Non-Confidential Information Presentation

September 2021

Oral and IV treatment for serious bacterial infections

Forward-looking Statements & Disclaimer

This Confidential Overview (this "Overview") contains forward-looking statements. These forward-looking statements include, without limitation, statements regarding the development, therapeutic and market potential of sulopenem, the granting or issuing of patents, the timing, progress and results of clinical trials, the expected timing of filings and the Company's plans, strategies and prospects for its business. In some cases, forward-looking statements can be identified by words such as "may," "believes," "intends," "seeks," "anticipates," "plans," "estimates," "expects," "should," "assumes," "continues," "could," "will," "future," "potential" or the negative of these or similar terms and phrases. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include all matters that are not historical facts. Actual future results may be materially different from what is expected due to factors largely outside the Company's control, including the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials, changes in regulatory requirements or decisions of regulatory authorities, commercialization plans and timelines if sulopenem is approved, the actions of third-party clinical research organizations, suppliers and manufacturers, the accuracy of the Company's expectation regarding how far into the future its cash on hand will fund its ongoing operations, the sufficiency of cash resources and the Company's ability to continue as a going concern, the impact of COVID-19 and related responsive measures thereto, risks and uncertainties concerning the outcome, impact, effects and results of the Company's evaluation of corporate, organizational, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, organizational, strategic, financial or financing alternative and the Company's ability to complete one at all and other factors discussed under the caption "Risk Factors" in the most recently filed Annual Report on Form 10-K or Quarterly Report on Form 10-Q (as the case may be) and other documents filed with the Securities and Exchange Commission from time to time. Forward-looking statements contained herein represent the Company's beliefs and assumptions only as of September 13, 2021. Except as required by law, neither we, nor the Company, assume any obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Certain information contained in this Overview relates to, or is based on, studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Overview, it has not been independently verified, and neither we nor the Company make any representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Overview involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while the Company believes its own internal research is reliable, such research has not been verified by any independent source.

Executive Summary

Overview of Lead Product - Sulopenem

Iterum is developing sulopenem, a penem antibiotic, in both oral and intravenous ('IV') formulations

- Oral sulopenem is a bilayer tablet combining the prodrug, sulopenem etzadroxil, with probenecid
- Oral sulopenem has the potential to be the first FDA-approved oral penem for use in the community

Sulopenem has a targeted spectrum of activity against relevant pathogens

- Active against common urinary and GI tract bacteria: *E. coli, K. pneumoniae, P. mirabilis and B. fragilis*
- Not active against *Pseudomonas aeruginosa* and *Acinetobacter baumannii*; unlikely to put pressure on these pathogens and lead to carbapenem resistance

Iterum has conducted three global Phase 3 clinical trials of sulopenem and Oral sulopenem in Uncomplicated Urinary Tract Infections ('uUTI'), Complicated Urinary Tract Infections ('cUTI') and Complicated Intra-Abdominal Infections ('cIAI')

- Oral sulopenem demonstrated superiority to ciprofloxacin in uUTI in patients not susceptible to quinolones (p-value < 0.001)
- Sulopenem did not achieve the non-inferiority endpoint in the uUTI or cUTI study solely due to the inclusion of asymptomatic bacteriuria ('ASB') in the FDA endpoint
- Iterum believes the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections

Iterum's NDA received a CRL from the FDA in July 2021; Type A Meeting to be held in September 2021

- FDA determined that additional data are necessary to support approval for the treatment of adult women with uncomplicated urinary tract infections caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone
  - FDA recommended that Iterum conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. Additionally, the FDA recommended that Iterum conduct further nonclinical investigation to determine the optimal dosing regimen, although the FDA stated that this recommendation does not raise an approvability issue.
- Meeting request for a Type A Meeting has been sent in and meeting scheduled in September 2021

Sulopenem Product Highlights

Multi-drug resistant ('MDR') bacteria are a significant and growing global health threat; desperate need for new therapies

- Quinolone-resistant bacteria are prevalent in urinary tract infections ('UTIs') with much of the U.S. resistance rates ranging from 20-40% by community
- Physicians have exhausted effective and safe oral options to treat uUTIs caused by MDR pathogens in the community or as IV stepdown
- No new oral antibiotics for uUTIs have been approved in over 20 years

Sulopenem has the potential to be a compelling treatment alternative for patients with quinolone-resistant uUTIs

- Demonstrated superiority to oral ciprofloxacin in a head-to-head pivotal clinical trial in quinolone-resistant uUTIs with p-value < 0.001
- Non-inferiority achieved in pre-specified analysis of all enrolled patients with a baseline pathogen
  - Not non-inferior in quinolone-susceptible uUTIs, the regulatory endpoint; however, equivalent outcome in clinical response and at end of treatment ('EOT')
- Favorable safety profile in over 3,000 patients treated with sulopenem

NDA received CRL from FDA in July 2021; Type A meeting scheduled in September 2021

- Type A meeting to understand FDA perspective on deficiencies of filing and to determine path forward to resubmission

Sulopenem addresses a significant commercial opportunity in U.S. uUTI

- ~33M annual TRx for uUTIs; ~9-10M estimated annual infections due to quinolone-resistant bacteria
- Sulopenem has the potential to provide a treatment option that is effective against resistant infections and keeps patients out of hospitals and infusion clinics
- Potential opportunity to expand sulopenem label over time

Initial sulopenem commercialization can be executed through resource-efficient model

- Target high-volume prescribers (PCPs, OB/GYNs, urologists, ER physicians) of uUTI TRx in areas with high rates of quinolone-resistance
- Expect large share of voice upon commercialization; minimal branded competition and the only treatment with superiority to cipro in quinolone-resistant isolates
- Modest field organization has potential to generate substantial revenue

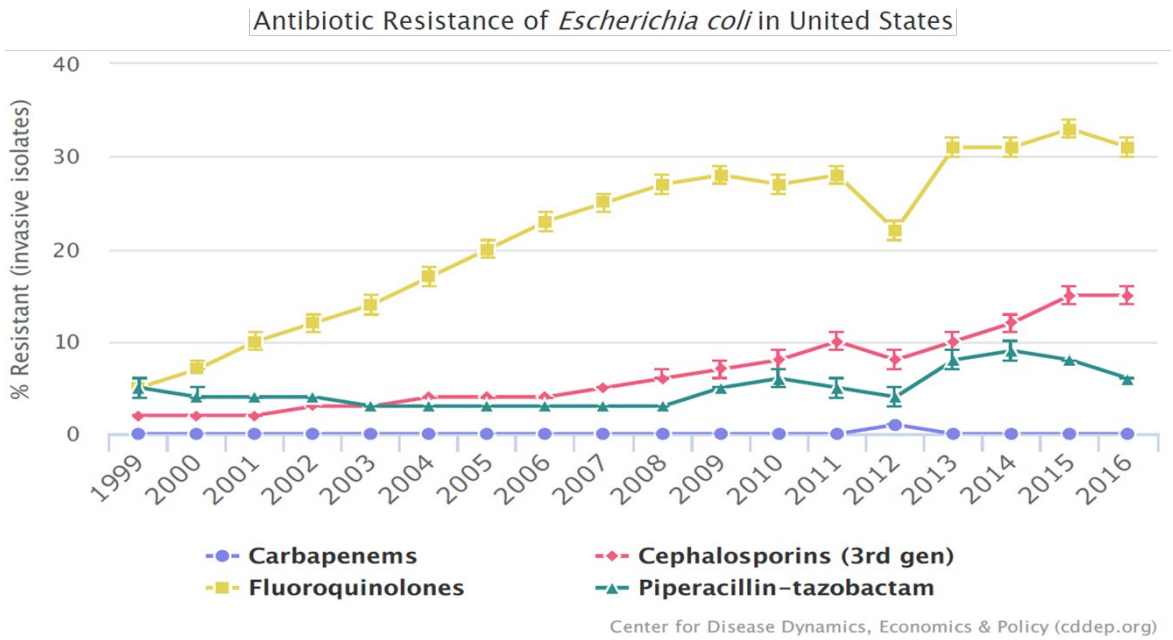
With statutory patent term extension upon filing, sulopenem will have U.S. patent protection into 2034 and new patent applications could potentially extend exclusivity into 2039; data exclusivity in EU & Japan extends into the early-to-mid 2030s

Bacterial Resistance Driving Need for New Oral Therapies

High resistance rates affecting the most populous regions of the U.S.

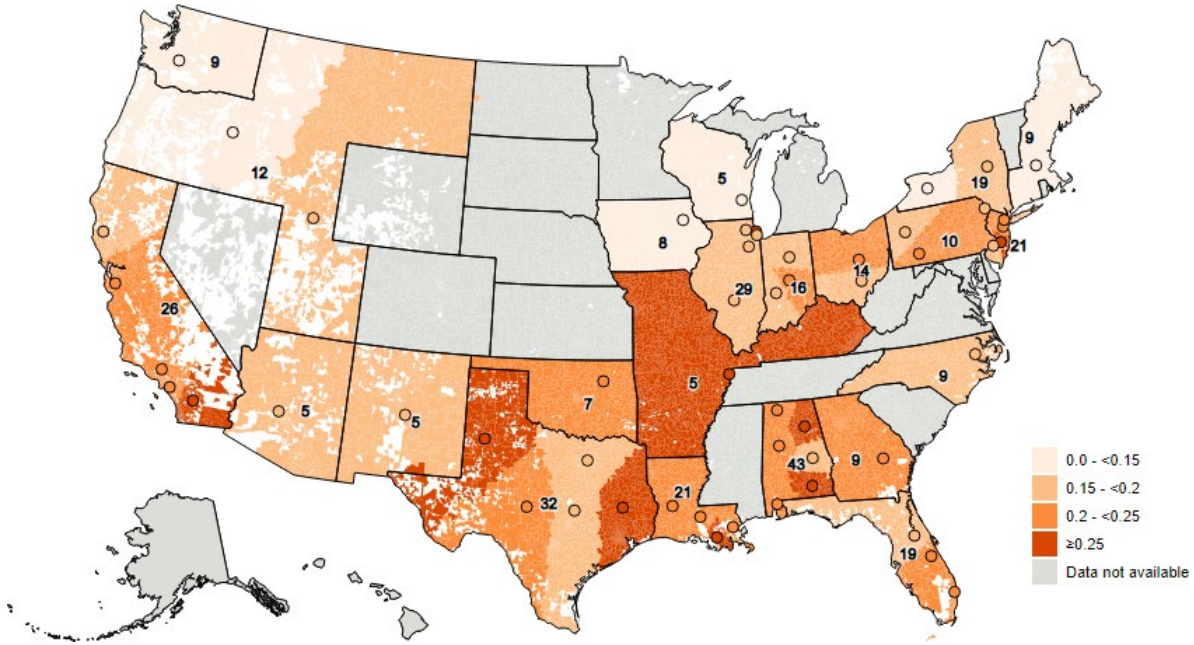
1999-2016 trends for antibiotic resistance in *E.coli* in hospitals in the United States

Antibiotic resistance continues to trend higher with quinolone and cephalosporin efficacy steadily eroding



2018 outpatient *Enterobacteriaceae* quinolone resistance, by zip code(1)

>20% of outpatient urinary gram negative isolates are resistant to quinolones in the most populous areas of the US



(1) Quinolone-non-susceptible and extended spectrum β-lactamase producing gram-negative pathogen rates from 379 acute care facilities across the United States; figures on the map reflect the number of acute care facilities in each state from which data was gathered.

Source: Center for Disease Dynamics, Economics Policy (CDDEP) & The Surveillance Network (TSN); Data analytics provided by BD Insights

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Efficacy and Safety Concerns with Existing Antibiotics

Doctors and patients are running out of effective oral options to treat UTI

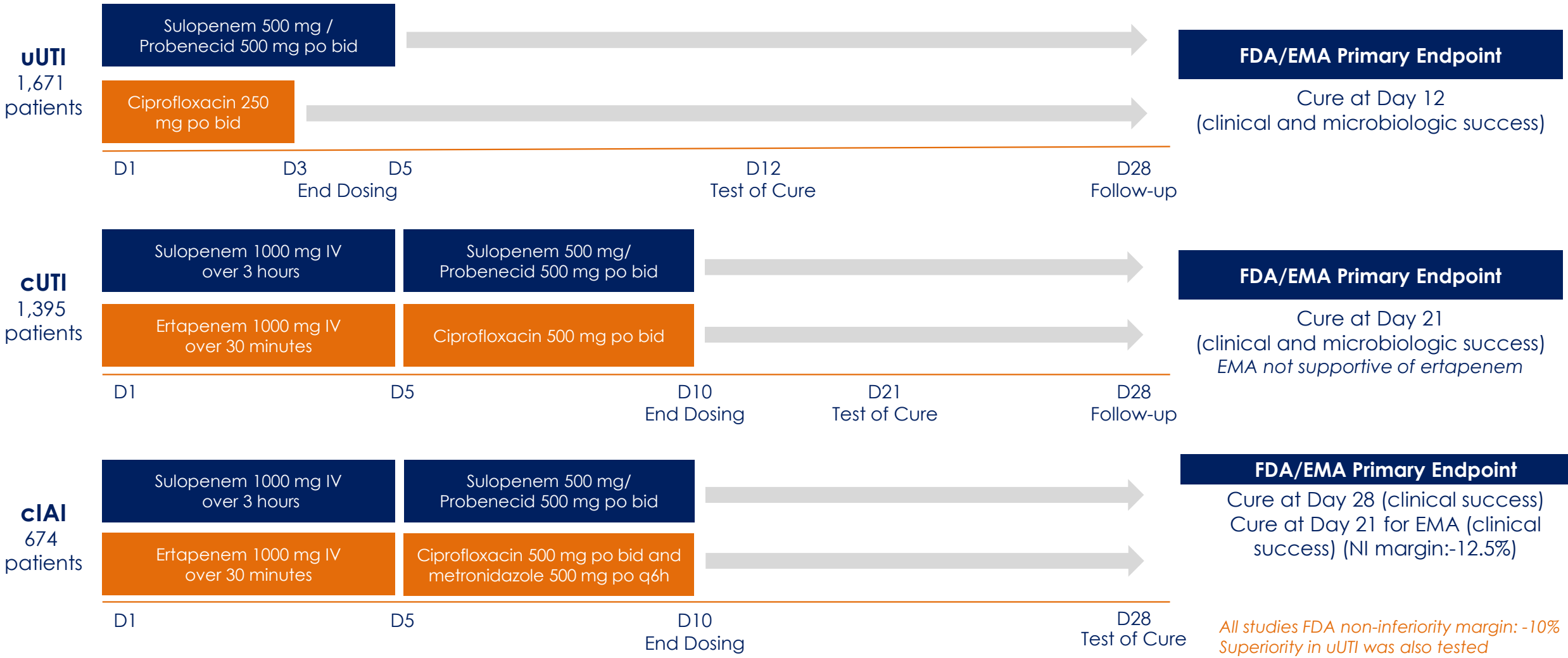
Antibiotic Class	UTI Pathogens				Prescribing Considerations
	All N=5,395 % S	*E. coli* N=4,081 % S	*K. pneumo* N=733 % S	P. mirabilis N=284 % S	
Quinolones	77	73	93	81	Should be reserved for patients who have no other treatment options for uUTI (risks outweigh benefits; Tendinitis, tendon rupture, peripheral neuropathy, central nervous system effects and exacerbation of myasthenia gravis; risk is further increased in older patients)
Nitrofurantoin	84	97	42	47	Should not be used for pyelonephritis; does not reach therapeutic concentrations in kidneys; avoid use in elderly due to age-related decline in renal function
TMP/SMX	72	67	87	84	Monitor patients for adverse events (rash, hyperkalemia) or use an alternate antibiotic
β-lactams	75	74	84	87	Inferior efficacy and more adverse effects compared with other UTI antimicrobials

Agents are no longer recommended for empiric treatment when resistance prevalence reaches 20%

Outpatient urine cultures 2015-2017; Iterum Therapeutics, Becton Dickinson Insights; Squadrito FJ, del Portal D. 2019 ; Smith, M. 2011: Hulisz, D. 2013;
FDA Drug Safety Update 2018; IDSA Guidelines 2010; examples of antibiotics in these classes: Quinolones (Ciprofloxacin); Nitrofurantoin (Macrobid); TMP/SMX (Bactrim); β-lactams (Augmentin; Keflex)

Completed Phase 3 Study Designs

Over 3,700 Patients Enrolled; Over 1,800 Patients Treated with sulopenem[1]



(1) Favorable safety profile in over 3,000 patients treated with sulopenem, including all P1 and P2 studies.

Snapshot of Oral Development Pipeline: uUTI and cUTI

Very limited competition under development results in highly attractive commercial landscape

- Pivmecillinam (Utility Therapeutics)
  - Using clinical data from historical European approval
  - Expected to file in 2H 2021 with potential approval in 2H 2022
  - Likely target non-elevated risk patients
- Gepotidacin (GSK)
  - Conducting two Phase three studies in uUTI, expected completion end of 2022/early 2023
  - Likely to file in mid-2023 with potential approval 1H 2024
- In the complicated urinary tract infection space, only one oral product currently under development in Phase 3
  - Tebipenem (Spero Therapeutics); expected to file in Q4 2021 with potential approval 2H 2022

uUTI Clinical Trial Summary

uUTI Study: Micro-MITT population

Results indicate that sulopenem would be an important new treatment for women with uUTIs

Micro-MITT population	Sulopenem n/N (%)	Ciprofloxacin n/N (%)	Difference (95% CI)	P value
Quinolone Non-susceptible Population				
Overall Response (TOC)	92/147 (62.6)	50/139 (36.0)	26.6 (15.1, 37.4)	< 0.001
Reason for Failure: Asymptomatic bacteriuria	27 (18.4)	38 (27.3)		
Clinical Response (TOC)	122/147 (83.0)	87/139 (62.6)	20.4 (10.2, 30.4)	< 0.001
Overall Response (EOT)	95/147 (64.6)	42/139 (30.2)	34.4 (23.1, 44.8)	< 0.001
Quinolone-susceptible Population				
Overall Response (TOC)	247/370 (66.8)	326/415 (78.6)	-11.8 (-18.0, -5.6)	
Reason for Failure: Asymptomatic bacteriuria	47 (12.7)	16 (3.9)		
Clinical Response (TOC)	300/370 (81.1)	349/415 (84.1)	-3.0 (-8.4, 2.3)	
Overall Response (EOT)	240/370 (64.9)	271/415 (65.3)	-0.4 (-7.1, 6.2)	
Combined (Quinolone-susceptible and Quinolone Non-susceptible Populations)				
Overall Response (TOC)	339/517 (65.6)	376/554 (67.9)	-2.3 (-7.9, 3.3)	
Reason for Failure: Asymptomatic bacteriuria	74 (14.3)	54 (9.7)		
Clinical Response (TOC)	422/517 (81.6)	436/554 (78.7)	2.9 (-1.9, 7.7)	
Overall Response (EOT)	335/517 (64.8)	313/554 (56.5)	8.3 (2.4, 14.1)	0.006

Overall Response at TOC by Resistance Class

~5% of Study population have infections with no available treatment options

Resistance Class	Sulopenem n/N (%)	Ciprofloxacin n/N (%)	Difference (95% CI)	P-value	% micro-MITT patients, N=1071
Quinolone-resistant	92/147 (62.6)	50/139 (36.0)	26.6 (15.1, 37.4)	<0.001	**26.7%**
Quinolone-resistant β-lactam-resistant	86/129 (66.7)	43/121 (35.5)	31.1 (18.9, 42.4)	<0.001	**23.3%**
Quinolone-resistant β-lactam-resistant TMP-SMX-resistant	38/ 63 (60.3)	16/ 47 (34.0)	26.3 (7.4, 43.2)	0.006	**10.3%**
Quinolone-resistant β-lactam-resistant TMP-SMX-resistant Nitrofurantoin-resistant	19/ 24 (79.2)	11/ 27 (40.7)	38.4 (11.4, 60.1)	0.005	**4.8%**

Sulopenem Has Demonstrated A Favorable Safety Profile

	Sulopenem n/N (%) N= 833	Ciprofloxacin n/N (%) N=827
Adverse Events	208 (25.0)	116 (14.0)
Treatment Emergent Adverse Events ('TEAEs')	207 (24.8)	115 (13.9)
Drug-related TEAE	142 (17.0)	51 (6.2)
TEAE leading to discontinuation of study drug	13 (1.6)	8 (1.0)
TEAE leading to discontinuation from study	0	1 (0.1)
Serious Adverse Events ('SAE')	**6 (0.7)**	**2 (0.2)**
Drug-related SAE	1 (0.1)(1)	0
SAE leading to premature discontinuation of study drug	1 (0.1)	0
SAE leading to death	1 (0.1)(2)	0
Treatment-Emergent Adverse Events Occurring in at Least 2% of Patients		
Diarrhea	103 (12.4)	21 (2.5)
Nausea	31 (3.7)	30 (3.6)
Headache	18 (2.2)	18 (2.2)

(1) Angioedema, resolved next day.
(2) Patient diagnosed with lung cancer on Day 5, died >5 months after completion of study from her cancer.

cUTI Clinical Trial Summary

Overall Response at the Test of Cure in cUTI Patients

Sulopenem non-inferior to ertapenem save for presence of ASB

Micro-MITT Population	Sulopenem n/N (%)	Ertapenem n/N (%)	Difference (95% CI)
Overall Response (TOC)	301/444 (67.8)	325/440 (73.9)	-6.1 (-12.0, -0.1)
Reason for Failure: ASB	93 (20.9)	59 (13.4)	
Clinical Response (TOC)	397/444 (89.4)	389/440 (88.4)	1.0 (-3.1, 5.1)
Overall Response (EOT)	385/444 (86.7)	391/440 (88.9)	-2.2 (-6.5, 2.2)
Patients With Ciprofloxacin Susceptible Isolates[1]			
Overall Response (TOC)	168/248 (67.7)	186/215 (86.5)	-18.8 (-26.1, -11.0)
Reason for Failure: ASB	54 (21.8)	10 (4.7)	
Patients With All Other Isolates[2]			
Overall Response (TOC)	133/196 (67.9)	139/225 (61.8)	6.1 (-3.1, 15.1)
Reason for Failure: ASB	39 (19.9)	49 (21.8)	

(1) Sulopenem patients treated with sulopenem-etzadroxil + probenecid, ertapenem patients treated with ciprofloxacin.
(2) Sulopenem patients treated with sulopenem IV only or sulopenem IV: sulopenem-etzadroxil + probenecid, ertapenem patients treated with ertapenem IV only or ertapenem IV: amoxicillin-clavulanate.

cIAI Clinical Trial Summary

Primary Endpoint at Test of Cure

Sulopenem did not achieve primary endpoint by 1 patient

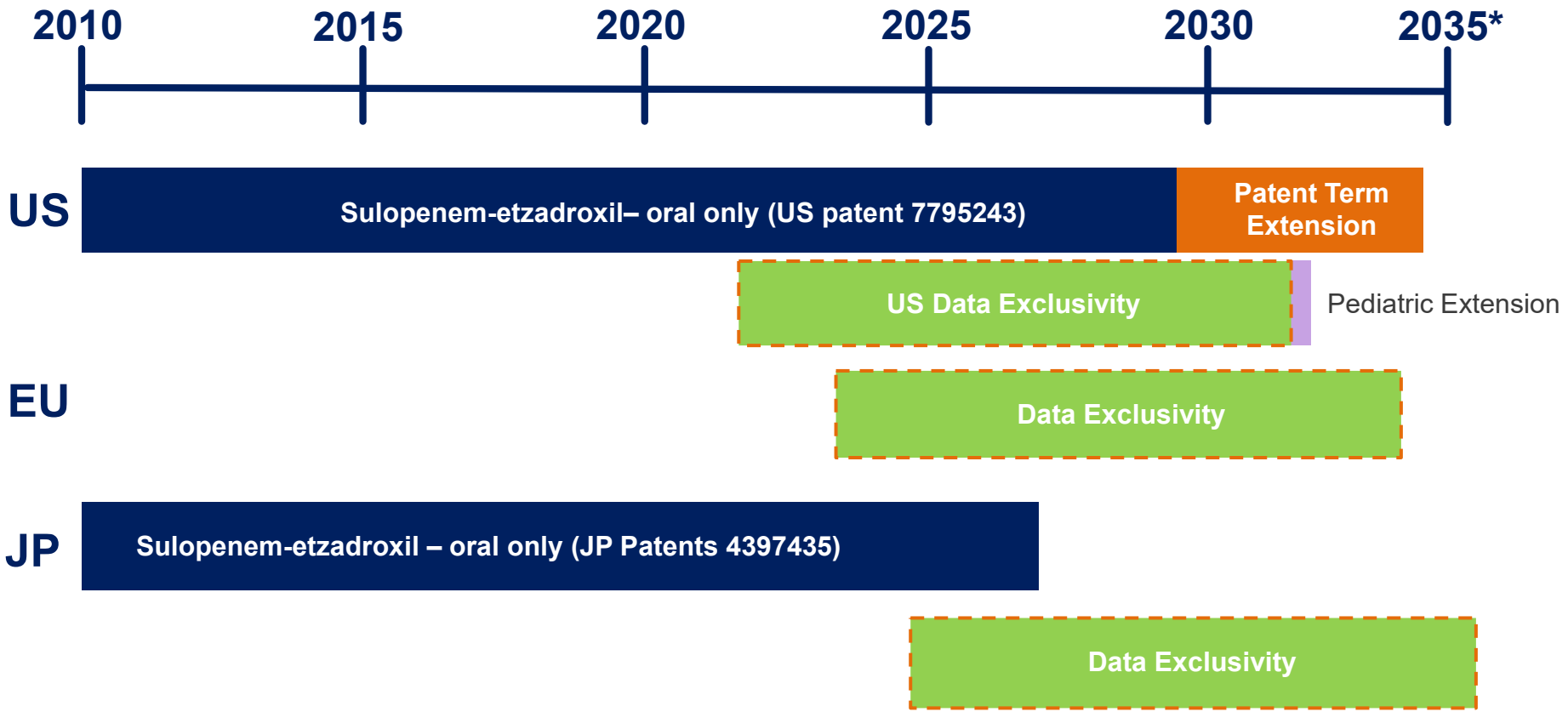
Population	Sulopenem n/N (%)	Ertapenem n/N (%)	Difference (95% CI)
Intention to Treat			
Micro-MITT			
Cure	213/249 (85.5)	240/266 (90.2)	-4.7 (-10.3, 1.0)
Fail	27/249 (10.8)	17/266 (6.4)	
Indeterminate	9/249 (3.6)	9/266 (3.4)	
ITT	292/338 (86.4)	300/336 (89.3)	-2.9 (-7.8, 2.0)
MITT	292/335 (87.2)	298/331 (90.0)	-2.9 (-7.7, 2.0)
Evaluable			
Clinical	265/283 (93.6)	265/277 (95.7)	-2.0 (-5.7, 1.7)
Microbiologic	196/212 (92.5)	212/222 (95.5)	-3.0 (-7.5, 1.4)

Note: FDA non-inferiority threshold of 10.0%; EMA non-inferiority threshold of 12.5%.

Intellectual Property

Long Runway to Capture Value

Sulopenem patents and regulatory exclusivity provide extensive length of protection



*Our patent portfolio also contains two U.S. and international patent applications, one addressing the effect of probenecid on the plasma concentrations of sulopenem after multi-day dosing and the second related to a method of preparing a bilayer tablet composed of sulopenem etzadroxil and probenecid. If granted, patent protection could extend into 2039.

Commercial Overview

Sulopenem U.S. Launch Planning On Hold

Partnered with Eversana to Execute Pre-Launch Activities

Advocacy Development

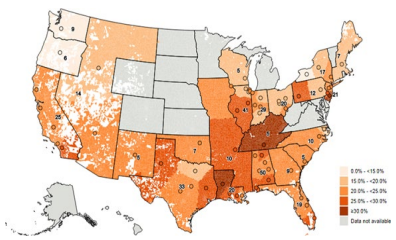
Collaborating with physician, pharmacist and patient organizations to fight growing resistance problem

KOL Support

Payer Reimbursement

Engaging with health plans and PBMs covering >250M US commercial and Medicare lives

Formulary Access



Sales Force Targeting

Mapping areas of greatest need through identification of bacterial resistance at the zip code level

Early Adoption

"Resistance" Campaign

Educating HCPs on geographic-specific bacterial resistance rates and ramifications of treatment failure

Physician Awareness

Manufacturing In Place

Oral sulopenem process development is complete; PV batches complete

Launch Readiness

Financials

Financial Overview

Key Metric	June 30, 2021
Cash, cash equivalents and short-term investments (millions)	$91.5
Term Loans, including PPP Loan (millions)	$4.9
6.500% Exchangeable Senior Subordinated Notes due 2025 (millions)*	$12.6
Ordinary shares outstanding (millions)	182.8

*The exchange rate is $0.7775 per ordinary share (or 16.2M shares [excluding interest] based on $12.6M of notes outstanding).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therapeutics