Investor Presentation

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Executive Summary

- **ORLYNVAH™, a penem antibiotic, for the treatment of uncomplicated urinary tract infections (uUTIs), was approved by the FDA in October 2024**
  - ORLYNVAH™ is a proprietary, patent-protected bilayer tablet combining the prodrug, sulopenem etzadroxil, with probenecid
  - First and only FDA-approved **oral penem;** indicated for treatment of uUTIs in the community
  - ORLYNVAH™ has a targeted spectrum of activity against relevant pathogens most likely to cause urinary tract infections
  - ORLYNVAH™ has demonstrated a favorable safety profile across four Phase 3 clinical trials
- **ORLYNVAH™ is the first new treatment commercially launched in the United States (August 2025) for uUTIs in the last 25 years**
  - Multi-drug resistant bacteria are a significant and growing global health threat
  - Significant U.S. market for uUTI therapies, estimated at approximately **40 million** prescriptions annually[1]
    - Approximately 2/3 or 26 million of those prescriptions[2] are written for at-risk patients[3], which would be the target patients for sulopenem
    - The four leading oral treatments for uUTI account for ~75% of the prescription market[4] but have resistance rates near or above **20%**[5] and all have additional safety concerns
    - Lack of innovation in an underserved area of women's health
    - ORLYNVAH™ is well positioned relative to other potential new market entrants
- **ORLYNVAH™ has a long runway to capture value**
  - Combination of patents and data protection in the U.S. expected to provide **protection into 2039**
    - Patent information for four U.S. patents for ORLYNVAH™ are listed in FDA's Orange Book
  - Foreign patent protection expiring no earlier than 2039 (JP, AU, KR, MX, CN)
  - Iterum also has an IV formulation of sulopenem for complicated infections in a hospital setting but does not plan to pursue U.S. approval, at this time

[1] Extrapolated from EVERSANA METYS Pharmacy Claims, EVERSANA ACTICS Data and Medical Claims and previous market research
[2] Extrapolated from Eversana longitudinal medical and pharmacy claims
[3] At-risk patients are elderly, diabetic, have a history of recurrent infections or other co-morbidities that negatively impact their immune system
[4] Extrapolated from EVERSANA METYS Pharmacy Claims, EVERSANA ACTICS Data and Medical Claims, and previous market research
[5] Dunne MW et al. A multicenter analysis of trends in resistance in urinary Enterobacterales isolates from ambulatory patients in the United States: 2011–2020. BMC Infect Dis. 2022;22:194

The Launch of ORLYNVAH™ Is a Significant Advance

- Despite growing rates of antimicrobial resistance, there have been no new antimicrobial therapies launched over the last three decades in the uUTI space.
- At-risk uncomplicated urinary tract infections (uUTI) patients – due to age, co-morbidities history of recurrent infections, or suspected resistance - are most in need of new alternatives.
- Orlynvah™ now provides at-risk adult women with uUTI with a potential novel solution that they have needed.
- As the first oral penem therapy, Orlynvah™ brings the demonstrated efficacy and safety of IV penem therapies used in the hospital, to at-risk patients in the community that are in need of new alternatives.
- Orlynvah™ is a proprietary, patent-protected bilayer tablet combining the prodrug, sulopenem etzadroxil, with probenecid
  - One tablet twice per day for 5 days
  - Orlynvah™ demonstrated higher response rates compared to amoxicillin clavulanate and increased response rates compared to ciprofloxacin in quinolone resistant infections
  - Orlynvah™ demonstrated safety in two pivotal uUTI clinical trials
- Orlynvah™ is a unique and highly differentiated new treatment as the first and only oral penem product approved by the FDA

Orlynvah Performance Highlights

- Launched on August 20, 2025
  - Q3 2025 product sales of $0.4M (includes some stocking of specialty pharmacy locations serving our geographies)
- Over 100 unique physician prescribers in the first few months post-launch
  - Approximately half of those physicians have prescribed Orlynvah to more than one patient
- Current fill rate of prescriptions is approximately 40% - expect that ratio to increase with payer decisions around coverage and access
- Health care providers see the utility in Orlynvah for their patients
  - Physicians are pleased to have a new, oral option to treat their uUTI patients
  - Clinical experience has been solid, as expected
- Early Orlynvah usage has included women with recurrent infections (more than 1 uUTI within 3 months) as well as usage to avoid hospital admissions to receive IV therapy
- High interest from key thought leaders and group practices which have generated follow-up discussions

Orlynvah Market Access Highlights

- Positive feedback from both Pharmacy Benefit Managers (PBMs) and health plans across both commercial and Medicare Part D formularies
- Iterum's National Account Managers continue to engage strategically with key stakeholders across the U.S. payer landscape, highlighting Orlynvah's differentiated value proposition
- Received a signed rebate agreement with one of the top 3 Medicare Part D PBMs; enables Orlynvah to be added to their Medicare Prescription Drug plan and Medicare prescription drug plan formularies for coverage beginning in 2026 or 2027, depending on individual plan structures
- Submitted bids to commercial and Medicare Part D PBMs; aiming to secure long term formulary positioning later this year and into Q1 2026
- Coverage now approximately 16% of insured lives, with increasing adoption by employer groups and payer formularies integrating Orlynvah into their standard benefit design

Orlynvah Sales Territory Coverage

- Specialty Pharmacy Distribution
  - We currently have 10 targeted geographies with field representatives; these representatives continue to call on their existing target physicians
  - Supplemental resources to be added during Q4 2025; additional field representatives as well as virtual sales representatives to increase reach and efficiency
  - With the combination of the existing and supplemental resources, we expect to provide equivalent coverage of at least 20 target geographies
- Traditional Specialty Distribution
  - In order to satisfy inquiries from physicians outside of our called-on network, specialty distribution has been established with McKesson and Cencora

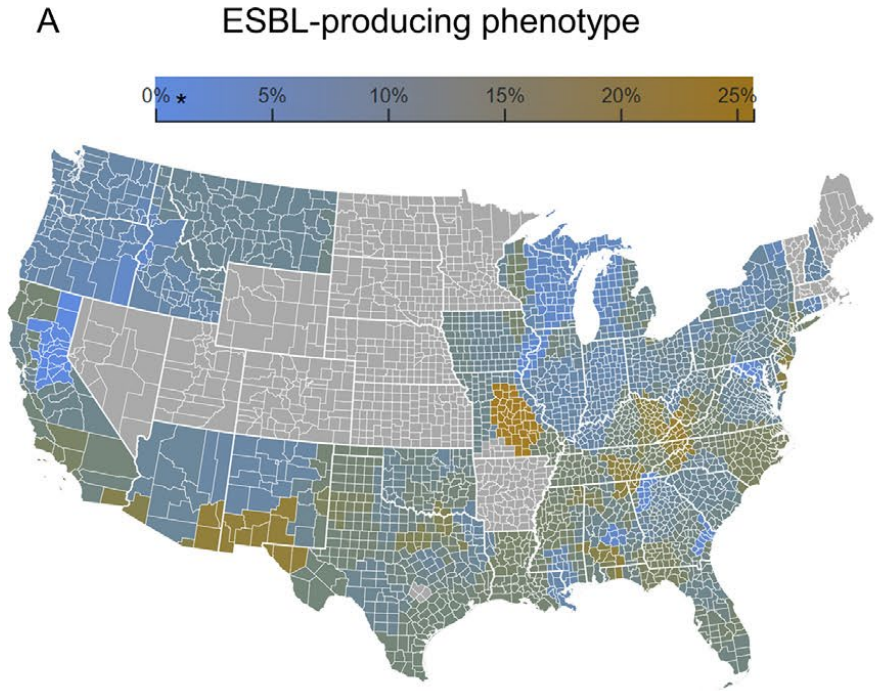
Bacterial Resistance Driving Need for New Oral Therapies

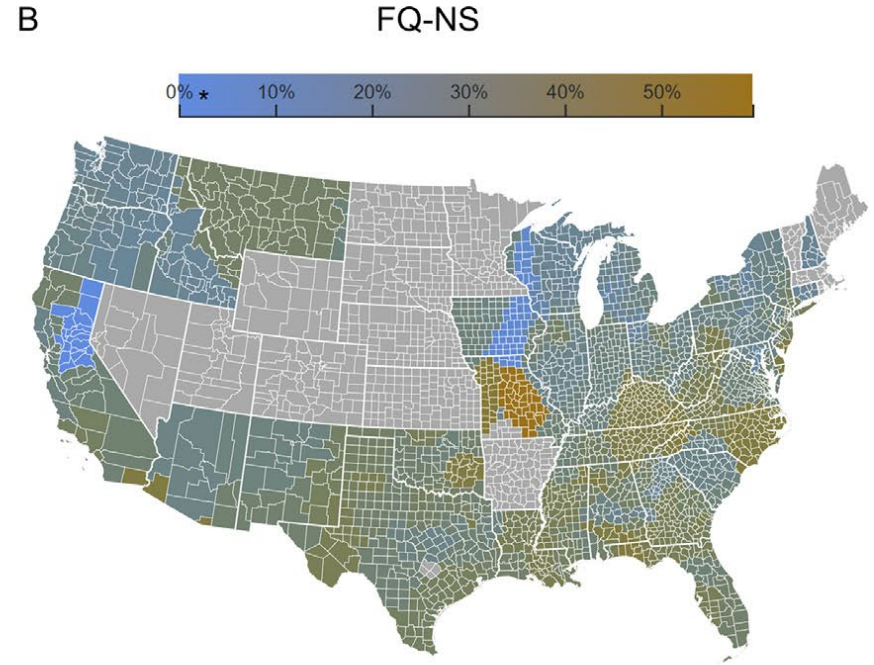
High resistance rates affecting the most populous regions of the U.S.

Geographic Distribution of Enterobacterales Resistance in Ambulatory Settings by Zip Code in the U.S., 2018-2020

- **Penems** are the recommended treatment for **ESBL-producing** Enterobacterales infections.
- ~10% of community urinary tract infections are due to an ESBL-positive organism
- **Orlynvah™** is the only approved **ORAL** penem antibiotic in the U.S.

>20% of outpatient urinary gram-negative isolates are resistant to quinolones in the most populous areas of the U.S.

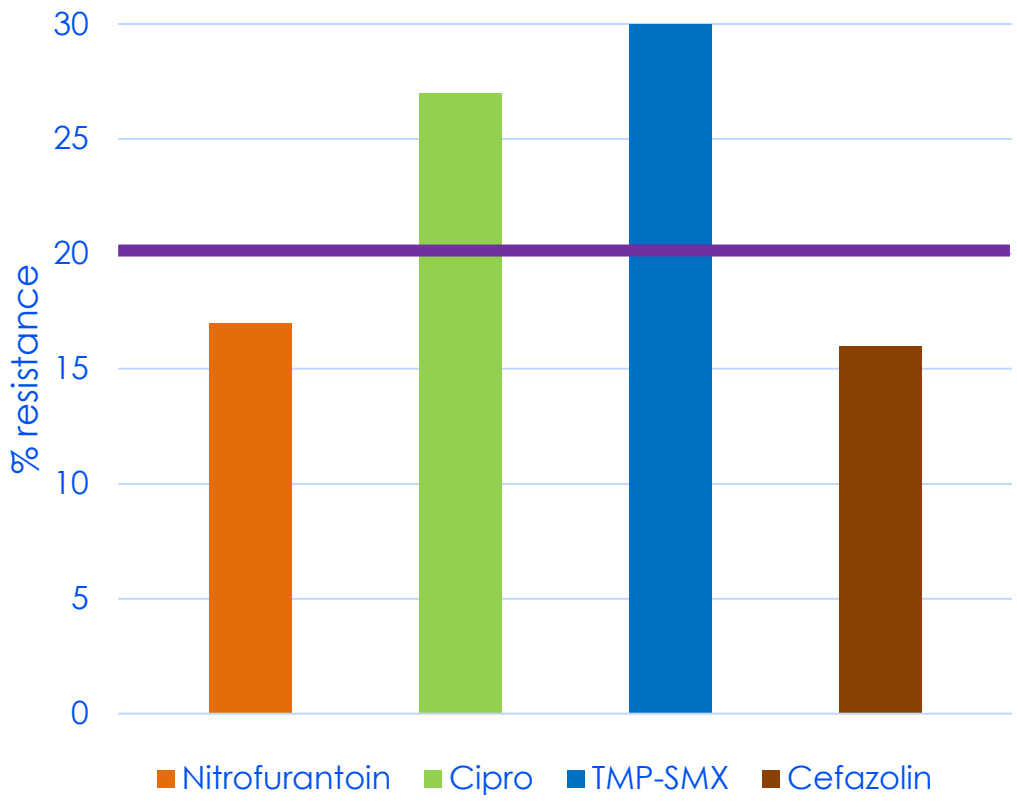




Nonduplicate (first isolate of a species within 30 days), noncontaminant Enterobacterales urinary isolates from ambulatory adult patients (≥18 years) from 338 ambulatory care facilities across the United States. [A] ESBL-producing (913,343 isolates) [B]Fluoroquinolone Nonsusceptible (970,219 isolates); Source: Aronin, et al International Journal of Infectious Diseases 2022;119:142-145; Data and analytics provided by BD Insights Research Database.

Prescribing Challenges for Key Oral Therapies in uUTI

At 20% resistance or above, Infectious Diseases Society of America (IDSA) no longer recommends empiric usage and physician research highlights need to change products prescribed; additionally, each of the below oral therapies have key safety challenges to consider



Prescribing Considerations

- **Nitrofurantoin (Macrobid)**
  - Should not be used for pyelonephritis, does not reach therapeutic concentration in kidneys, contraindicated in patients with creatinine clearance <60mL/min (~ 30% of patients)
- **Ciprofloxacin (Cipro)**
  - FDA/EMA does not recommend usage in uncomplicated infections; should be reserved for patients who have no other treatment options (product shown to have potential risk of tendonitis, tendon rupture, peripheral neuropathy, CNS effects and exacerbation of myasthenia gravis) and risk is further increased in older patients
- **Trimethoprim-Sulfamethoxazole (Bactrim)**
  - Monitor patients for adverse events (rash, hyperkalemia) or use alternative antibiotic
- **Cephalexin (Keflex)**
  - Has drug interaction with metformin that can lead to hypoglycemia; potential to trigger seizures, especially if dose not reduced in renal failure patients

*Resistance rates for Enterobacterales from Iterum's 301 and 310 studies combined using urinary breakpoints; per the FDA, CLSI-published urinary cefazolin breakpoints should be used to predict the susceptibility of oral cephalosporins including cephalexin (Keflex)

uUTI Oral Development Pipeline

ORLYNVAH™ is well positioned on both product profile and potential launch timing

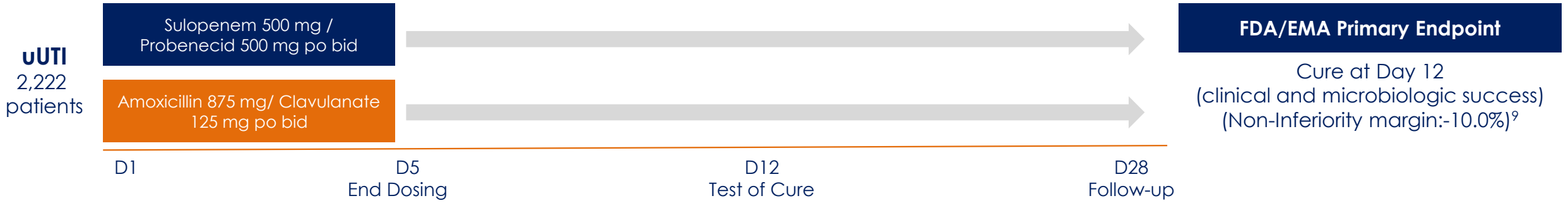
- Gepotidacin (GlaxoSmithKline) - uUTI
  - NDA approved by FDA on March 25, 2025; potential commercial launch in Q4 2025

- Pivmecillinam (Alembic Pharmaceuticals, Inc.)
  - NDA approved by FDA on April 24, 2024; potential commercial launch in Q4 2025

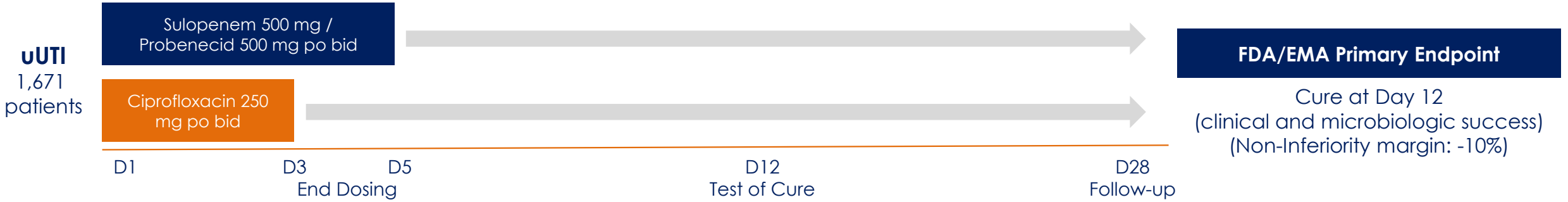
Phase 3 Study Designs - uUTI

Conducted under Special Protocol Assessment (SPA) Agreements with FDA

REASSURE



SURE-1



[9] The number of patients with Augmentin® resistant pathogens was inadequate to test for superiority in this population

REASSURE uUTI Study: Micro-MITT population

Non-inferior to Augmentin® in the Augmentin®-susceptible population, as well as statistically superior

Micro-MITT population	Sulopenem n/N (%)	Augmentin® n/N (%)	Difference (95% CI)	P value
Augmentin®-susceptible Population				
Overall Response (TOC)	296/480 (61.7)	243/442 (55.0)	6.7 (**0.3**, 13.0)	0.019
Clinical Response (TOC)	371/480 (77.3)	339/442 (76.7)	0.6 (-4.8, 6.1)	
Microbiological Response (TOC)	361/480 (75.2)	295/442 (66.7)	8.5 (2.6, 14.3)	
Combined (Augmentin®-susceptible and Augmentin® Non-susceptible Populations)				
Overall Response (TOC)	**318/522 (60.9)**	**260/468 (55.6)**	**5.4 (-0.8, 11.5)**	0.044
Clinical Response (TOC)	397/522 (76.1)	358/468 (76.5)	-0.4 (-5.7, 4.9)	
Microbiological Response (TOC)	390/522 (74.7)	315/468 (67.3)	7.4 (1.8, 13.1)	

Micro-MITT = microbiological modified intention to treat
TOC = Test of Cure
CI = Confidence Interval

SURE-1 uUTI Study: Micro-MITT population

Micro-MITT population	Sulopenem n/N (%)	Ciprofloxacin n/N (%)	Difference (95% CI)	P value
Quinolone Non-susceptible Population				
Overall Response-Test of Cure (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-End of Treatment (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

Microbiologic eradication was defined as $<10^3$ CFU/mL of baseline pathogen isolated at a follow-up visit, as determined by using whole genome sequencing;
Green circle represents outcome within the specified non-inferiority margin

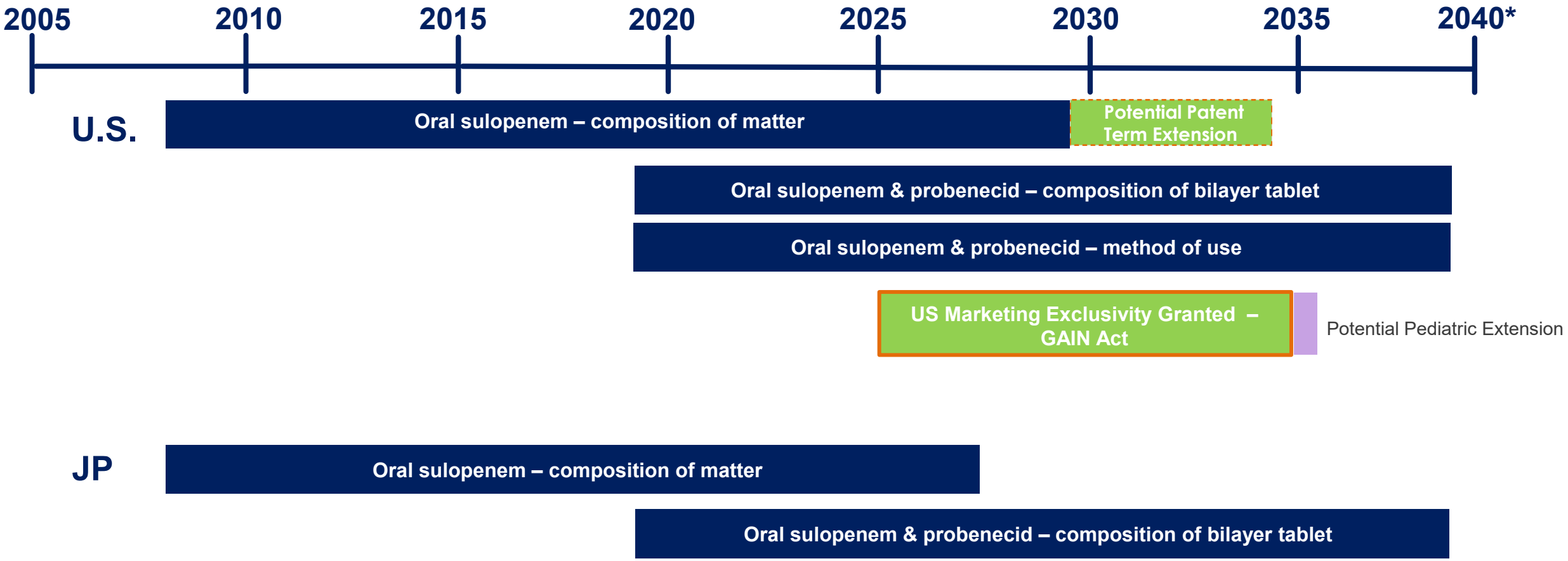
ORLYNVAH™ Has Demonstrated A Favorable Safety Profile[10]

	Sulopenem N= 1940 n/N (%)	Augmentin N= 1107 n/N (%)	Ciprofloxacin N=827 n/N (%)
Treatment Emergent Adverse Events ('TEAEs')	416 (21.4)	136 (12.3)	115 (13.9)
Drug-related TEAE	297 (15.3)	85 (7.7)	51 (6.2)
TEAE leading to discontinuation of study drug	21 (1.1)	4 (0.4)	8 (1.0)
TEAE leading to discontinuation from study	4 (0.2)	1 (0.1)	1 (0.1)
Serious Adverse Events ('SAE')	**6 (0.3)**	**5 (0.5)**	**2 (0.2)**
Drug-related SAE	1 (0.1)[11]	0	0
SAE leading to premature discontinuation of study drug	1 (0.1)	2 (0.2)	0
SAE leading to death	1 (0.1)[12]	0	0
Treatment-Emergent Adverse Events Occurring in at Least 2% of Patients			
Diarrhea	193 (9.9)	45 (4.1)	21 (2.5)
Nausea	79 (4.1)	32 (2.9)	30 (3.6)
Headache	42 (2.2)	17 (1.5)	18 (2.2)

[10] Data from both SURE-1 and REASSURE uUTI studies; sulopenem column is a combined total for the sulopenem arm from SURE-1 and REASSURE studies
[11] Angioedema, resolved next day.
[12] Patient diagnosed with lung cancer on Day 5, died >5 months after completion of study from their cancer.

Long Runway to Capture Value

ORLYNVAH™ patents and regulatory exclusivity provide extensive protection



Iterum's patent portfolio also contains additional patents granted in the US, Australia, Canada, Mexico, China and South Korea and pending patent applications in a number of other jurisdictions including Europe and Brazil. Note, the Company submitted patent information for four U.S. patents for ORLYNVAH™ have been listed in FDA's Orange Book.

Financial Overview

Key Metric	September 30, 2025
Cash and cash equivalents (millions)	$11.0
Pfizer Promissory Note*	$21.2
Ordinary shares outstanding (millions)**	~52.8

Iterum has sufficient cash to fund its operating expenses into the second quarter of 2026

* Pursuant to our exclusive license with Pfizer for sulopenem we were obligated to make a regulatory milestone payment of $20m to Pfizer upon approval of oral sulopenem. In accordance with the license we elected to defer payment for two year and delivered promissory note to Pfizer in the amount of $20.0 million in October 2024. In May 2025, the promissory note was amended and extends the repayment of the note to October 2029. This note accrues interest at an annual rate of eight percent for the first two years and then ten percent for the next three years on a daily compounded basis until paid in full.

** Based on shares outstanding as of November 13, 2025


ITERUM
therapeutics