's preclinical studies and clinical trials and its research and development programs, including management’s assessment of such results; the direct and indirect impact of the pandemic caused by an outbreak of a new strain of coronavirus on the Company’s business and operations; the timing of the availability of data from the Company’s clinical trials; the timing of the Company’s filings with regulatory agencies; product candidate benefits; competitive position; business strategies; objectives of management; potential growth opportunities; potential market size; reimbursement matters; possible or assumed future results of operations; projected costs; and the Company’s cash forecast and the availability of additional non-dilutive funding from governmental agencies beyond any initially funded awards. In some cases, forward-looking statements can be identified by terms such as “may,” “will,” “should,” “expect,” “plan,” “aim,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. All statements other than statements of historical facts contained in this presentation are forward-looking statements. The Company may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: the Company's ability to timely complete related Phase 1 trials for its planned NDA submission for tebipenem HBr, taking into account the possible effects of the COVID-19 pandemic; the Company’s need for additional funding; the lengthy, expensive, and uncertain process of clinical drug development; the Company’s reliance on third parties to manufacture, develop, and commercialize its product candidates, if approved; the ability to develop and commercialize the Company’s product candidates, if approved; the potential impact of the COVID-19 pandemic; the Company’s ability to retain key personnel and to manage its growth; whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials and whether preliminary data from the Company’s clinical trials will be predictive of final results from such trials; whether the Company’s product candidates will advance through the preclinical development and clinical trial process on a timely basis, or at all, taking into account such factors as the effects of possible regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, clinical trial design, clinical data requirements and clinical outcomes; whether the results of such clinical trials will warrant submission for approval from the FDA or equivalent foreign regulatory agencies; decisions made by the FDA and equivalent foreign regulatory agencies with respect to the development and commercialization of the Company's product candidates; the commercial potential of the Company's product candidates; the Company's ability to obtain adequate third-party reimbursement for its product candidates; whether the Company will satisfy all of the pre-conditions to receipt of the development milestone payment under its agreement with Everest Medicines; whether BARDA elects to exercise its second option under the Company's agreement with BARDA; the Company’s ability to implement its strategic plans; the Company’s ability to obtain, maintain and enforce intellectual property and other proprietary rights for its product candidates; the risks and uncertainties related to market conditions; whether the Company’s cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; and other factors discussed in the “Risk Factors” section of the Company's periodic reports filed with the U.S. Securities and Exchange Commission (SEC), and risks described in other filings the Company may make with the SEC in the future. The forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company’s views as of any date subsequent to the date of this presentation.
Spero: Robust Infectious Disease and Rare Disease Portfolio led by Oral Tebipenem HBr

**Tebipenem HBr (previously SPR994): oral carbapenem**

ADAPT-PO Phase 3 met its primary endpoint in landmark trial – Oral tebipenem HBr demonstrated noninferiority to IV ertapenem in cUTI and AP; safety results similar to intravenous ertapenem

NDA submission planned for 2H21

**Pipeline of assets supported by positive Phase 1 data**

**SPR720:** First potential oral therapy for NTM infections; granted orphan designation; Data from Phase 2a trial in NTM-PD patients expected in 1H22

**SPR206:** Novel therapy for MDR Gram-negative infections; Phase 1 BAL study planned for 1H21

**Multi-billion dollar opportunity for cUTI and NTM**

Large unmet needs in infectious disease

No approved branded or generic oral competition within carbapenem class

Marketed primarily outside the hospital

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cUTI = complicated urinary tract infections; ancillary supportive studies also required for tebipenem HBr in addition to single Phase 3 trial;

NTM = non-tuberculous mycobacterial; PK = Pharmacokinetic; MDR = multidrug resistant infections; Tebipenem HBr = tebipenem pivoxil hydrobromide (formerly SPR994)
Leadership Team

**Ankit Mahadevia, MD**  | **Chief Executive Officer**
---|---
Prior Venture Partner at Atlas Venture; Arcion Therapeutics, Genentech, McKinsey
Formed eight companies in the life sciences sector; three as Acting CEO
Background in healthcare policy

**Cristina Larkin**  | **Chief Operating Officer**
---|---
Prior Vice President, Infection, Forest Laboratories
25+ years of commercial expertise with multiple antibiotic launches including Teflaro, Dalvance, Avycaz, Levaquin
Launched seven products across variety of therapeutic categories in retail and hospital

**David Melnick, MD**  | **Chief Medical Officer**
---|---
Prior Vice President Clinical Development for anti-infectives; Allergan, AstraZeneca
18 years in anti-infective drug development including 16 Phase 3 trials
Seven successful anti-infective drug approvals

**Tom Parr, PhD**  | **Chief Scientific Officer**
---|---
Prior CSO at Fedora Pharma and Targanta; Microcide, Head of Antibacterials, Eli Lilly
Worked on a broad range of antibiotic classes and marketed antibiotics (oritavancin, vancomycin, ceftazidime, daptomycin, cephalexin, cefaclor, loracarbef, anidulafungin)

**Timothy Keutzer**  | **Chief Development Officer**
---|---
Prior VP Program and Portfolio Management, Cubist
Extensive antibiotic development experience from pre-clinical to approval
Over 20 years in the pharmaceutical industry

**Sath Shukla**  | **Chief Financial Officer**
---|---
Prior CFO at Ziopharm Oncology; VP and Global Head of Finance at Vertex
Over 20 years of financial leadership, executing within commercial and clinical companies

**Tamara Joseph**  | **Chief Legal Officer**
---|---
Over 20 years of leadership and legal experience in the biotech sector
Prior General Counsel at several biotechnology companies including Millendo Therapeutics, Enzyvant Therapeutics, InVivo Therapeutics, and Cubist

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## Multiple Catalysts Across the Pipeline

**Positive Tebipenem HBr ADAPT-PO Phase 3 Topline Data Supports Expected NDA Submission in 2H21**

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Upcoming Milestone</th>
<th>Partnerships/Alliances</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Carbapenem for Gram Negative Multidrug Resistant (MDR) Infections</strong></td>
<td>Tebipenem HBr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NDA submission for the treatment of cUTI planned for 2H21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Complicated UTI (cUTI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral DNA Replication Inhibitor for Non-tuberculous Mycobacterial (NTM) Disease</strong></td>
<td>SPR720</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Data from Phase 2a trial in NTM-PD patients expected in 1H22</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NTM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Direct Acting IV Potentiator for Gram Negative MDR Infections</strong></td>
<td>SPR206</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1 BAL study planned for 1H21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MDR Infections</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

As of January 6, 2021
Spero Pipeline Assets Share Common Attributes With Other Successful ID Drugs

High unmet need with strong economic benefit

$1 B+ Sales*

Non-DRG reimbursement

*Estimated Peak Year Worldwide Sales
*Trademarks are properties of their respective owners
Oral Carbapenem
Tebipenem HBr
Tebipenem HBr: Positive ADAPT-PO Phase 3 Trial Results

Robust Results Support NDA Submission and Potential Treatment Shift from IV to Oral in cUTI

**Landmark ADAPT-PO Trial Met Primary Endpoint**
- Positive results in landmark study unprecedented for the field
- Overall combined response rate: Oral tebipenem HBr response rate of 58.8% versus 61.6% for IV ertapenem (-3.3%; -9.7, 3.2; -12.5% NI margin)*
- Tebipenem HBr safety results similar to ertapenem

**Potential to Transform How cUTI Patients are Treated**
- Tebipenem HBr, if approved as the first oral carbapenem, could allow appropriate patients the opportunity to receive treatment in the community setting
- Provides an important value proposition that could benefit patients, hospitals and payers

**Positive ADAPT-PO Trial Results Support an NDA Submission in 2H21**
- One well-controlled pivotal trial to form the basis for an NDA submission as per FDA interactions
- Expect completion of a new drug application (NDA) submission to the FDA in the second half of 2021

If approved, tebipenem HBr would be the only oral carbapenem approved for treatment of complicated urinary tract infections (cUTI) and acute pyelonephritis (AP)

NI, non-inferiority; NDA, new drug application
* The trial at 95% confidence interval (CI) achieved success (a -9.7 NI margin) within the original -10% NI margin
Pivotal Phase 3 Trial Design: Evaluation of Oral Tebipenem HBr compared to IV Ertapenem

Innovative Trial Design Compares an Oral-Only Regimen Directly Against an IV Regimen for cUTI and Acute Pyelonephritis (AP)

**Randomization**
- Adult patients ≥18 years

**Screening**
- All Oral Tebipenem HBr 685 patients
- All IV Ertapenem 687 patients

**Head-to-Head Comparison: Oral vs. IV†**
- Duration of therapy 7-10 days
- Oral Only Tebipenem HBr (600mg q8h)
- IV Only Ertapenem (1g q24h)

**Primary Endpoint**
- Overall Response‡ rate at TOC in micro-ITT population (17-21 days after first dose of study drug)

†Showing active treatment arms only; study is placebo-controlled double-blind, double-dummy
‡ Combined Clinical Cure and Microbiological Eradication
Additional evaluation at LFU (23-27 days after first dose of study drug)
Non-inferiority margin of -12.5%
Masked individual and composite PK data reviewed by an independent review committee after enrolling the first 70 patients to confirm dose

cUTI, complicated urinary tract infection; ITT, intent-to-treat; IV, intravenous; LFU, long-term follow-up; q24h, every 24 hours; TID, three times daily; TOC, test-of-cure
ADAPT-PO Met Its Primary Efficacy Endpoint
Tebipenem HBr Demonstrated Statistical Non-inferiority Compared to Ertapenem

ADAPT-PO primary endpoint:
Clinical cure + microbiological eradication at test-of-cure in micro-ITT population

<table>
<thead>
<tr>
<th>Endpoint (micro-ITT Population)</th>
<th>TBP-PI-HBr N = 449</th>
<th>Ertapenem N = 419</th>
<th>Treatment Difference (%) (TBP-PI-HBr minus ERT, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response at TOC (%/n)</td>
<td>58.8% 264</td>
<td>61.6% 258</td>
<td>-3.30 (-9.7, 3.2)</td>
</tr>
</tbody>
</table>

Micro-ITT = microbiologically modified intent-to-treat; TOC = test of cure.

Demonstrated non-inferiority at margin of -12.5%*
Results were similar between treatment arms across all subgroups of patients

* The trial at 95% confidence interval (CI) achieved success (a -9.7 NI margin) within the original -10% NI margin
TBP-PI-HBr, tebipenem HBr; ERT, ertapenem
ADAPT-PO Key Secondary Endpoints Evaluating Patient Outcomes

Clinical cure rate is a key determinant in routine clinical management of cUTI patients

Clinical cure rates at test-of cure (TOC) for micro-ITT groups comparable between the oral tebipenem HBr and IV ertapenem treatment arms

Durable clinical response observed with high clinical cure rates at TOC sustained through late follow-up visit

Median duration of therapy was similar for both treatment groups

![Comparable Clinical Cure Rates at TOC](image)
ADAPT-PO Safety and Tolerability Results

Safety and tolerability profiles similar across the oral tebipenem HBr and IV ertapenem arms

<table>
<thead>
<tr>
<th></th>
<th>Oral Tebipenem HBr</th>
<th>IV Ertapenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with at least one TEAE</td>
<td>25.7%</td>
<td>25.6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5.7%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Headache</td>
<td>3.8%</td>
<td>3.8%</td>
</tr>
<tr>
<td>ALT increase</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>AST increase</td>
<td>1.0%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Serious TEAEs</td>
<td>1.3%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Drug-related SAEs</td>
<td>0.0%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

- TEAE rates generally consistent with that of the carbapenem/beta-lactam class
- Diarrhea and headache were the most commonly reported TEAEs in both treatment groups
- No *C. difficile* infections in tebipenem HBr arm
- No deaths reported
**ADAPT-PO: Landmark Trial with Potential to Change Clinical Practice**

- **Landmark trial demonstrating value of all oral regimen**
  - First all oral regimen for cUTI in 26 years, if approved

- **Non-inferior efficacy to IV ertapenem**
  - Met primary endpoint of combined clinical cure and microbiological response at TOC

- **Safety results similar to IV ertapenem**
  - No drug related SAEs for tebipenem HBr; comparable GI TEAE rates

**Head-to-head results support regulatory submission of tebipenem HBr for the treatment of cUTI/AP**
Lack of Oral Options for cUTI is Widespread, Costly, and Addressable

If approved, tebipenem HBr could help shift care back to outpatient setting: Helping patients to **Go Home or Stay Home**

### Growing Fluoroquinolone Resistance

<table>
<thead>
<tr>
<th></th>
<th>Hospital</th>
<th>Community</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2004</td>
<td>3.5%</td>
<td>0%</td>
</tr>
<tr>
<td>2019</td>
<td>30.8%</td>
<td>21.2%</td>
</tr>
</tbody>
</table>

### Major Unnecessary Cost

- 76% Increase in hospitalizations
- +2 Days Longer Stays in Hospital

Resistance + No Viable Oral cUTI Option = 2.3M Potentially Avoidable Hospitalizations

Tebipenem HBr has the Potential to be a Highly Differentiated Therapy if Approved

- No branded or generic oral substitutes in the carbapenem class
- Existing, large, and growing unmet need
- Primary reimbursement outside of the hospital
- Current practice and financial incentives support usage
- Prescriber base beyond infectious disease specialists
Tebipenem HBr Developed to Address a Large and Existing UTI Population

**Stay Home: Hospital Avoidance**

*Katrina,* college student at the University of Kansas, experienced “a U.T.I. that did not respond to three different rounds of antibiotics.” “It got so bad that I was out of school for months and had to get a medical withdrawal,” she said.

**Go Home: Get Home Sooner From Hospital**

“Theodore, a medical student, was hospitalized with E. coli that was highly resistant to a wide variety of antibiotics. His discharge was delayed because the resistant nature of the bacteria would require insurance approval of home IV antibiotics.”

**Treatment currently includes:**
- Evaluation for systemic involvement requiring hospitalization
- Referral to urologist to evaluate structure abnormalities
- Cycling through available oral antibiotics to avoid hospital admittance

**Treatment currently includes:**
- Full course of IV antibiotics within the hospital
  OR
- Transition from hospital to outpatient IV antibiotic therapy and monitor for complications

Sources: NYT Aug 20, 2019; IDSA Faces of Antimicrobial Resistance
OPAT: Outpatient parenteral antimicrobial therapy
Carbapenem Market Estimated at $3B in United States Alone*

Carbapenem use in UTI and in outpatient setting has increased significantly

![Carbapenem DOT 2011-2017](chart1.png)

*9M DOT x $350/day = $3 billion

Source: IQVIA NDS Database, Accessed 11/06/2018; AMR data on use by indication; 2017 UTI data projected

Outpatient calculated as volume in "Clinics" and "Home Health and Long Term Care" channels

*Analysis excludes Meropenem – price, dosing regimen and stability data do not make it a widely used outpatient option
Large Market Opportunity for Patients Able to Be Treated at Home

Targeted patients often cycle through multiple therapies

Lack of effective oral treatment options has resulted in increased...
• Outpatient visits
• Emergency department visits
• Unwarranted outpatient IV use
• Unnecessary hospitalizations
• Hospital days
• Home Health and LTC stays post-hospitalization

7.9 M UTI Patients in the US

5.2 M
1st line Oral

1.6 M
2nd line Oral
(Resistant/Failed)

1.1 M
IV Therapy/3rd+
line Oral
(Resistant/Failed)

1.9 M
>2nd line Oral
(Resistant/Failed)

780 K
IV Carbapenem
Pip/tazo

Spero Focus
2.7M UTI prescriptions 2nd line+ Oral or IV therapy

Source: IQVIA 2019; Komodo 2020 data; Becton Dickinson Market Research, 2020
Pip/tazo = Piperacillin and tazobactam
Targeted Launch Based on Concentrated Prescribers and Focus on Urology

Initial sales team focused on high volume retail practices and hospitals

Source: IQVIA 2019; 1.35 = 50% of volume (deciles 6-10) from IQVIA 2019; Komodo 2020 data; Becton Dickinson Market Research, 2020

Pip/tazo = Piperacillin and tazobactam

Spero will implement staged ~100-125 FTE field force by further segmenting for:
- Resistance (zip code level data)
- Favorable payer mix
- Adoption readiness, e.g. use of carbapenems

Spero Focus
50% patients in high-decile accounts
Highly concentrated opportunity in both retail (4,000 accounts) and hospital (1,000 accounts)

Urologists:
Largest treaters for 2nd line UTI patients across retail and hospital outlets

7.9 M UTI Patients in the US

- 5.2 M 1st line Oral
- 1.6 M 2nd line Oral (Resistant/Failed)
- 1.1 M IV Therapy/3rd+ line Oral (Resistant/Failed)
- 1.9 M >2nd line Oral (Resistant/Failed)
- 780 K IV Carbapenem Pip/tazo

1.5 M 2nd line Oral
(Resistant/failed)

1.1 M IV Therapy/3rd+ line Oral
(Resistant/Failed)
Unmet Need Identified by Healthcare Providers; Expect Broad Access Across Payer Channels

Interactions with 100+ Health Care Professionals and 150M Payer Lives

There is high agreement that relapsed, failed cUTI patients could be treated at home

HCPs identify carbapenems as a preferred drug class for our target patients

HCPs and Payers see potential value of tebipenem HBr

If approved, payers expect to broadly cover tebipenem HBr due to unmet need for new oral therapy

“We need more drugs for UTI beyond Macrobid for lower UTI, Keflex and Cipro. There is a lot of resistance to FQ, so if we want an oral, we need something new.” - Urologist

“Switching to PO would be far preferable to a PICC and Home Health or having them return to an infusion center...” - KOL

“We don’t have any oral carbapenems now to send them home. This would shorten length of stay markedly and it covers ESBLs for hospital and community!” – Hospitalist

“The value proposition here is that you can avoid using the IV which I think certainly has some clinical benefit and may be even some economic benefit as well.” - National Payer

Source:: IQVIA 2019; Precision Payer Landscape Research 2020; Key Opinion Leader Interviews, 2020
Tebipenem HBr Well Positioned to Recognize Significant Market Opportunity Upon Approval

- **Value-Based Pricing**
  Consistent with other unmet need antibiotics

- **Anticipated Favorable Payer Coverage**
  Primarily reimbursed as a pharmacy benefit and not under hospital DRG

- **Largest Unmet Need in Infection Today**
  2.7 Million resistant or failed cUTIs

- **Targeted Commercial Footprint**
  Urology is primary treater for relapsed, refractory or failed cUTI patients in the community or hospital

- **Robust IP**
  Coverage through 2038; Granted QIDP and Fast Track designation

- **Commercial Support**
  Tebipenem HBr for the treatment of cUTI

- **Lack of Competition**
  No branded or generic oral substitutes approved or in late-stage development

- **Commercial Support**
  Tebipenem HBr for the treatment of cUTI

- **Robust IP**
  Coverage through 2038; Granted QIDP and Fast Track designation

- **Value-Based Pricing**
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- **Anticipated Favorable Payer Coverage**
  Primarily reimbursed as a pharmacy benefit and not under hospital DRG

- **Largest Unmet Need in Infection Today**
  2.7 Million resistant or failed cUTIs
Zyvox $1.4 B Peak Year “Go-Home/Stay Home” Analogue for Tebipenem HBr Launch

### Zyvox Launch Curve-Time to Peak
5 Years to Peak

<table>
<thead>
<tr>
<th>Quarters Since Launch</th>
<th>Linezolid: Retail</th>
<th>Linezolid: Non-retail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q9</td>
<td></td>
<td></td>
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<tr>
<td>Q13</td>
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<tr>
<td>Q17</td>
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<tr>
<td>Q21</td>
<td></td>
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<tr>
<td>Q25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q29</td>
<td></td>
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</tbody>
</table>

Retail reaches peak share by Q20

### Market Size

<table>
<thead>
<tr>
<th>Mkt size (pts)</th>
<th>Zyvox MRSA Gram-positive Market</th>
<th>Tebipenem HBr FQ-R Gram-negative Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8 M</td>
<td>2.2 M</td>
<td></td>
</tr>
</tbody>
</table>

### Resistance to Oral Options

<table>
<thead>
<tr>
<th>Resistance to oral options at launch</th>
<th>Zyvox</th>
<th>Tebipenem HBr</th>
</tr>
</thead>
<tbody>
<tr>
<td>29%</td>
<td>36%</td>
<td></td>
</tr>
</tbody>
</table>

### Reimbursement Landscape

<table>
<thead>
<tr>
<th>Reimbursement landscape</th>
<th>Zyvox</th>
<th>Tebipenem HBr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restricted</td>
<td></td>
<td>Restricted</td>
</tr>
</tbody>
</table>

### Pricing Model

<table>
<thead>
<tr>
<th>Pricing model</th>
<th>Zyvox</th>
<th>Tebipenem HBr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premium</td>
<td></td>
<td>Premium</td>
</tr>
</tbody>
</table>

*Estimated for tebipenem HBr column based on 5.5% growth rate

Next Steps for Tebipenem HBr

- **Complete NDA package** - Meeting with FDA and finalizing Phase 1 trials
- **Exploring lifecycle management opportunities** – Microbiological surveillance and clinical studies
- **Manufacturing readiness** – Process validation and launch planning
- **Launch readiness** – Market development work, pricing research, distribution strategy, key hires
Rare Disease Pipeline
SPR720
Severe cough
“It [coughing] could go on for a good 90 minutes, and I'm just down on the floor, on my knees, grabbing my ribs, hacking.”

Fatigue
“I've been in the grocery store with the shopping cart, but I didn't have the energy to wait in line to check out.”

Dyspnea
Limits the types of activities that people are able to do, including walking, shopping, or traveling.

Non-tuberculous mycobacterial disease (NTM) causes chronic and serious lung disease with debilitating symptoms that leads to a decline in lung function. It can have a significant physical and emotional impact on patients.

SPR720 has orphan drug designation and could be the first and only oral treatment for NTM.

## Current Therapies for NTM Have Limitations

<table>
<thead>
<tr>
<th></th>
<th>Arikayce® (Approved Inhaled Therapy)</th>
<th>Generic Standard of Care</th>
<th>SPR720 (Oral Product Candidate)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tolerability</strong></td>
<td>Poor</td>
<td>Poor</td>
<td>Tolerability in Phase 1 supports advancing 1000 QD dose</td>
</tr>
<tr>
<td><strong>Proven Activity in Naïve and Newly Treated Patients</strong></td>
<td>No</td>
<td>Limited</td>
<td>Will assess in ongoing Phase 2a trial</td>
</tr>
<tr>
<td><strong>Oral Therapy</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Better options are needed for the more than 75% of non-refractory patients without approved therapies

QD = Daily; *Trademarks are properties of their respective owners
SPR720: First Novel Oral Candidate Designed to Treat NTM Infections

**Broad spectrum, oral candidate: applicable to both non-refractory and refractory patients**

More than 75% of NTM patients are non-refractory; lack any approved options to treat NTM

**Planned once daily dose supported by clinical and non-clinical studies**

Selected 500 - 1000mg once daily dose range for Phase 2 supported by concordant in vivo and in vitro PK/PD models

BAL study in non-human primates supports lung exposure; macrophage data shows intracellular and extracellular activity

**Safety/tolerability data**

Data at 500 - 1000mg once daily in Phase 1 SAD/MAD studies supportive of advancement to Phase 2 clinical studies
### SPR720 Patient Focus

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Treatment Inexperienced</th>
<th>Refractory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial hygiene/ clearance, exercise, education</td>
<td>No specific NTM treatments approved; SOC consists of poorly tolerated antibiotic regimens</td>
<td>Inhaled Arikayce® approved for NTM</td>
</tr>
<tr>
<td><strong>Colonization</strong></td>
<td><strong>Inflammatory disease (tissue burden drives inflammatory response)</strong></td>
<td><strong>Anatomical disease (fixed lung injury)</strong></td>
</tr>
<tr>
<td></td>
<td>Delay treatment due to:</td>
<td>Treatment benefits limited by:</td>
</tr>
<tr>
<td></td>
<td>▪ Intolerability</td>
<td>▪ Declining lung function</td>
</tr>
<tr>
<td></td>
<td>▪ Inconvenience</td>
<td>▪ Additional co-morbidities</td>
</tr>
<tr>
<td></td>
<td>▪ Ineffectiveness</td>
<td></td>
</tr>
</tbody>
</table>

**SPR720 target population**
SPR720 Development Plan Overview

FDA meeting supportive of stepwise development plan

- Acknowledged Phase 2a trial including the clinical trial endpoints and duration of therapy as an appropriate next development step
- Longer-term development of SPR720 as part of a combination regimen will incorporate patient reported outcomes

**In vitro and in vivo studies**
- Demonstrated activity, tissue penetration

**PD modeling**
- Identified predicted therapeutic exposure range

**Safety pharmacology, preclinical toxicology**
- Safety supportive of selected dose range

**SAD/MAD Phase 1**
- 500mg - 1000mg QD supports Phase 2 development

**Phase 2a monotherapy trial in NTM patients**
- PK, safety, tolerability and microbiology over 28 days

**Phase 2b/3 combination trial in NTM patients**
- Evaluating efficacy, safety, tolerability over longer duration
Phase 2a Clinical Trial: Early and Robust Clinical Proof of Concept

### Phase 2a Trial in NTM

If trial results are positive, SPR720 would be the only agent shown to drive early microbiological response as a stand-alone agent versus placebo.

<table>
<thead>
<tr>
<th>Treatment Population</th>
<th>Treatment Arms</th>
<th>Objectives</th>
</tr>
</thead>
</table>
| Treatment inexperienced patients | Placebo  
SPR720 – 500mg  
SPR720 – 1000mg  
Standard of Care | Over 28 Days Evaluate:  
Safety  
Tolerability  
Plasma PK  
Microbiological response |

Next Steps for the Development Plan

Data from Phase 2a trial expected in 1H22
Phase 1 SAD/MAD Data Supports Advancement to Phase 2 Trial

Data indicates therapeutic exposure can be attained with dose associated with low incidence of adverse events (500 – 1000mg once daily)

### Single Ascending Dose Cohorts (N = 56)
- No SAEs reported; Mild GI symptoms at >1500mg

### Multiple Ascending Dose Cohorts (N = 40)
- PK analysis shows dose dependent increase in plasma exposure
- No clinically significant differences in safety or PK between healthy elderly and healthy non-elderly subjects
- 500mg and 1000mg doses evaluated over 7- and 14-day dose ranges
  - No SAEs reported; Most common AE among all cohorts was mild diarrhea not requiring discontinuation of therapy
  - No clinically significant lab findings: ALT levels >1.5x ULN noted in 3 subjects; maximum values <3x ULN and rapidly reversible. No Hy’s law cases
- One discontinuation in 1500mg dose cohort: pancreatic enzyme elevation that was asymptomatic, monitorable and reversible

Notes: Patients randomized 3:1 to SPR720 or Placebo
Once Daily Phase 2 Treatment Dose is Supported by Several Models

SPR720 500mg – 1000mg QD dose range supported by:

| **In vitro models** | • Inhibitory concentrations (MIC90) <4mg/mL for clinically relevant NTM strains. Favorable to amikacin |
| **In vivo models** | • Activity comparable to amikacin and clarithromycin in murine NTM infection models  
  • Additive effect in combination regimens |
| **Hollow fiber *M. avium* infection model** | • Dose-related bactericidal activity comparable to clarithromycin  
  • PD driver AUC/MIC with suppression of resistance at attainable plasma exposure |
SPR720 Demonstrated Dose Response
Lung Infections in Multidrug Resistant *M. abscessus* Strains in Murine Models

Multidrug resistant *M. abscessus* strain infection set for 27 days, dosing in SCID mice days 27 to 61. AMK=Amikacin SQ dosed every 24h. SPR720 dosed every 48h at the doses listed above
Direct Acting IV
Potentiator:
SPR206
SPR206 Phase 1 Data and Preclinical Potency Against XDR Gram-Negative Pathogens Support Advancement

Phase 1 SAD/MAD Preliminary Data (N = 96)

- Successful Phase 1 doses likely to be within a therapeutic range for MDR Gram-negative bacterial infections
- Mean plasma drug exposures concordant with models predictive for clinical efficacy against target Gram-negative pathogens

Preclinical Data Supports Increased Efficacy Beyond Traditional Antibiotics

![Graphs showing % isolates inhibited for MDR A. baumannii, MDR P. aeruginosa, and MDR K. pneumoniae against MIC values for SPR206, Meropenem, and Amikacin]
Financial Overview

$ in 000’s

### Income Statement

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Revenue</td>
<td>$3,995</td>
<td>$7,423</td>
</tr>
<tr>
<td>R&amp;D Expense</td>
<td>$17,706</td>
<td>$53,798</td>
</tr>
<tr>
<td>G&amp;A Expense</td>
<td>$5,309</td>
<td>$13,942</td>
</tr>
<tr>
<td>Loss from Operations</td>
<td>$(19,020)</td>
<td>$(60,317)</td>
</tr>
<tr>
<td>Net Loss Attributable to Common Stockholders</td>
<td>$(18,936)</td>
<td>$(60,244)</td>
</tr>
</tbody>
</table>

### Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>As of September 30, 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, Cash Equivalents and Marketable Securities</td>
<td>$127,244</td>
</tr>
</tbody>
</table>

- Funded into the second quarter of 2022, through the NDA submission for tebipenem HBr
- BARDA/DTRA non-dilutive funding award for tebipenem HBr up to $56.7M; additional awards and alliances provide funding for pipeline
Key Investment Highlights

- Experienced management team
- Accelerated path to market
- Significant near-term catalysts
- Pipeline products with a solid value proposition
- Multiple drugs in clinical development
- Large and existing market opportunities