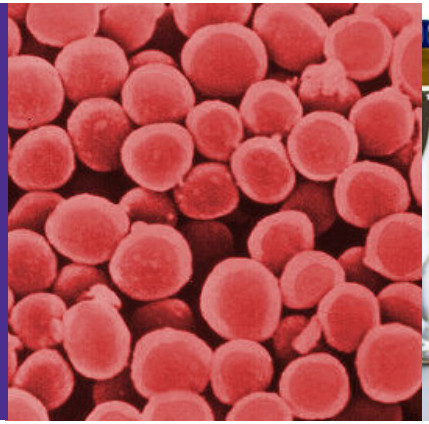
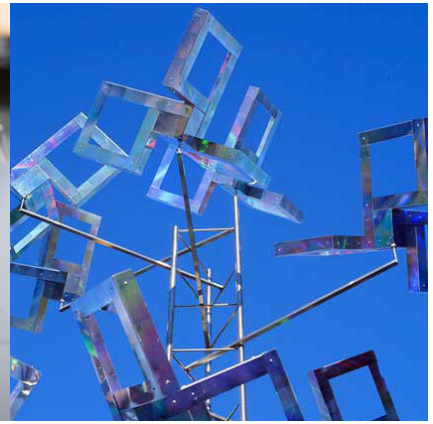
CUBIST
PHARMACEUTICALS





Cubist Pharmaceuticals

The Shape of Cures to Come™

Corporate Presentation

September 2012

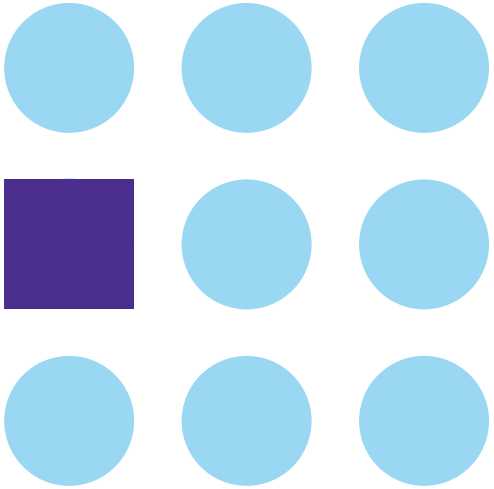
Forward-Looking & Non-GAAP Statements

This presentation includes forward-looking statements, including statements regarding our future financial and operating results, including product revenues for CUBICIN® and ENTEREG®; the development plans, timing of regulatory approvals, timelines and potential commercialization of our product candidates; our expectations for compensation related to our co-promotion arrangement with Optimer for DIFICID®; and expectations that by 2017 our global revenue will grow to $2 billion, we will have four product candidates in late-stage clinical trials, and we will generate $700 million in non-GAAP annual adjusted operating income. Any statements that are not statements of historical fact (including statements containing the words "believe," "plan," "project," "forecast," "expect," "estimates" and similar expressions) should also be considered to be forward looking statements. Each forward-looking statement contained in this presentation is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statement. Applicable risks and uncertainties include, among others: our ability to continue to grow revenues from the sale of CUBICIN, which depends on such factors as the ability of our third-party suppliers to produce and deliver adequate amounts of CUBICIN and competition from generic drug companies such as Teva, with whom we have settled our previously-disclosed Hatch-Waxman litigation regarding CUBICIN, and Hospira, whom we have filed suits against in response to its ANDA filing regarding CUBICIN; our ability to successfully market and sell ENTEREG; our ability to successfully develop, gain marketing approval for and commercially launch CXA-201 and our other product candidates for their planned indications and on the timelines that we expect; our ability to find opportunities and successfully negotiate and execute deals for the in-licensing or acquisition of new products and product candidates or the acquisition of companies; our ability to achieve and manage the growth in our business; and those additional factors discussed under the caption "Risk Factors" in our recent periodic filings with the Securities and Exchange Commission. We caution investors not to place considerable reliance on the forward-looking statements contained in this presentation. These forward-looking statements speak only as of the date this presentation was given, and Cubist does not undertake any obligation to update or revise any of these statements.

Within this presentation, in order to provide greater transparency regarding Cubist's performance, we refer to certain non-GAAP financial measures that involve adjustments to GAAP measures. Any non-GAAP financial measures presented should not be considered an alternative to measures required by GAAP, should not be considered measures of Cubist's liquidity and are unlikely to be comparable to non-GAAP information provided by other companies. A reconciliation between our non-GAAP financial measures and GAAP financial measures is included on our web site at www.cubist.com on the Investor Relations page.

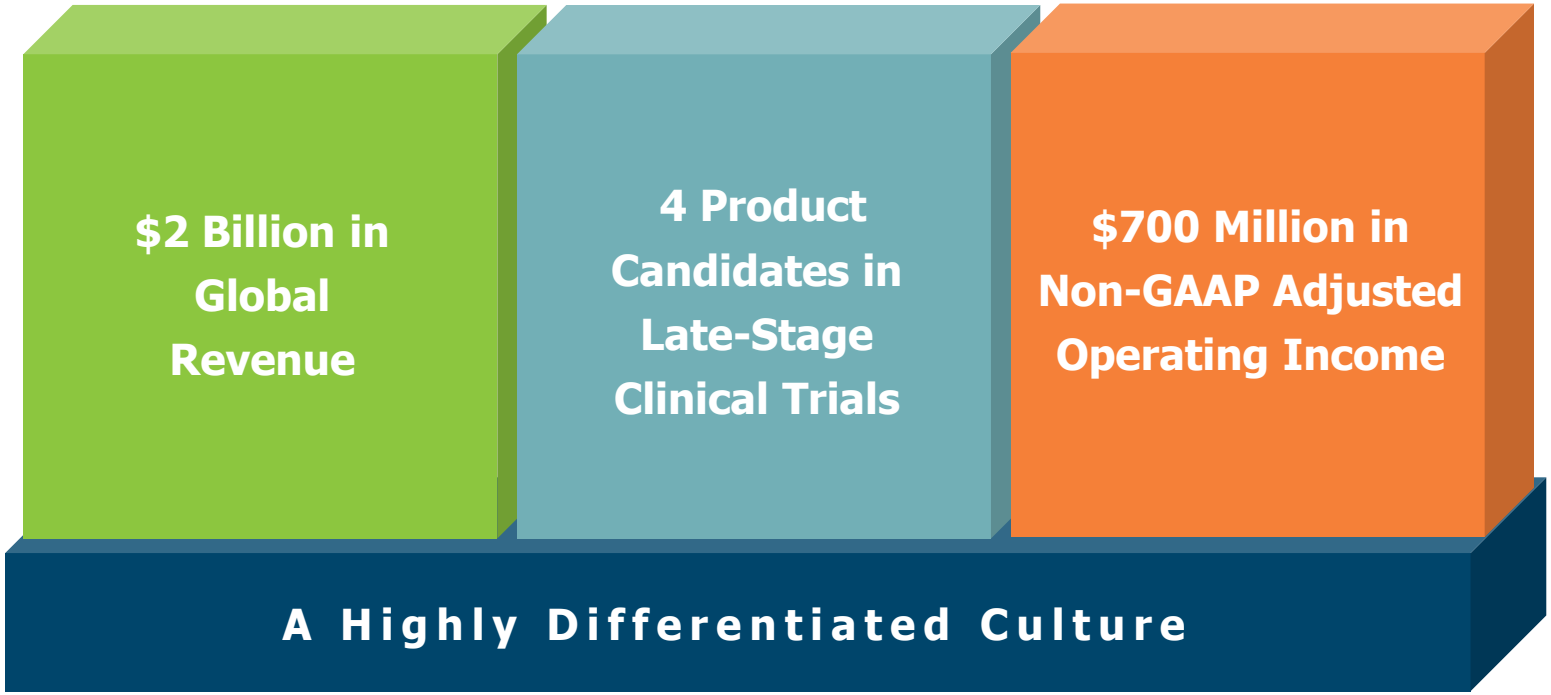
Cubist Mission

What sets us apart



Through our highly differentiated products and culture, our mission is to be the global leader in transforming the lives of patients in the acute care / hospital environment.

Building Blocks of Growth – 5 Year Goals*

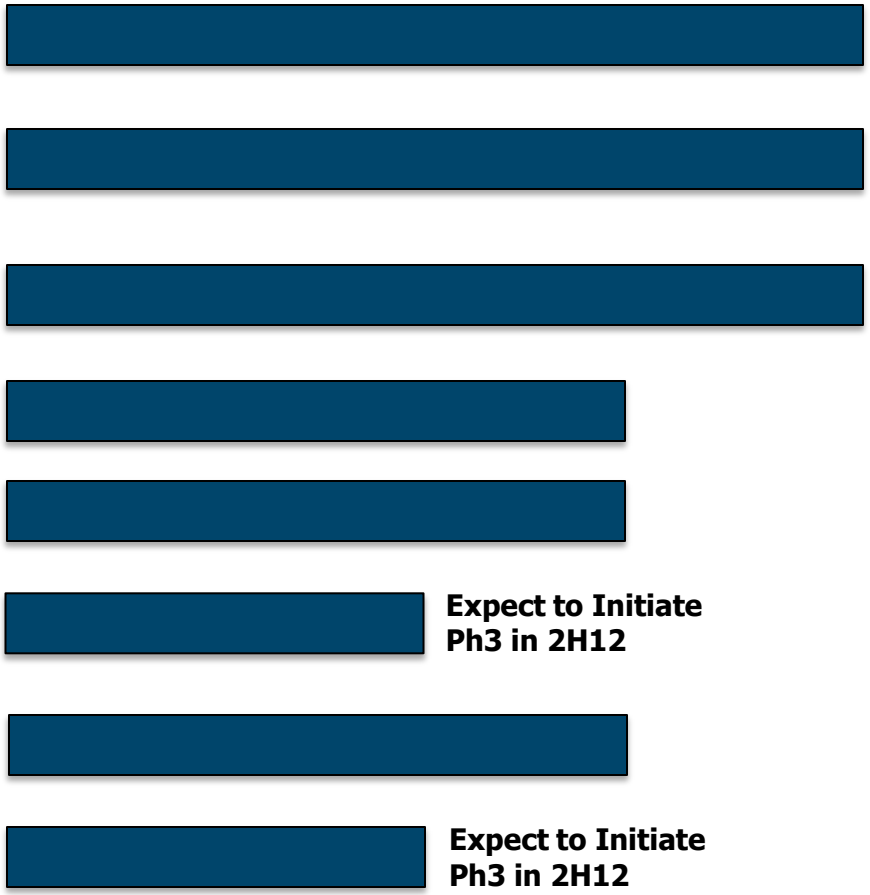


*5 year goals (2012 – 2017)

Three Drivers of Profitable Revenue Growth in 2012

Late-Stage Pipeline Continues to Advance

Therapy	Indication
CUBICIN® (daptomycin for injection)	Certain Gram-positive infections including MRSA: cSSSI/SAB
ENTEREG® (alvimopan)	Accelerated GI motility bowel resection surgery with primary anastomosis
DIFICID®* (fidaxomicin)	*Clostridium difficile*-associated diarrhea (CDAD)
Ceftolozane/tazobactam** (combo IV)	cUTI (complicated urinary tract infection)
	cIAI (complicated intra abdominal infection)
Infections caused by MDR Gram-negative pathogens including *Pseudomonas aeruginosa*	HABP/VABP (hospital-acquired/ventilator-associated bacterial pneumonia)
CB-315 (Oral novel lipopeptide)	*Clostridium difficile*-associated diarrhea (CDAD)
CB-5945 (Novel *mu*-opioid receptor antagonist)	Opioid-induced constipation (OIC)



*Agreement with Optimer Pharmaceuticals for Cubist to co-promote DIFICID in the U.S.
**Commercialization rights worldwide, except for select Asia-Pacific and Middle East territories, under a license from Astellas Pharma Inc. Development rights are worldwide. cSSSI = complicated skin & skin structure infections; SAB = *Staphylococcus aureus* bacteremia.
Information as of July 19, 2012.

2012 Cubist Guidance*

	as of April 18, 2012	as of July 19, 2012
Total net revenue range:**		**$900 – 930M**
– **U.S. net CUBICIN**		**$790 – 815M**
– **International CUBICIN**		**~$45M**
– **U.S. net ENTEREG**		**$40 - 45M**
– **Service and other revenues (includes DIFICID)**		**~$25M**
Gross margin (On total product revenue)	**~76%**	**~75%**
Cost of goods sold	**~24%**	**~25%**
Operating expenses+:		
– **R & D (including milestone payments)**	**$285 – 295M**	**$275 - 285M**
– **Contingent consideration++**		**~$10M**
– **SG & A**		**$165 - 175M**
Operating income (GAAP)	**$230 - 235M**	**$235 – 245M**
Adjusted Operating income (Non-GAAP)	**$260 - 265M**	**$265 – 275M**
Other income (expense)		**~($33)M**

	12/31/11 (Actual)	12/31/12 (Projected)	
Cash, cash equivalents and investments	**$868M**	**~$980M**	**~$925M**
Convertible debt	**$559M**	**$559M**	**$484M**

* Does not include impact of any future product or company acquisitions, or other one-time events.
** Assumes no wholesaler stocking; + Expense ranges include around $26 million for stock-based compensation expenses.
++ Expense is based on current expectations for the related ceftolozane/tazobactam and CB-5945 programs, which are subject to change.

2012 Milestones
As Announced on January 19, 2012

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- Clinical Development
  - Ceftolozane/tazobactam
    - Progress enrollment in cUTI and cIAI trials to stay on track for NDA filing by YE 2013
    - Initiate Phase 3 trial in HAP/VAP in 2H12
  - ✓ CB-315: Initiate Phase 3 CDAD program in 1H12
  - CB-5945: Initiate Phase 3 OIC trials by end of 2012
  - CB-625: Complete initial Phase 1 studies by 2H12

- Operations
  - ✓ Realize $30 Million in efficiencies from integration of Adolor acquisition by mid-2012
  - Identify a 3rd fill finish facility for CUBICIN by YE 2012

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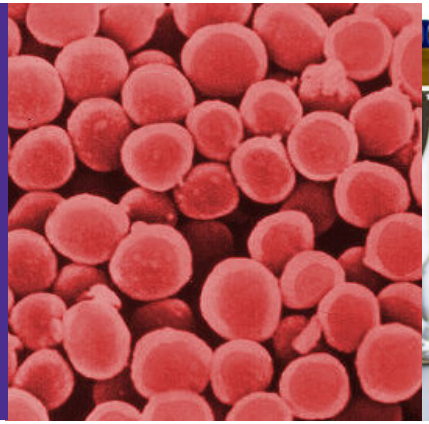

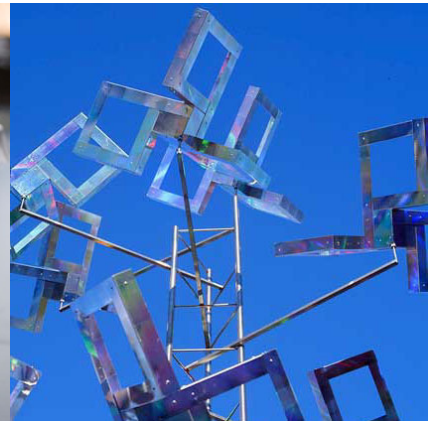

Cubist Pharmaceuticals

The Shape of Cures to Come™

CUBICIN® (daptomycin for injection)

A first-in-class cyclic lipopeptide approved as treatment for serious skin and bloodstream infections caused by certain Gram-positive organisms including MRSA

CUBICIN® (daptomycin for injection)

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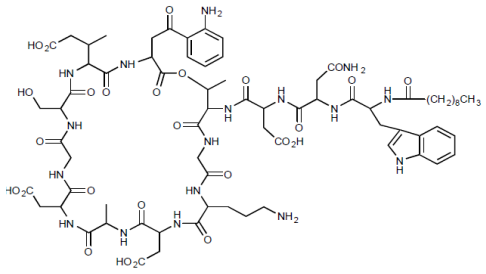
Compound



daptomycin for injection

Mechanism of Action

- Rapid depolarization of membrane potential

Stage

- FDA approved September 12, 2003

Indications (U.S.)

- Complicated skin and skin structure infections (cSSSI)
- *Staphylococcus aureus* bacteremia (SAB), including right-sided infective endocarditis (RIE) caused by MRSA and MSSA

In Vitro Microbiology

Gram (+)	Potent broad Gram+ *Staph aureus* MIC_{90} = 0.25-1 ug/mL Enterrococci MIC_{90} = 1-4 ug/mL
Cidality	Rapidly bactericidal

Pharmacokinetics

- Generally linear and time-independent at IV doses of 4 to 12 mg/kg q24h (healthy adults)

Dosing

Can be administered intravenously either by injection over a 2 min. period or by infusion over a 30 min. period

- cSSSI – 4mg/kg IV
- SAB/RIE – 6mg/kg IV

How Supplied

- Single-use 500mg vial (U.S.)

Commercial Outlook

- Projected peak annual U.S. revenues of >$1 billion
- Approved in more than 70 countries
- Distributed Ex-U.S. through partners:
  - Novartis (EU/Latin America)
  - Astra Zeneca (Asia/Mid East)
  - Merck(Japan)
  - Medison (Israel)
  - Sunovion (Canada)
  - TTY (Taiwan)
  - Kuhnil (Korea)

U.S. IP Protection: OB-listed patents

- Method of treatment patent with protection until September 2028
- Two high purity composition patents with protection until November 2020
- Two method of administration patents with protection until September 2019
- Pharmaceutical composition patent protection through June 2016

Teva license settlement: granted Teva a license to sell generic daptomycin in U.S. either as of 6/24/18 — if CUBICIN is granted pediatric exclusivity extension, or as of 12/24/17.

CUBICIN: On Historic Path to Blockbuster Status

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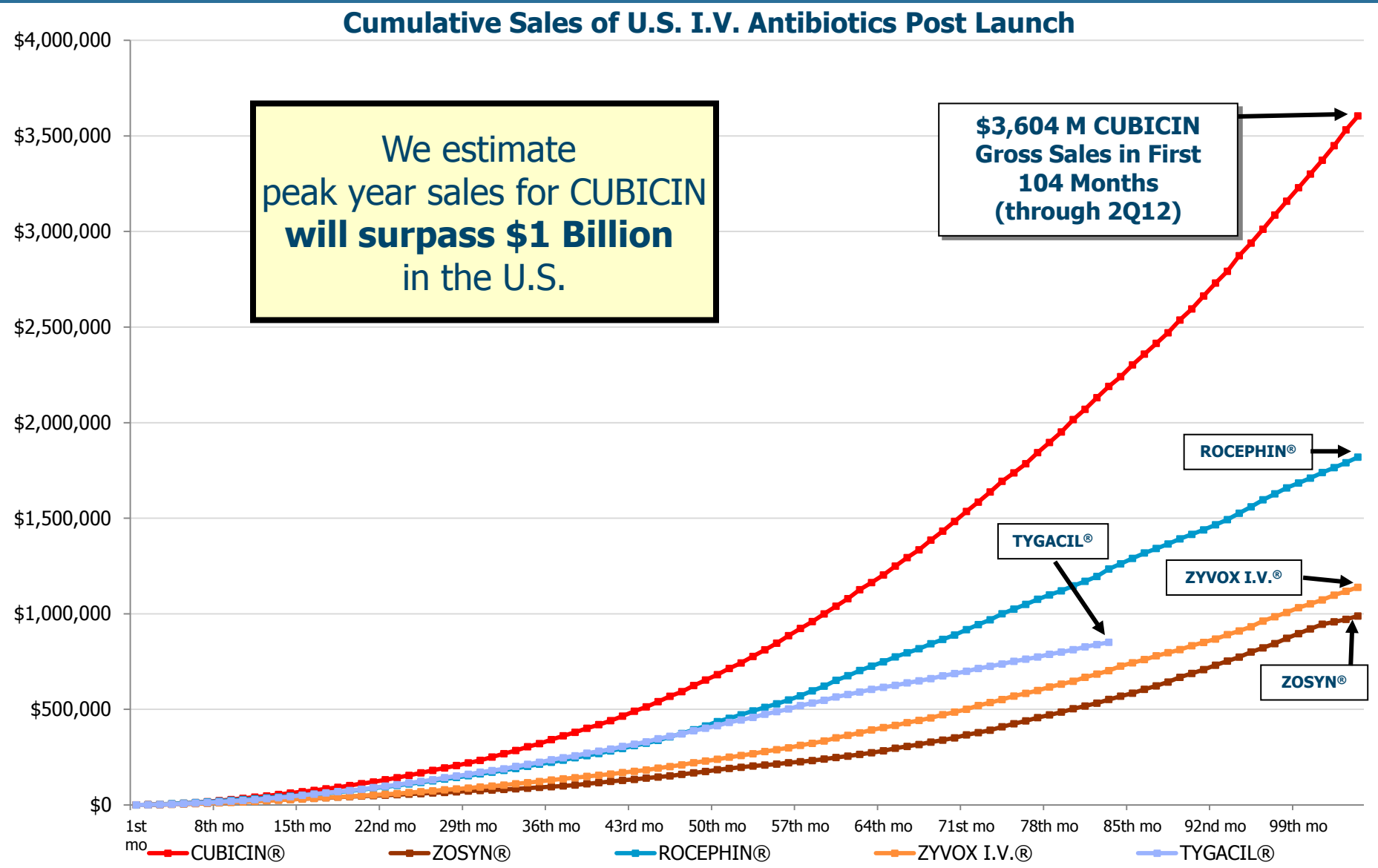

Source: ICS Gross orders for CUBICIN, IMS Gross Sales for other products

Cubist Annual Total Net Revenues

We Estimate Peak Year Sales of CUBICIN will surpass $1B in the U.S

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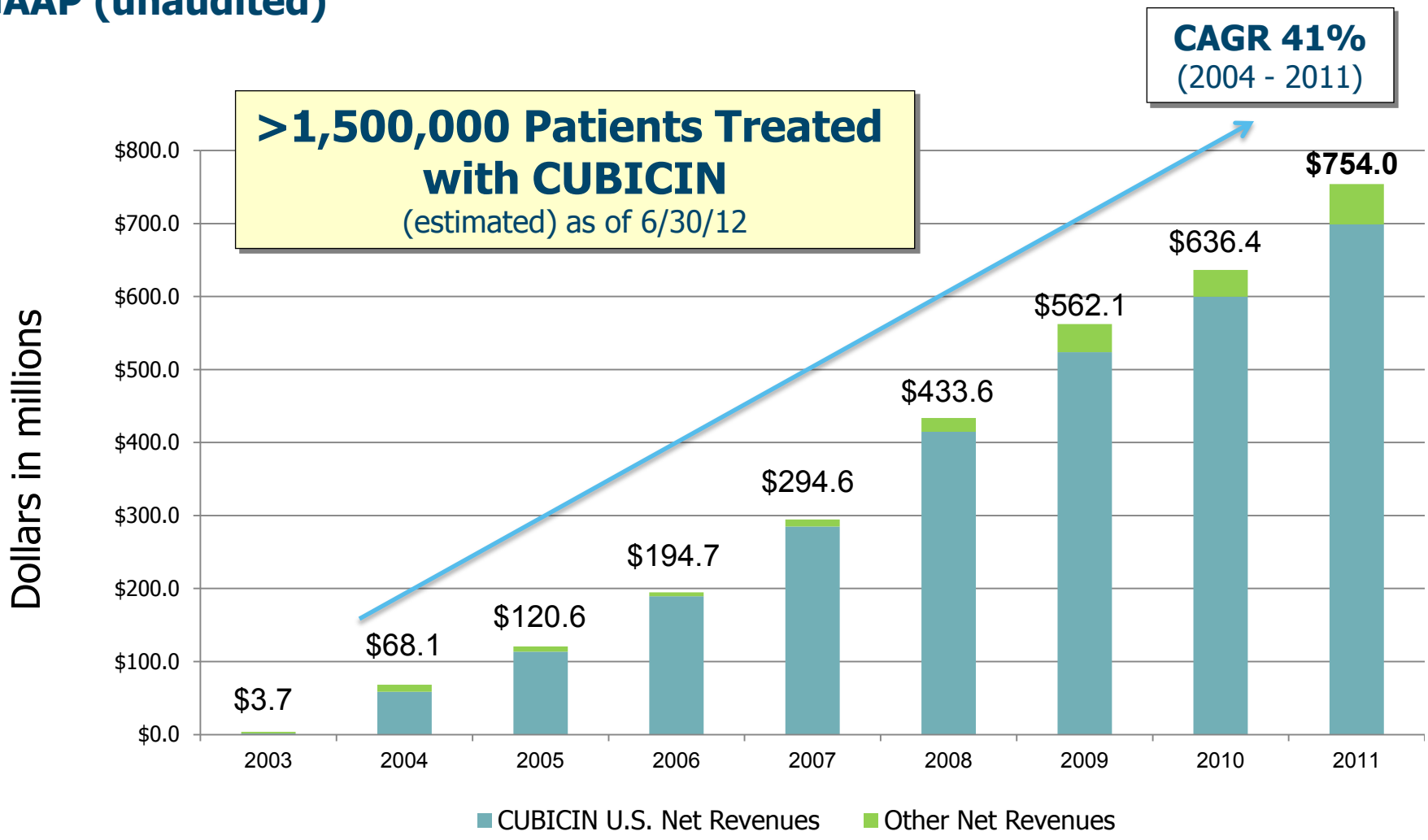
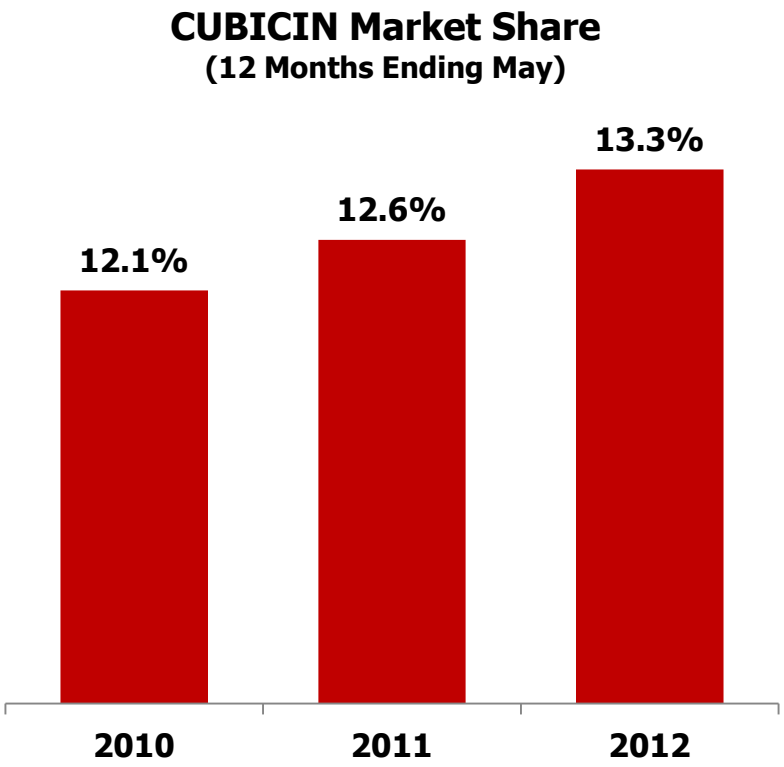
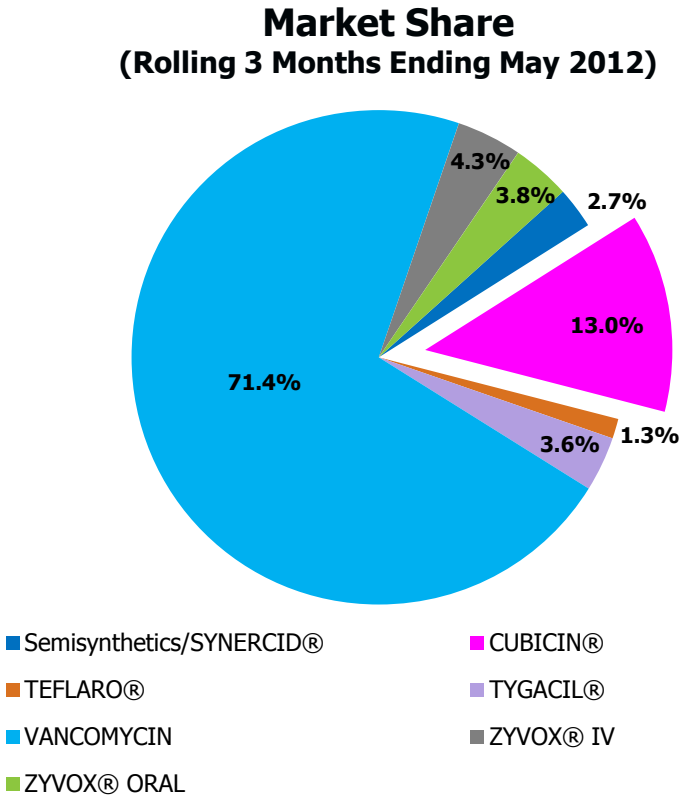
GAAP (unaudited)



CUBICIN U.S. Market Share

Based on Days of Therapy





Data through: May 2012
Source: CUBICIN®: ICS - CUBICIN Gross vials converted to days of therapy; WKH - Competitor Non-Retail grams converted to days of therapy
Defined market includes: Semi-Synthetics (Nafcillin and Oxacillin); SYNERCID®; TYGACIL®; ZYVOX ORAL®; ZYVOX I.V.®;VIBTIV®;CUBICIN; and Vancomycin.
CUBICIN is not approved for use in all of the indications captured within this market

CUBICIN – Expected to Surpass $1B in U.S.

We Get To $1 B With <6.2%* CAGR

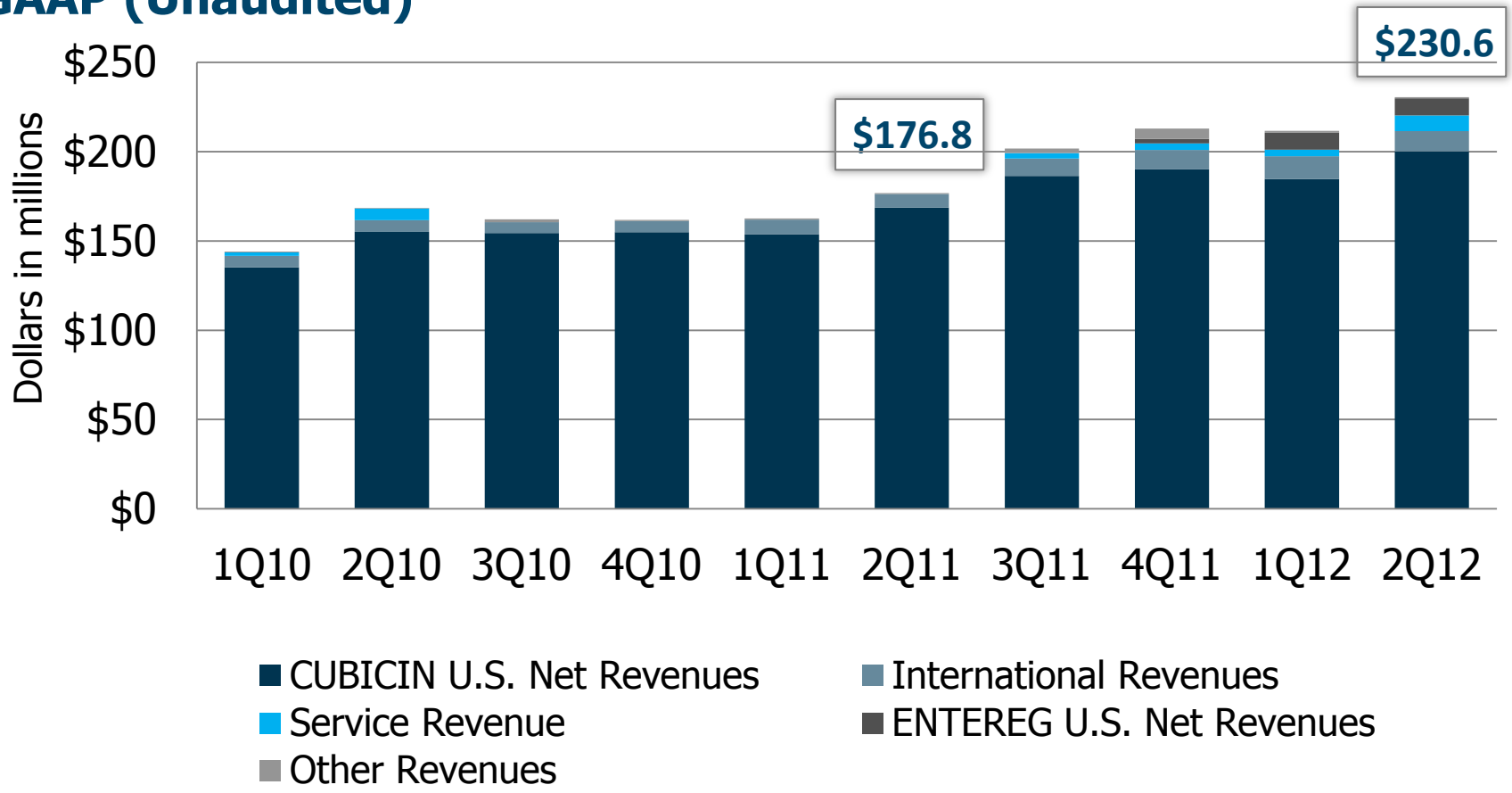
- Growth drivers
  - CUBICIN's value proposition
  - IDSA guidelines
  - Outpatient fit
  - 2-min injection
- Reasonable price increases (8 – 10% annually historically)
- Assumptions:
  - MRSA persists
  - Vancomycin effectiveness continues its slow decline
  - Teva launches generic under agreement no earlier than 12/17

*Required CAGR is 6.2% (through FY 2017) calculated from reported full year 2011 US CUBICIN net product revenue ($698.8MM).

2Q12: Continued Momentum

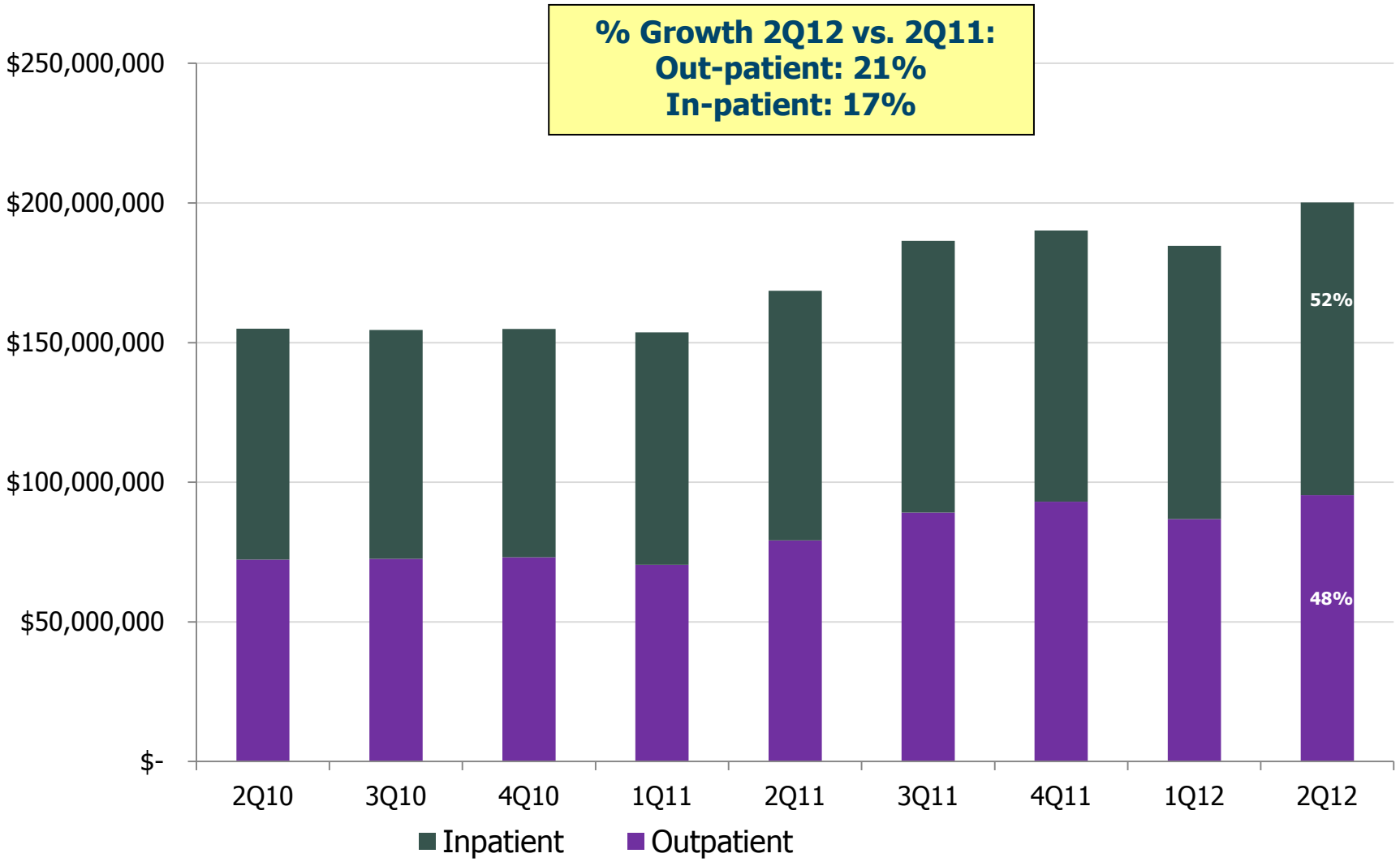
- 2Q12 U.S. net product revenues of $209.9M were up 24.5% vs. 2Q11
- 2Q12 U.S. CUBICIN net product revenues of $200.2M were up 18.7% vs. 2Q11
- 2Q12 CUBICIN vials sold up 8.0% in U.S. vs. 2Q11

GAAP (Unaudited)



CUBICIN Growth: In-Patient and Out-Patient

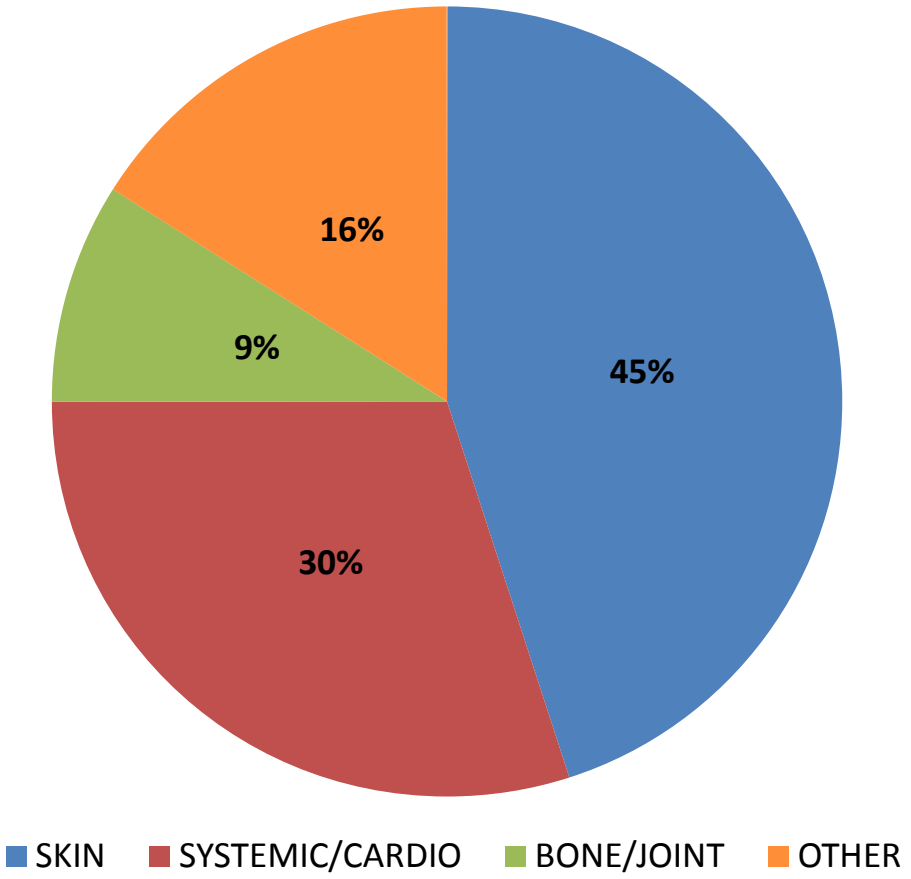
(Net U.S. Product Revenue)



Source: ICS: Cubicin Vials

CUBICIN Usage By Indication

In Days of Therapy – 12 months through Dec 2011



Source: The U.S. Hospital Antibiotic Market Guide, Jan 2011 – Dec 2011 by AMR/Arlington Medical Resources, Inc

Concerns with clinical outcomes for vancomycin at higher end of its susceptible range

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Late 2011 publications:

- Moore, Zervos et al: *Daptomycin Versus Vancomycin for Bloodstream Infections Due to Methicillin-Resistant* Staphylococcus aureus *With a High Vancomycin Minimum Inhibitory Concentration: A Case-Control Study.* Published in CID with accompanying editorial 11/21/2011

- J. Brown, K. Brown, Forrest: *Vancomycin AUC_{24}/MIC in MRSA Complicated Bacteremia and Infective Endocarditis Patients with Attributable Mortality during Hospitalization.* Published in AAC 11/28/2011.

IDSA Issues Its First Clinical Practice Guidelines for Treatment of MRSA Infections[1]

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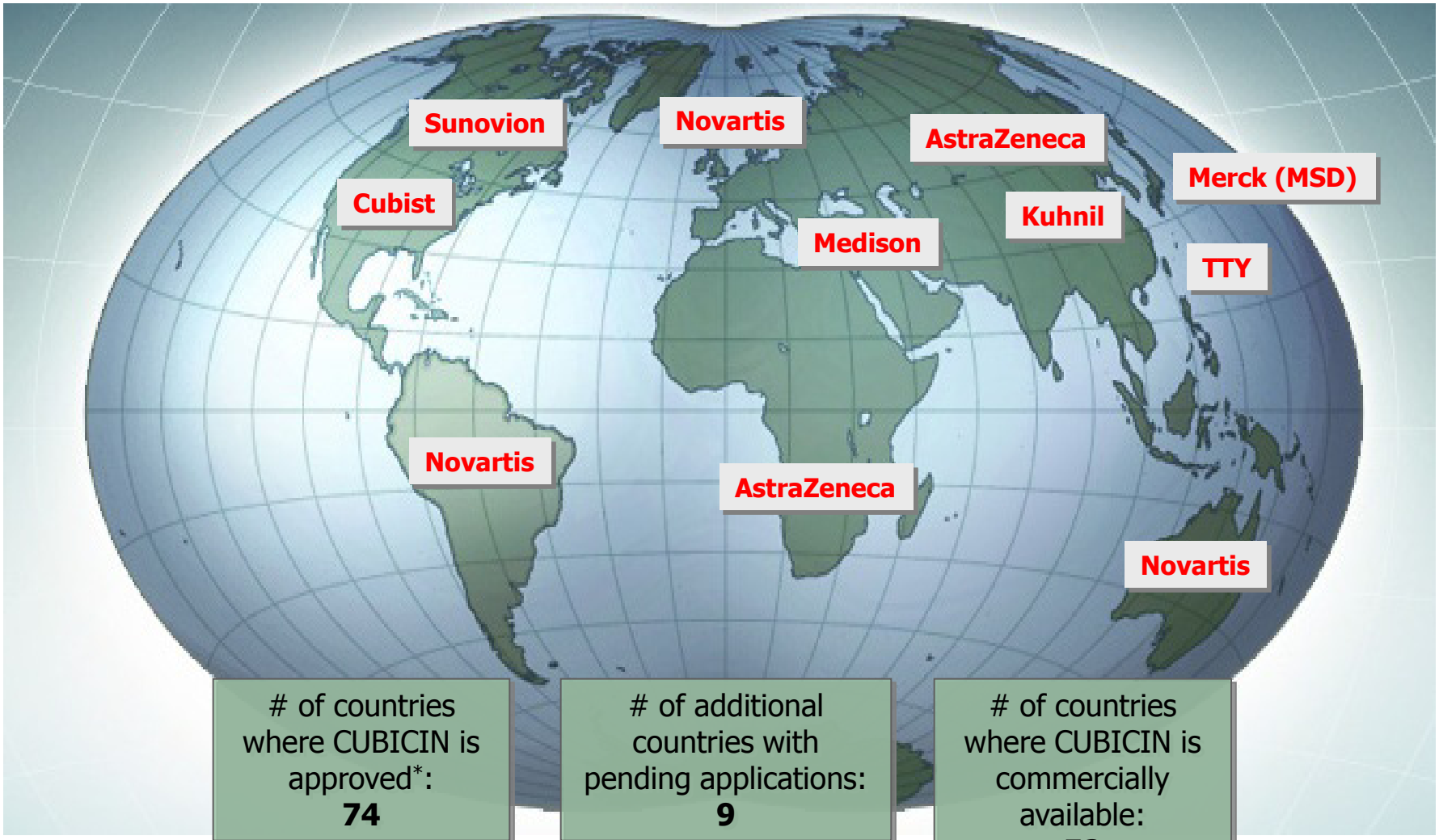
- Recommendations are provided regarding:
  - Vancomycin dosing and monitoring
  - Management of infections due to MRSA strains with reduced susceptibility to vancomycin, and vancomycin treatment.

- Once-a-day CUBICIN (6 mg/kg) is included in the IDSA Guidelines as an option for the initial therapy of MRSA bacteremia (AI) as in vancomycin(AII)
  - Strength of recommendation "A" defined as good evidence to support a recommendation for or against use;
  - Quality of evidence "I" defined as evidence from $\geq$ 1 properly randomized, controlled trial

- The IDSA Guidelines include once-a-day CUBICIN (4 mg/kg) as an option for the empiric therapy of MRSA cSSTI (AI) as well as vancomycin (AI), linezolid (AI), televancin (AI) and clindamycin (AIII), in addition to surgical debridement and broad-spectrum antibiotics for hospitalized patients with cSSTI.

Source: Liu C et al. "Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* Infections in Adults and Children." *Clinical Infectious Diseases* 2011:52 (published on line January 4, 2011.)

CUBICIN International Commercialization Advances



# of countries where CUBICIN is approved*: **74**	# of additional countries with pending applications: **9**	# of countries where CUBICIN is commercially available: **52**

*Or import license has been issued. Information is as of July 19, 2012

Competitive Landscape (1 of 2)
Gram-positive with MRSA Coverage

	CUBICIN	Vancomycin	ZYVOX® IV/oral	VIBATIV™ (telavancin)	Dalbavancin	Oritavancin	Tedizolid
Company	Cubist	Generic	Pfizer	Theravance	Durata Therapeutics	The Medicines Company	Trius Therapeutics
Class	Lipopeptides	Glycopeptides	Oxazolidinones	Lipoglycopeptide	Glycopeptides	Glycopeptides	Oxazolidinone
Dosing, form	QD, IV	BID, IV	BID, IV and oral	QD, IV	Weekly, IV	QD, IV	IV, PO
Indications	cSSSI, SAB/RIE	cSSSI, endo, bone, LRTI, septicemia	HAP, CAP, cSSSI, uSSSI, DFI, VREF	cSSSI, HAP (filed)	ABSSI (acute bacterial skin and skin structure infections)	ABSSI	ABSSI
Cidality	Bactericidal	Static	Static	Bactericidal	Bactericidal	Bactericidal	Static
Status	Market	Market	2012 Worldwide sales were $325MM up 2% 2012 US Sales were $154MM up 5% (6/2012)	Vibativ continues to be available but only from residual inventories (6/2012); Astellas announced termination of agreement for Vibativ (1/2012)	Two Phase 3 trials on-going est. completion Q4-2012 (6/2012) Paperwork Filed for IPO of ~$86M (3/2012)	Two Phase 3 clinical trials on-going: SOLO 1 – Results exp. Q4 -2012 (6/2012); SOLO -2 Results TBD NDA submission exp 2013 (5/2012)	Continued enrollment in the second Phase 3 trial in ABSSSI and remain on track to report top line data in early 2013 (6/2012)

On Market Not on Market

NOTE: In 2010, when FDA reevaluated the types of skin infections to be included in clinical trials to support an indication, the term *acute bacterial skin and skin structure infections* or ABSSI was adopted, replacing cSSSI. Information is as of July 3, 2012

Competitive Landscape (2 of 2)

Broad Spectrum with MRSA Coverage

	Tygacil	Teflaro™ (Ceftaroline)	Ceftobiprole	Omadacycline
Company	Pfizer	Cerexa/Forest Laboratories	Basilea	Paratek
Class	Tetracycline	Cephalosporin	Cephalosporin	aminomethylcyclines
Dosing, form	BID, IV	BID, IV	BID or TID, IV	QD oral and IV
Indications	cSSSI, cIAI, CAP HAP, VRE, DFI* (P3 completed)	cSSSI, CABP	cSSSI (filed) HAP, VAP, CAP, DFI (P3 completed), fever and neutropenia (P3 terminated)	Active against ABSSSI, CABP and UTI, including resistant strains such as MRSA (methicillin-resistant
Cidality	Mostly static	Bactericidal	Bactericidal	Bactericidal
Status	2012 Worldwide sales were $81MM up 12% 2012 US Sales were $40MM up 11%	Q4 -2012 sales were $6.5 million - slightly below Forest exp. Sales breakdown by indication is currently Skin – 70% Pneumonia – 30% Target is to move to a 50/50 split (6/2012)	Filed MMA in EU for the treatment of severe community and hospital acquired pneumonia (7/2012) Preparing to file in the US, timing TBD (6/2012)	Paratek announced the FDA has approved SPA related to their Ph 3 (ABSSSI and CABP) program design (3/2012)

On Market Not on Market

Information is as of July 31, 2012

Cubist Pharmaceuticals

The Shape of Cures to Come™

ENTEREG® (alvimopan)

Only FDA-approved therapy to accelerate upper and lower GI recovery following partial large or small bowel resection surgery with primary anastomosis

ENTEREG® (alvimopan)

Compound

alvimopan

Mechanism of Action

- Peripherally-acting μ opioid receptor antagonist
- First, and only, approved product to accelerate GI recovery following bowel resection

Stage

- FDA approved May 2008

Indications (U.S.)

- Restoration of bowel function following GI surgery

In Vitro Pharmacology

μ Opioid Receptor Binding*	K_i = 0.27nM
μ Opioid Receptor Antagonist Potency*	K_B = 0.17nM

* **human cloned receptors**

Pharmacokinetics

- High degree of peripheral selectivity
- Orally bioavailable
- BID dosing

How Supplied

- Capsules are available in unit-dose packs of 30 capsules (30 doses)

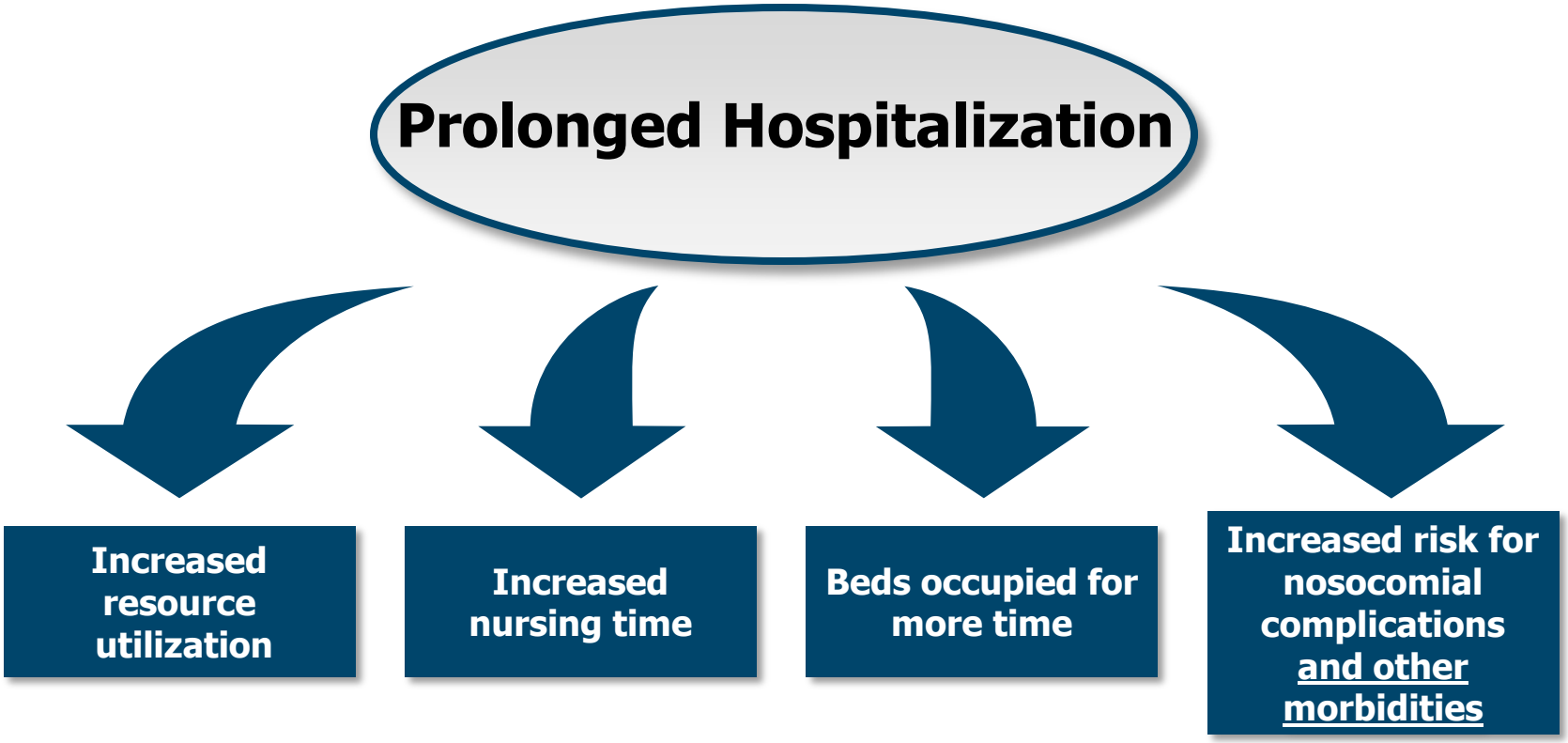
Commercial Outlook

- Approximately 400,000 to 450,000 bowel resections performed annually in the U.S.
- At least $100 million in U.S. peak year sales expectation

IP Protection

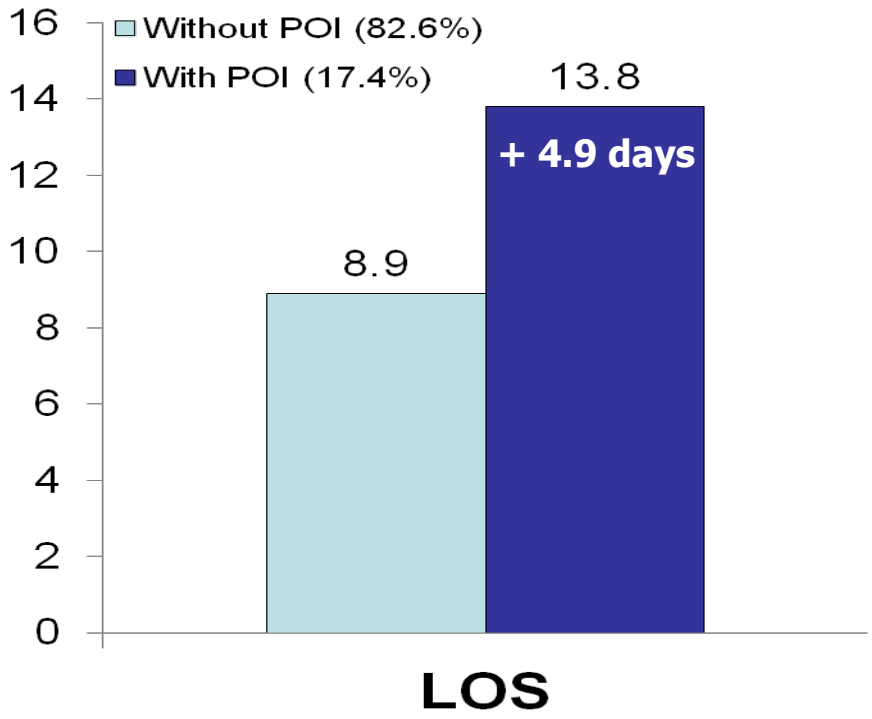
- Composition of matter patent protection until March 2016
- Two method of treatment patents (expiring November 2020 and July 2030)

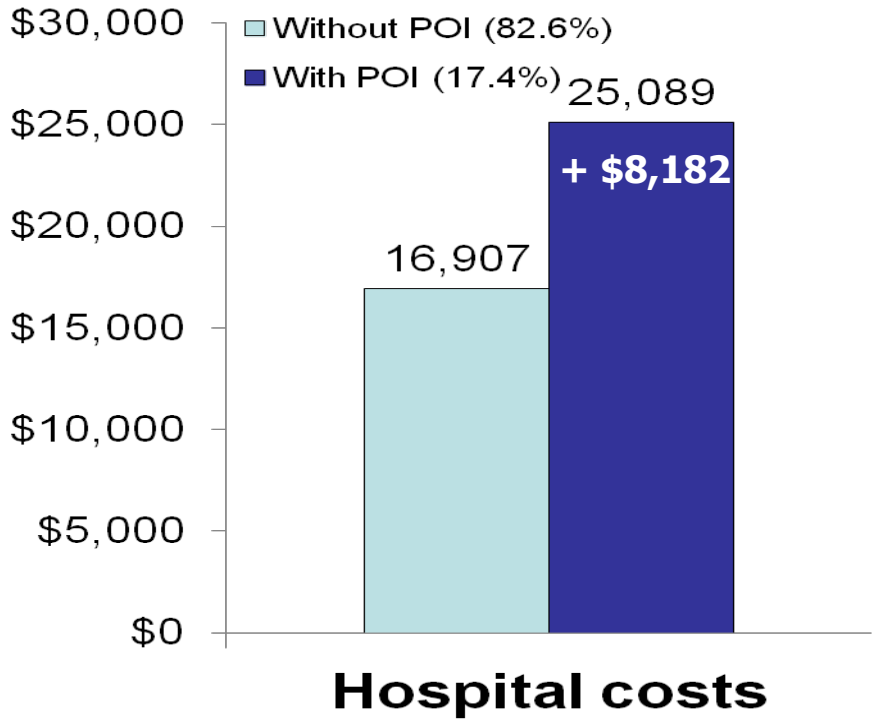
Overall Potential Impact of Delayed GI Recovery and Postoperative Ileus



Sources: Schuster TG, Montie JE. *Urology*. 2002;59:465. Holte K, Kehlet H. *Br J Surg*. 2000;87:1480; [c] Chang SS, et al. *J Urol*. 2002;67:208; Sarawate CA, et al. *Gastroenterology*. 2003;124:A-828; Behm B, et al. *Clin Gastroenterol Hepatol* .2003;1:71-80; Bosio RM, et al. *Semin Colon Rectal Surg*. 2005;16:235-238; Kehlet H, et al. *Am J Surg*. 2001;182(suppl 5A):3S-10S.

Consequences of Delayed GI Recovery After Colectomy



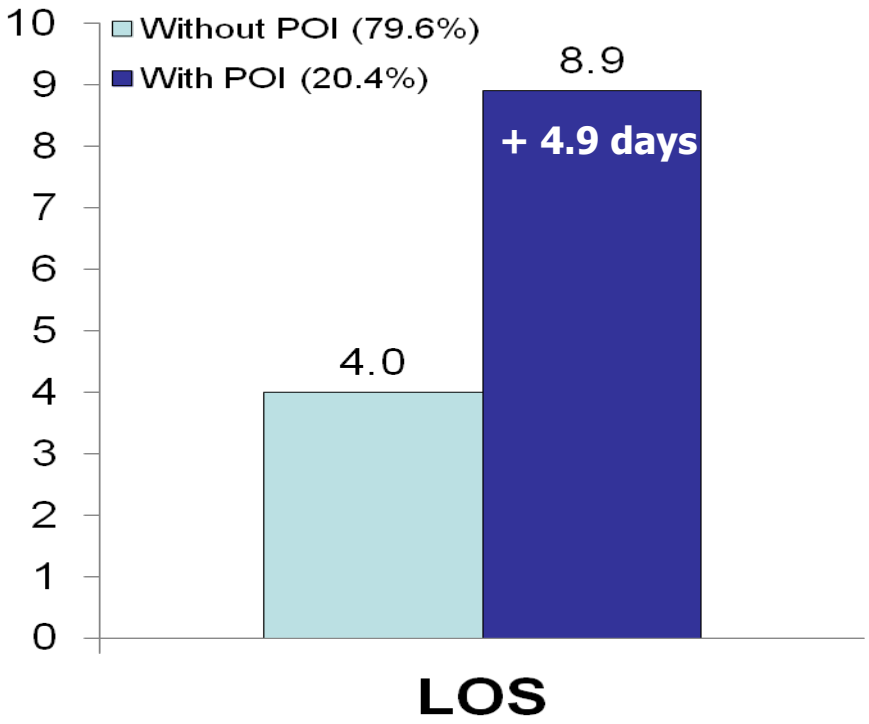


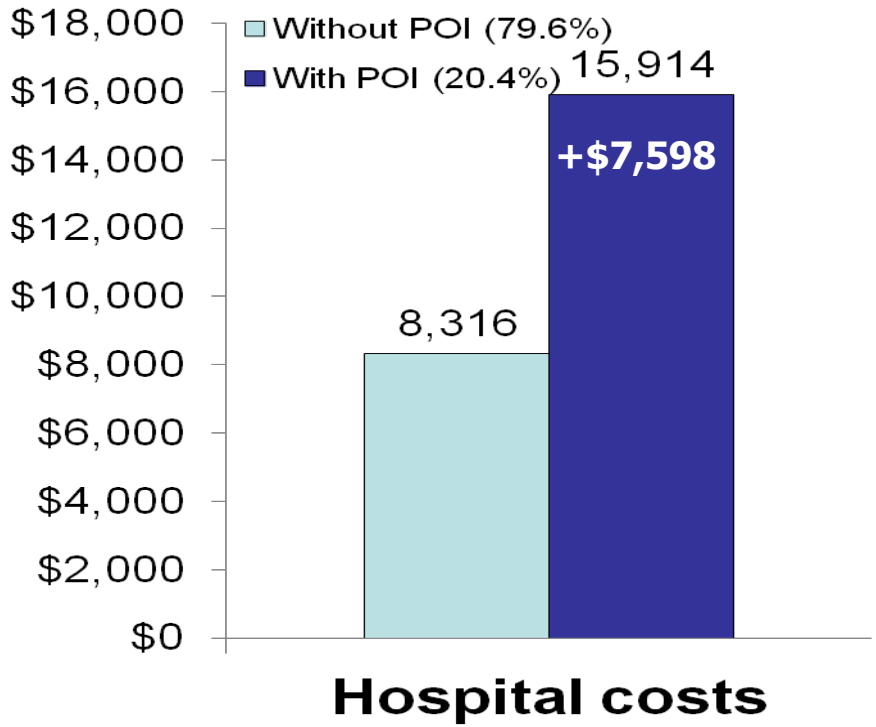
Cumulative Costs of a Coded POI*: $ 1,460,000,000[2]

* Total hospitalization plus readmission.

Sources: Data from Premier Perspective database and includes both open and laparoscopic colectomies.
POI = Postoperative ileus; defined using ICD-9-CM codes for paralytic ileus (560.1) and/or digestive system complications not elsewhere classified (997.4)
Iyer S, et al. *J Man Care Pharm*. 2009;15:485-494; 2. Goldstein JL, et al. *P & T*. 2007 32(2):82-89;.

Consequences of Delayed GI Recovery After Colectomy - Data from 1 Institution





Readmission rate; 27% in patients with POI; 11% in patients without POI

Sources: 31% of the included colectomies were performed via open technique.
POI = Postoperative ileus defined as > 3 episodes of emesis (vomiting) in 24 hours with return to NPO (nothing by mouth) status and/or insertion of a nasogastric tube. SOURCE: Asgeirsson T, et al. *J Am Coll Surg.* 2010 Feb;210(2):228-31.

Potential Care Pathway Elements

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Preoperative

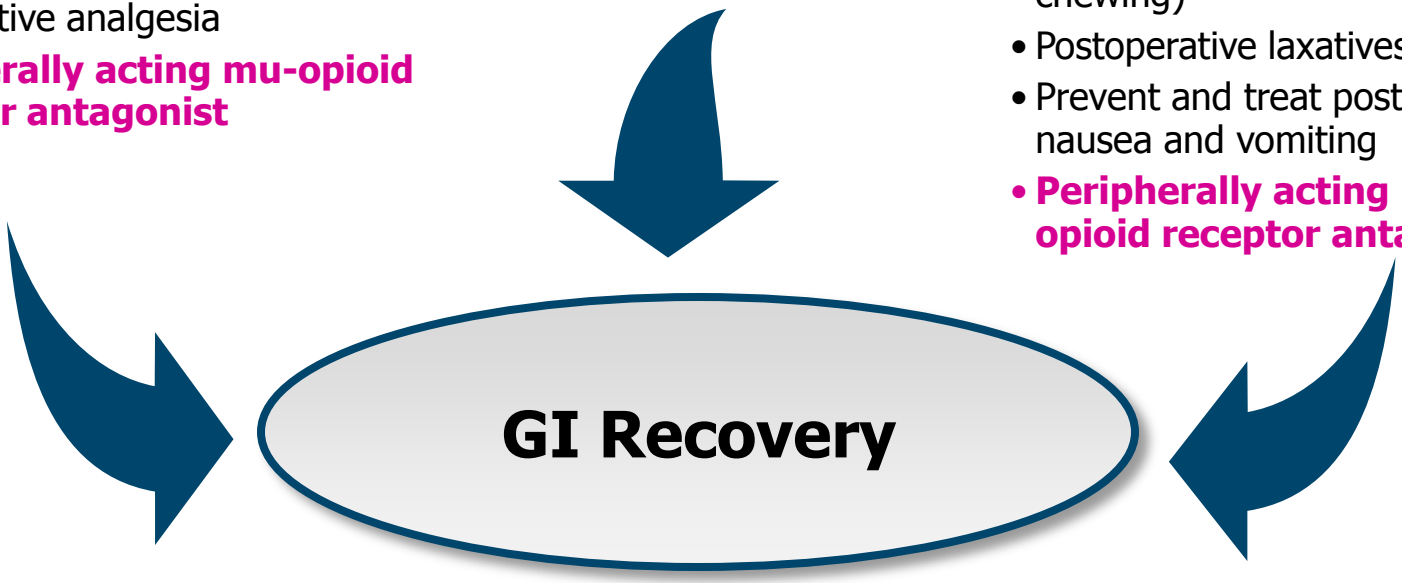
- Preoperative counseling
- Avoidance of bowel preparation
- Preoperative nutritional support/ carbohydrate loading
- Pre-emptive analgesia
- **Peripherally acting mu-opioid receptor antagonist**

Intraoperative

- Minimally invasive surgery
- Fluid management

Postoperative

- Multimodal analgesia
- Selective NGT use / early removal
- Early mobilization
- Postoperative feeding
- Sham feeding (e.g., gum chewing)
- Postoperative laxatives
- Prevent and treat postoperative nausea and vomiting
- **Peripherally acting mu-opioid receptor antagonist**



Sources: 1. Lassen K, et al. *Arch Surg*. 2009;144:961-969; 2. Wolff BG, et al. *J Am Coll Surg*. 2007;205:43-51; 3. Kehlet H. *Curr Opin Crit Care*. 2009;15:355-358; 4. Mukherjee A, et al. *Col Rect Surg*. 2005;16:215-227; 5. Gouvas N, et al. *Int J Colorectal Dis*. 2009; 24:1119-1131; 6. ENTEREG (alvimopan) prescribing information. 2009, Adolor Corporation; 9. Delaney CP, et al. Evaluation of Alvimopan in Clinical Practice: A National Matched-Cohort Study of 30-Day Postoperative In-Hospital Morbidity and Mortality in Patients Undergoing Bowel Resection. *Dis Colon Rectum*. 2011;54(4):195. poster presentation at ASCRS, Mtg. May 14 – 18, 2011, Vancouver, British Columbia.

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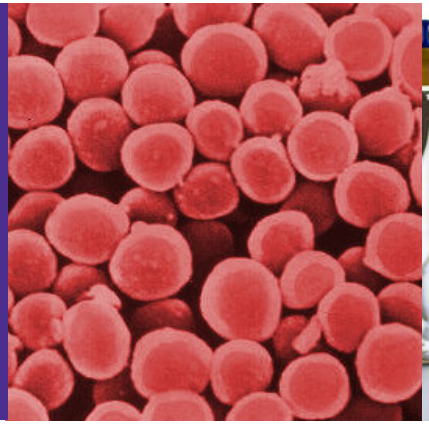

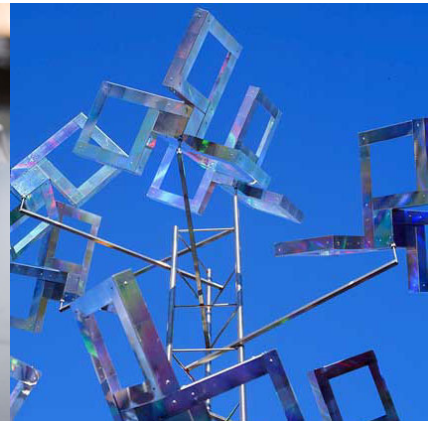

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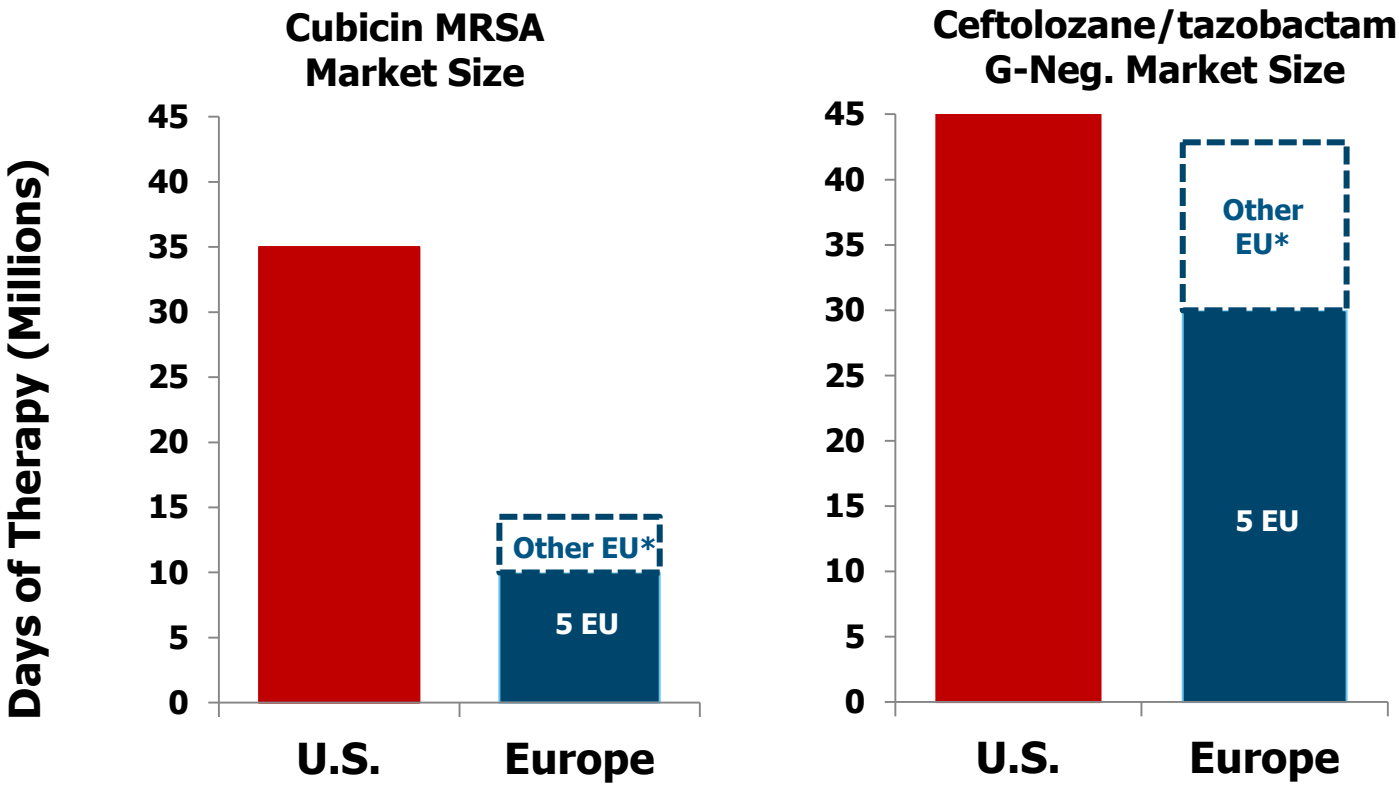
Gram-negative Infections

Gram-negative Market Opportunity

U.S. & EU: 80% more days of therapy than MRSA Market



Sources: The U.S. Hospital Antibiotic Market Guide, Jan 2011-Dec 2011 and the European Hospital Antibiotics Market Guide, Jan 2010 – Jun 2010 by AMR/Arlington Medical Resources, Inc; IMS sales data *Other EU is estimated at 30% of Total EU based on select brand antibiotic reported sales, complete IMS sales data not available

Ceftolozane/Tazobactam G-Neg. Market Size includes days of therapy from the following antibiotics: Piperacillin-tazobactam, Levofloxacin (IV Only), Ciprofloxacin (IV Only), Cefepime, Ceftazidime, Meropenem, Doripenem and Imipenem-cilistatin

5 EU = UK, France, Germany, Italy, and Spain

Gram-negative Infections Competitive Market Overview

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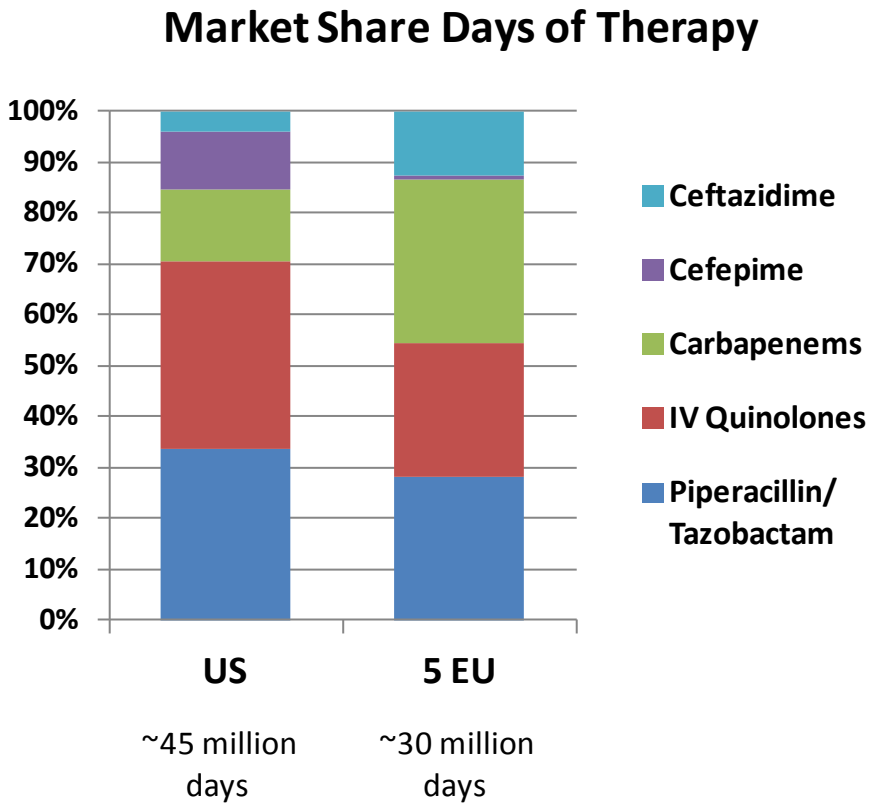
U.S. & 5 EU Days of Therapy (Defined by select IV Antibiotics)



Carbapenems are used much more widely in Europe than in the US, while quinolones are used less often

Ceftolozane/tazobactam competitive market is identified based on relevant infection and pathogen treatment using IV antibiotics:

- Zosyn® – Piperacillin/Tazobactam
- Levaquin® – Levofloxacin IV
- Cipro® – Ciprofloxacin IV

(Levaquin® and Cipro® – IV Quinolones)

- Merrem® – Meropenem
- Primaxin® – Imipenem-Cilastatin
- Doribax® – Doripenem

(Merrem®, Primaxin®, Doribax® – Carbapenems)

- Fortaz® – Ceftazidime
- Maxipime® – Cefepime

Sources: IMS U.S. Non-Retail grams January 2011 - December 2011 converted to days of therapy;
IMS 5EU Hospital and Retail grams January 2009 - December 2009 converted to days of therapy
Defined market includes: piperacillin/tazobactam, ciprofloxacin IV, levofloxacin IV, meropenem, imipenem/cilastatin, doripenem, cefepime, and ceftazidime
5 EU = UK, France, Germany, Italy, and Spain

Key Infections Caused by Gram-negative Pathogens

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% Days of Therapy	U.S.	EU
Lower Respiratory	34%	37%
Skin	13%	8%
Genitourinary	15%	11%
Systemic	16%	15%
GI / Biliary	10%	11%
Abdominal / Pelvic	5%	6%
Other	7%	12%

% Hospital Days of Therapy Treated Empirically	
U.S.	64%
EU	67%

Sources: The U.S. Hospital Antibiotic Market Guide, January 2011-December 2011 and the European Hospital Antibiotics Market Guide, January 2010-June 2010 by AMR/Arlington Medical Resources, Inc

Defined market includes: piperacillin/tazobactam, ciprofloxacin IV, levofloxacin IV, meropenem, imipenem/cilastatin, doripenem, cefepime, and ceftazidime

P. aeruginosa a Pathogen of Concern in U.S. & EU

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Incidence Higher in EU

	% of Identified Pathogens	
	U.S.	**EU**
Lower Respiratory	25%	45%
Skin	12%	30%
Genitourinary	13%	15%
Systemic	15%	17%
GI / Biliary	1%	8%
Abdominal / Pelvic	9%	8%
Other	5%	42%

Sources: The U.S. Hospital Antibiotic Market Guide, January 2011-December 2011 and the European Hospital Antibiotics Market Guide, January 2010-June 2010 by AMR/Arlington Medical Resources, Inc

Defined market includes: piperacillin/tazobactam, ciprofloxacin IV, levofloxacin IV, meropenem, imipenem/cilastatin, doripenem, cefepime, and ceftazidime

MDR Pa is a Substantial Problem in U.S. Hospitals

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% of Isolates Showing Resistance

Antimicrobial resistant pathogen	% isolates showing resistance		
	ICU	Non-ICU	Outpatient
Methicillin-resistant *Staphylococcus aureus* (MRSA)	52.9	46.0	31.1
Ciprofloxacin/ofloxacin-resistant *Pseudomonas aeruginosa*	34.8	27.7	23.4
Levofloxacin-resistant *P aeruginosa*	35.3	30.5	24.5
Imipenem-resistant *P aeruginosa*	19.1	12.3	7.0
Ceftazidime-resistant *P aeruginosa*	13.9	8.8	4.6
Piperacillin-resistant *P aeruginosa*	17.5	11.6	6.0

"These are life-threatening drug-resistant infections, and we're seeing them every day. What is worse is that our ammunition is running out and there are no reinforcements in sight." - *IDSA President, Martin J. Blaser, MD*

Sources: CDC National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004*; Am J Infect Control*; 2004 (32):470.

Gram-negative Competitive Landscape (1 of 2)
Marketed Products

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	ZOSYN®	DORIBAX®	PRIMAXIN®	MERREM I.V.®	FORTAZ®	MAXIPIME®	CIPRO®	LEVAQUIN®
Company	Pfizer; Generics	J&J	Merck; Generics	AstraZeneca	GSK; Generics	BMS; Generics	SP/Bayer; Generics	J&J
Generic name	Piperacillin+ tazobactam	Doripenem	Imipenem+ cilastatin	Meropenem	Ceftazidime	Cefepime	Ciprofloxacin	Levofloxacin
Class	Ampicillin + β-lactamase inhibitor	Carbapenem	Carbapenem	Carbapenem	3rd generation Cephalosporin	4th generation Cephalosporin	Quinolone	Quinolone
Dosing, form	3 – 4x/day; IV	3x/day; IV	3 - 4x/day; IV, IM	3x/day; IV	3x/day; IV	2x/day; IV	2-3x/day; PO & IV	1x/day; PO & IV
Indications:								
NP	✓		✓		✓	✓	✓	✓
UTI		✓	✓		✓	✓	✓	✓
IAI	✓	✓	✓	✓	✓	✓		
cSSSI	✓		✓	✓	✓	✓	✓	✓
Pediatrics	Yes	No		In bacterial meningitis in peds >3mos of age	Yes	Yes	Yes	No
Cidality	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Notes	Generic available as of Sep 2009	Approved Oct 2007 in U.S.	IV available as generic; IM patent expired Sep 2009	Hospira rcvd FDA approval for generic version June 2010	Approved July 1985 in U.S. Patent expired 2003	IV Patent expired 2008	Approved Oct 1987 in U.S. Patent expired 2003	Approved Dec 1996; Patents expired March 2011

Information as of July 3, 2012

Gram-negative Competitive Landscape (2 of 2)
Known Compounds in Development

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	Ceftolozan/ Tazobactam	Ceftazidim/ Avibactam	KB001	Plazomicin	Ceftaroline/ Avibactam	TP-434
Company	Cubist	Forest	KaloBios/ Sanofi	Achaogen	Forest	Tetraphase
Stage	Phase 3	Phase 3	Phase 2	Phase 2	Phase 2	Phase 2
Class	Cephalosporin + β-lactamase inhibitor	Cephalosporin + β-lactamase inhibitor	PcrV antibody	Aminoglycoside	Cephalosporin + β-lactamase inhibitor	Tetracycline
Dosing form	IV	IV	IV	IV	IV	IV, PO
Indications: **NP** **cUTI** **cIAI** **Other**	 P1 P3 P3 n/a	 ? P3 P3 ?	 VAP P2 n/a n/a CF P2	P2	P2	P2 (IV Only)
Cidality	Cidal	Cidal	n/a	Cidal	Cidal	Static
Notes		NDA submission is planned for 2014 (6/2012)	Phase 2a trial with KB001 suggests potential in Ventilator Associated Pneumonia (VAP) (6/2012)	Phase 2 met objectives of safety and efficacy compared to levofloxacin (6/2012)	Phase 3 is to start in Q2 2013 NDA submission is planned for 2015 (6/2012)	

Information as of July 3, 2012

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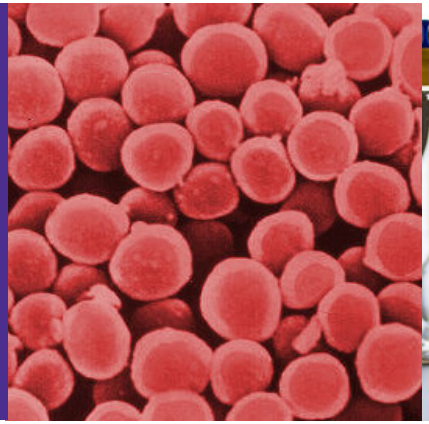

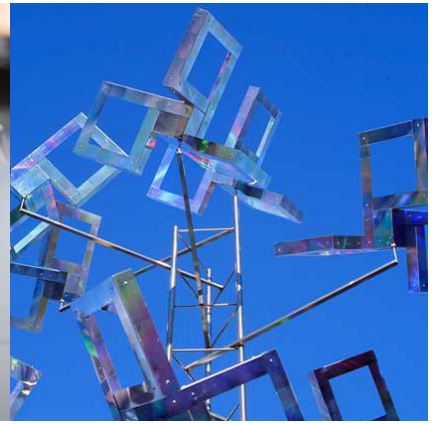

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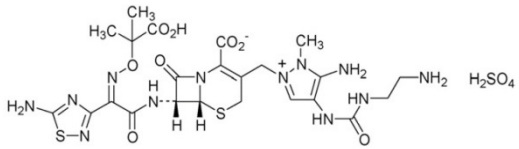
Ceftolozane/tazobactam Program

A Promising New Weapon Against a Very Bad Bug:
Pseudomonas aeruginosa

Ceftolozane/tazobactam* Overview

Compound

- Ceftolozane/tazobactam
- Fixed 2:1 ratio



Ceftolozane

Mechanism of Action

- Cell wall synthesis inhibition (Ceftolozane)
- β-lactamase inhibitor (tazobactam)

Stage

- Phase 3

In Vitro Microbiology

Cidality	Rapidly Bactericidal
P. aeruginosa *K.pneumoniae* *E. coli*	MIC_{90} = 4 µg/mL MIC_{90} = 4 µg/mL MIC_{90} = 0.5 µg/mL (U.S. data)
Resistance	Low mutation frequency in Pseudomonas biofilm

Human Safety

- Well tolerated in > 385 subjects/patients studied to date

Pharmacokinetics

- Linear PK
- Rapid tissue distribution
- No accumulation
- Renal excretion
- Low protein binding

Phase 2 Efficacy

- High clinical response rate in cIAI and cUTI Phase 2 studies

Commercial Outlook

- Approximately 45 million days of therapy U.S. and 30 million days of therapy EU
- At least $1 Billion in U.S./EU peak year sales expectation; assuming clinical and regulatory success

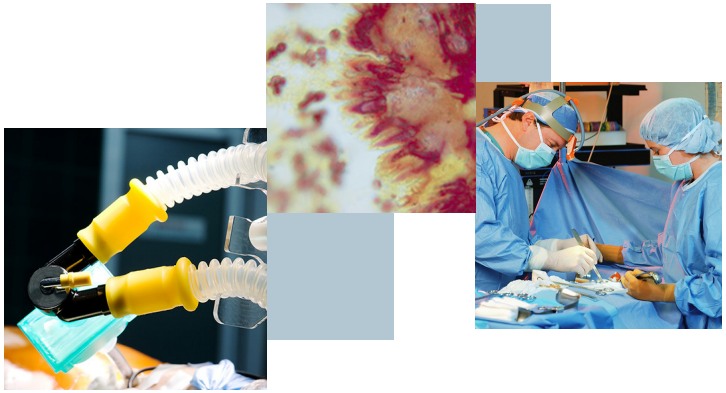
IP Protection

- U.S. IP through 2024
- EU IP through 2023

Sources: IMS: Non-Retail grams Jan2009-Dec 2009 converted to days of therapy
Defined market includes: piperacillin/tazobactam: Zosyn & generics; IV quinolones: ciprofloxacin IV, levofloxacin IV; carbapenems: meropenem, imipenem/cilastatin, doripenem; cephalosporins: cefepime, and ceftazidime.
•Rights under a license from Asetllas Pharma Inc. acquired with Cubist's acquisition of Calixa Therapeutics Inc.* Ceftolozane/tazobactam was formerly known as CXA-201
•PACTS: Program to Assess Ceftolozane/Tazobactam Susceptibility; JMI laboratories 2011

Pseudomonas aeruginosa (PA) is a killer

- Increased mortality associated with inadequate therapy in infections in ICU
- Significant rates of mortality associated with VABP
- *Pseudomonas aeruginosa* is the most common Gram-negative pathogen associated with HABP or VABP
- Concerning levels of multi-drug-resistance associated with *Pseudomonas aeruginosa*



Pseudomonas aeruginosa is Commonly Resistant to Antibiotic Therapy

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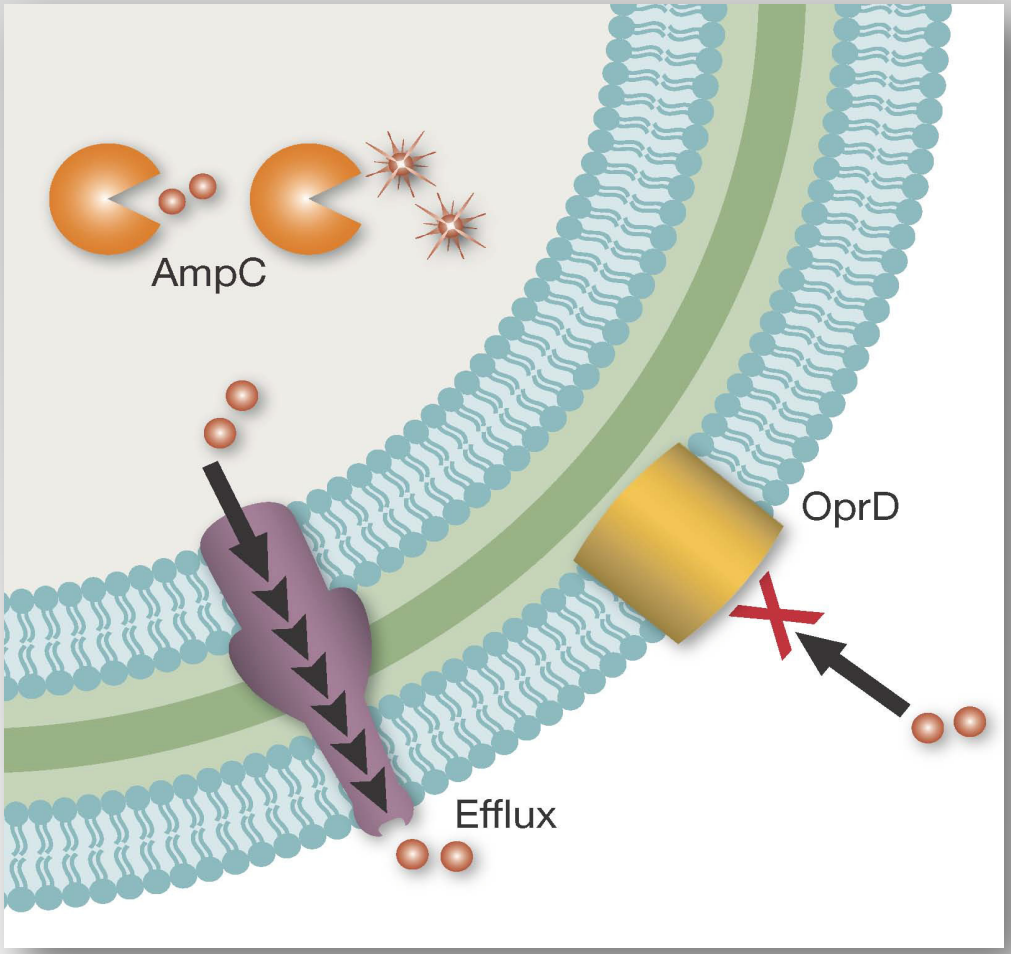
PA Utilizes Several Mechanisms of Resistance



Ceftolozane/tazobactam (CXA-201) Potent Antipseudomonal Activity

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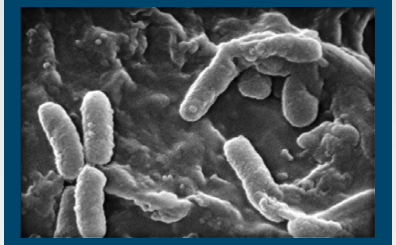
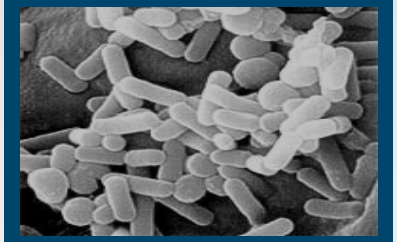
CXA-201 Coverage

Multidrug resistant *P. aeruginosa*

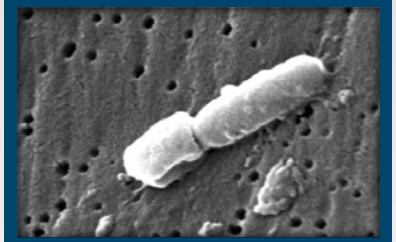
ESBL-producing Enterobacteriaceae



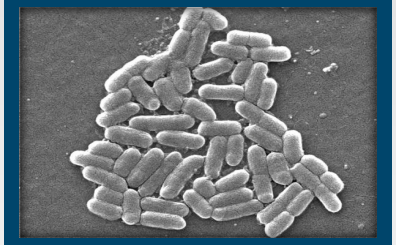
P. aeruginosa



Enterobacter



K. pneumoniae



Escherichia (E. coli)

Ceftolozane — Highly Differentiated Profile

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- Ceftolozane demonstrated excellent activity *in vitro* against a panel of >900 *Pa* strains, including cephalosporin- and carbapenem-resistant isolates

Agent	% Susceptible[a]	
	US	**5 EU**
Ceftolozane/tazobactam[b]	97.7	97.0
Cefepime	80.7	83.5
Ceftazidime	80.9	78.0
Meropenem	78.3	77.6
Doripenem	82.7	81.1
Zosyn® (piperacillin/tazobactam)	74.6	73.9

Source: Data for 973 *P. aeruginosa* from 2011 PACTS surveillance program (JMI laboratories)
a. Criteria as published by CLSI [2012]
b. MIC ≤ 8ug/mL
5 EU = UK, France, Germany, Italy, and Spain

Broad Gram-negative Spectrum of Activity

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	Ceftolozane/tazobactam		Ceftazidime	Piperacillin/ tazobactam
Species (N)	MIC_{50}	% MIC≤8 µg/mL	%S	%S
P. aeruginosa (973)	1	97.7	80.9	74.6
E. coli (1244)	0.25	99.3	91.5	94.5
K. pneumoniae (668)	0.25	90.4	83.7	86.2
Enterobacter spp. (525)	0.25	93.1	77.7	81.9
Citrobacter spp. (174)	0.25	90.8	83.3	85.1
Serratia spp. (287)	0.5	99.3	96.9	97.6
Proteus mirabilis (203)	0.5	100	99.5	99.0

- Combination of ceftolozane with tazobactam broadens spectrum to better cover other important Gram-negative bacteria
- The addition of tazobactam substantially enhances activity against beta-lactam-resistant *Enterobacteriaceae* strains

Source: PACTS: Program to Assess Ceftolozane/Tazobactam Susceptibility; JMI laboratories 2011

Ceftolozane/tazobactam

Broad Gram-negative Spectrum of Activity

	US			5 EU		
Species	**N**	**MIC $_{90}$ (µg/mL)**		**N**	**MIC $_{90}$ (µg/mL)**	
		Ceftolozane	**Ceftolozane/ tazobactam**		**Ceftolozane**	**Ceftolozane/ tazobactam**
P. aeruginosa	973	4	4	491	4	4
E. coli	1244	4	0.5	1056	8	0.5
K. pneumoniae	668	>32	4	271	>32	>32
Enterobacter spp.	525	16	8	228	16	4
Citrobacter spp.	174	16	8	100	16	8
S. marcescans	287	1	1	120	2	1
Acinetobacter spp.	208	>32	>32	96	>32	>32

2011 PACTS surveillance program (JMI laboratories)

Combination of ceftolozane with tazobactam (in fixed 2:1 ratio)

- Does not alter strong activity of ceftolozane against Pa
- Substantially enhances activity against beta-lactam-resistant *Enterobacteriaceae* strains

Ceftolozane/tazobactam

In Vitro Studies Show Lower Potential for Resistance Emergence

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- *In vitro* antibiotic resistance development can be predictive of the tendency for development of resistance in the clinic
  - Two methods are commonly used:
    - Single-step selection or multiple-step selection
- Single-step selection
  - Culture P.A. with ceftolozane (or other drugs) at 4x, 8X and 16X MIC then look for resistant mutants
    - At 4X, 8X and 16X the ceftolozane MIC no spontaneous mutants were detected
    - Ceftolozane has a lower incidence of selecting for spontaneous resistance in *P. aeruginosa* than ceftazidime, imipenem and ciprofloxacin
- Multi-step selection

  – Serial passage P.A. with ceftolozane (or other drugs) and look for *increase* in MIC after 16 passages
    - The increase in MICs in cultures exposed to ceftolozane was slower than for cells exposed to ceftazidime or meropenem
    - At day 16, there was only a slight increase in the MIC of ceftolozane

Ceftolozane/tazobactam Clinical Data to Date

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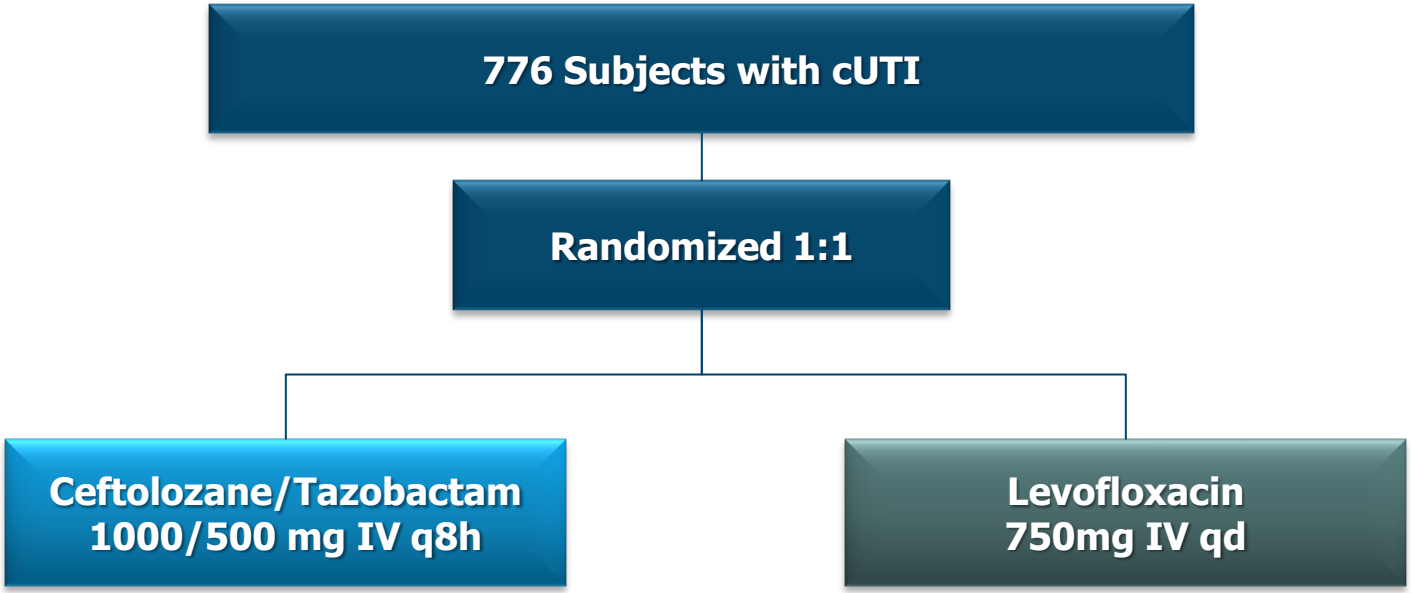
- Plasma concentrations at tolerated doses well within projected efficacious target
- High clinical response rate in patients with cUTI and with cIAI
- Demonstrated excellent lung penetration of ceftolozane – exceeded our expectations
- Safe and well tolerated in the 385 subjects or patients in phase 1 and 2 studies conducted to date
- Phase 3 Trial Status
  - cUTI trials first patient enrolled 7/29/11
  - cIAI trials first patient enrolled 12/8/11
  - Ventilator-associated pneumonia (VAP) trial expected to begin 2H12

Phase 3 cUTI Global Study Enrolling

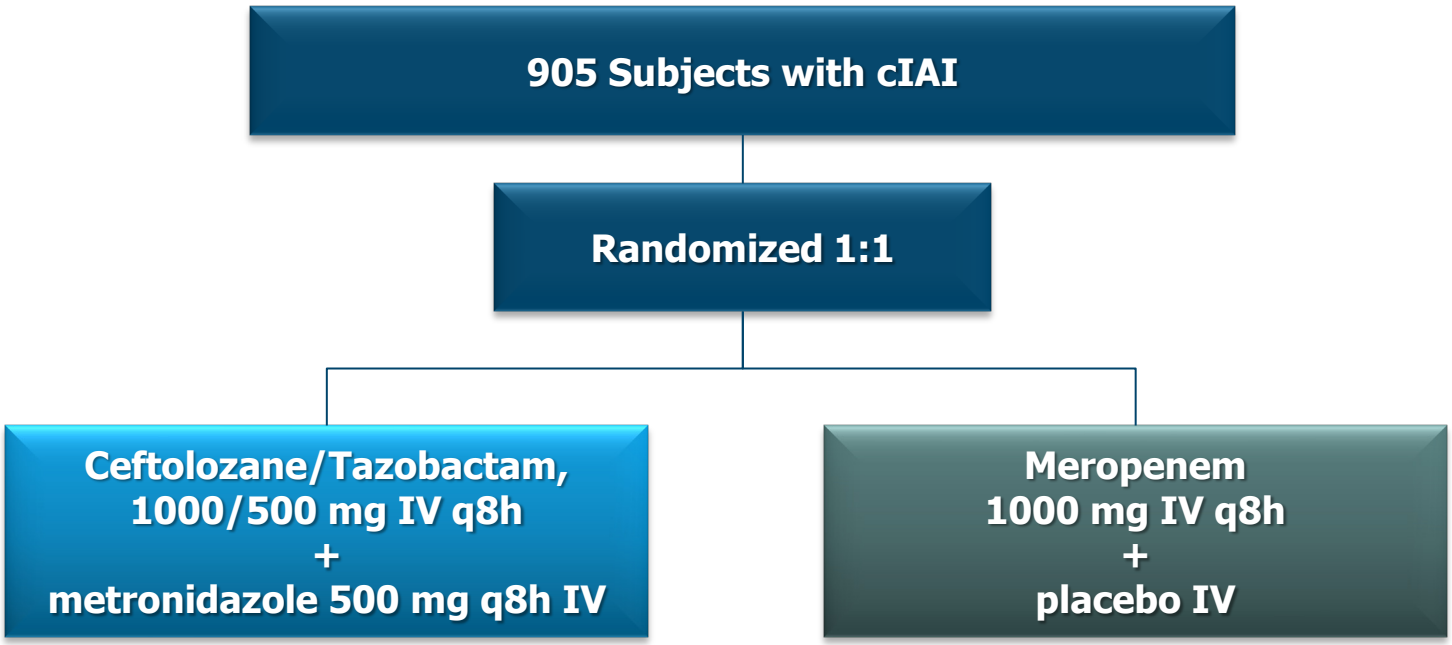
- Two, randomized, controlled, double-blind, multi-center Phase 3 trials in adult patients with cUTI
  - Primary Objective: To demonstrate the non-inferiority of ceftolozane/tazobactam versus comparator (levofloxacin) in adult subjects with cUTI using a non inferiority margin of 10%





Phase 3 cIAI Global Study Also Enrolling

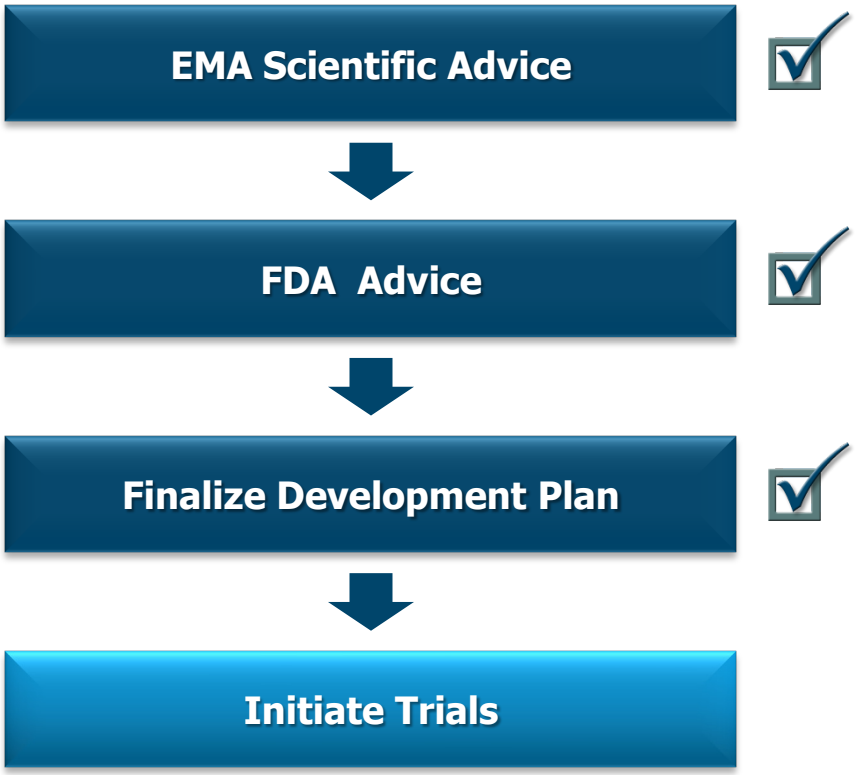
- Two, randomized, controlled, double-blind, multi-center Phase 3 trials in adult patients with cIAI
  - Primary Objective: To demonstrate non-inferiority of ceftolozane/tazobactam and metronidazole vs. meropenem in adult patients with cIAI





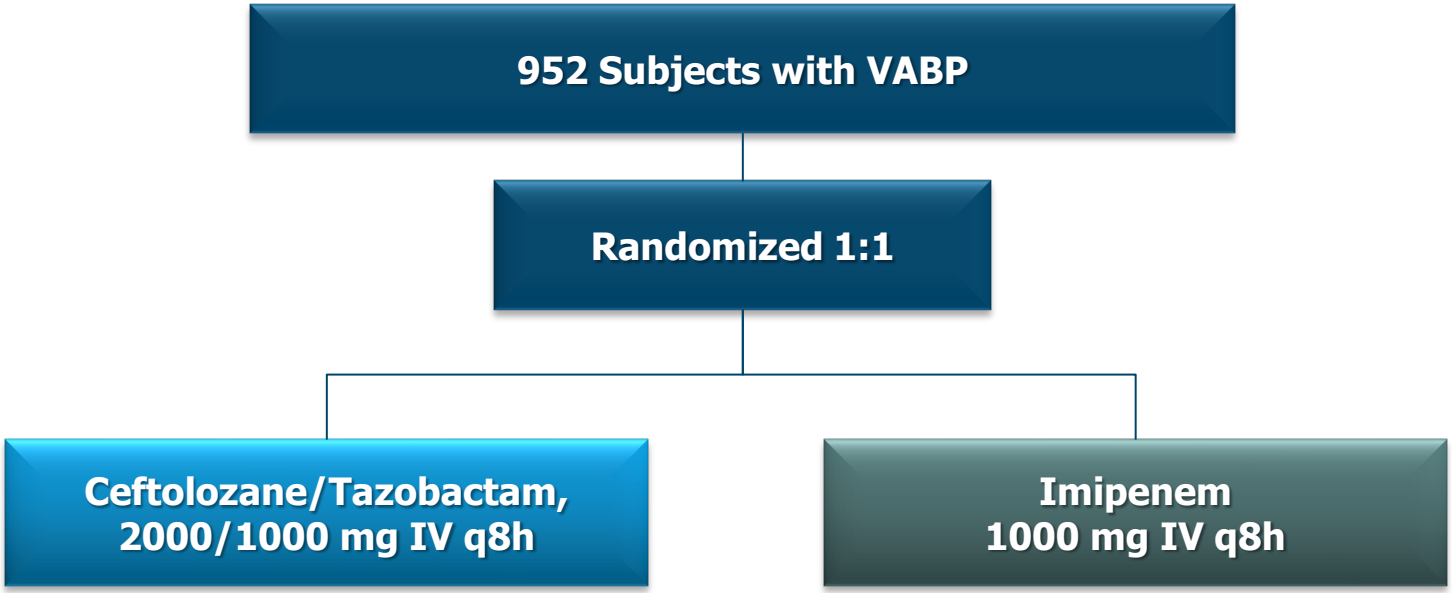
NOW: HABP/VABP Phase 3 Path Forward Clarified

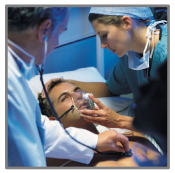
- Clarity achieved on regulatory path
- On target to initiate VABP Phase 3 this year

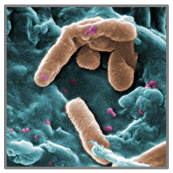


Phase 3 VABP Global Study Design

- One, randomized, controlled, double-blind, multi-center Phase 3 trials in adult patients with VABP
  - Primary Objective: To demonstrate non-inferiority of ceftolozane/tazobactam vs. imipenem in 28-day mortality rates in adult patients with VABP, using a non-inferiority margin of 10%







Ceftolozane/tazobactam Development Timeline on Target

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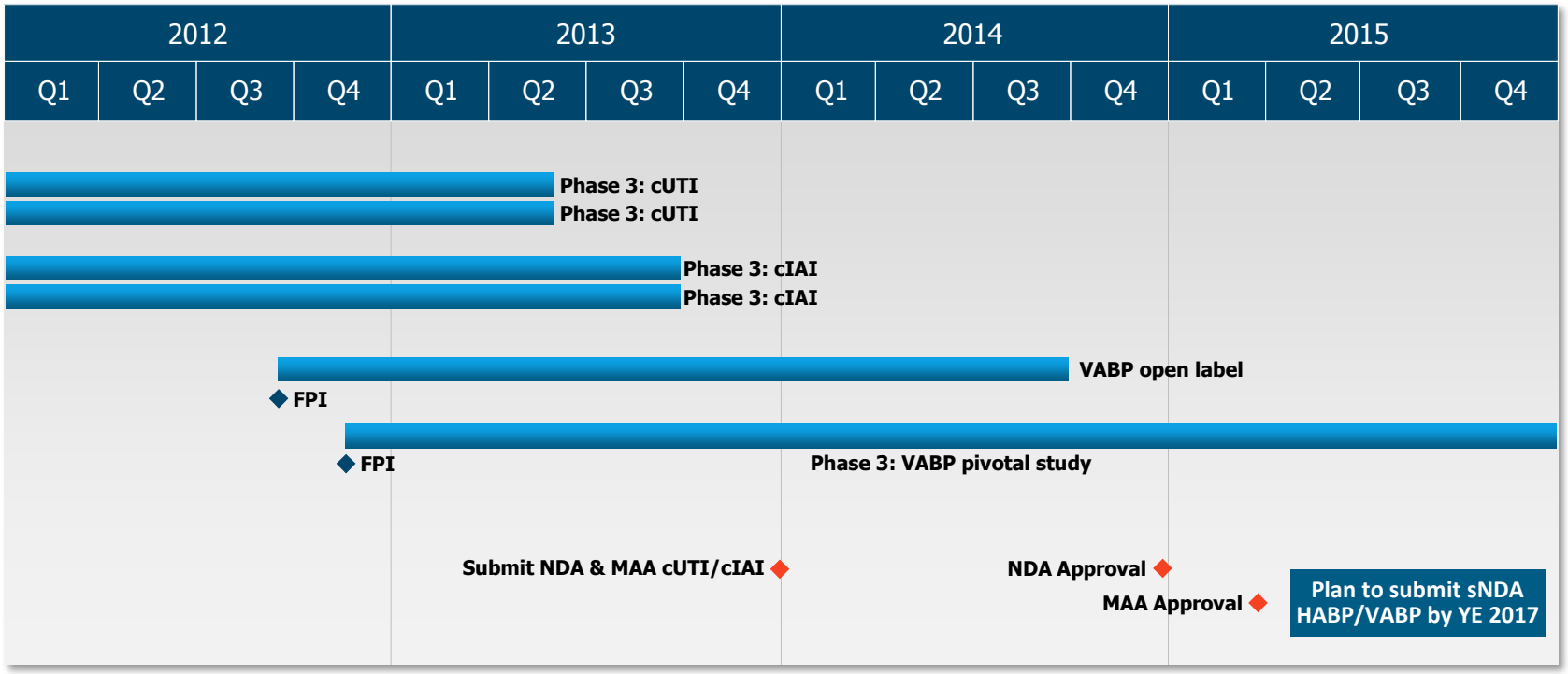
Development Timeline



Ceftolozane/tazobactam Summary

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Product Description

- Ceftolozane/tazobactam is a novel broad spectrum anti-pseudomonal cephalosporin combined with a beta-lactamase inhibitor
- Highly differentiated profile covering multidrug-resistant Gram-negative bacteria

Development Status

- Phase 2 trials completed in cIAI/cUTI
- Phase 3 trials ongoing in cIAI/cUTI

Next Steps

- Phase 3 trial in HABP/VABP expected to start this year
- Data from cUTI and cIAI Phase 3 trials—mid 2013
- Anticipated NDA in 2013 for indications in cUTI and cIAI
- Supplementary filing in HABP/VABP target: YE 2017



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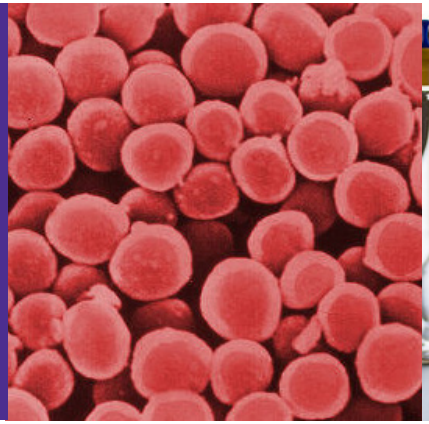
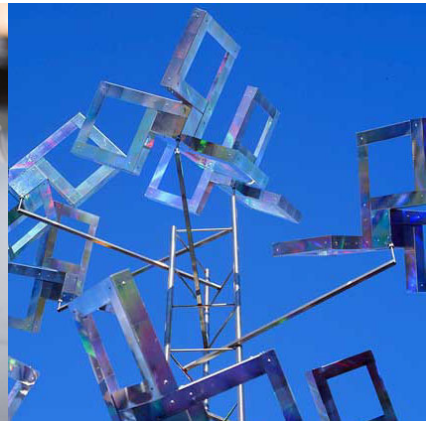
PHARMACEUTICALS





Cubist Pharmaceuticals

The Shape of Cures to Come™

CB-315

A potent, oral, cidal lipopeptide in development for the treatment of *Clostridium difficile*-associated diarrhea

CB-315 Overview

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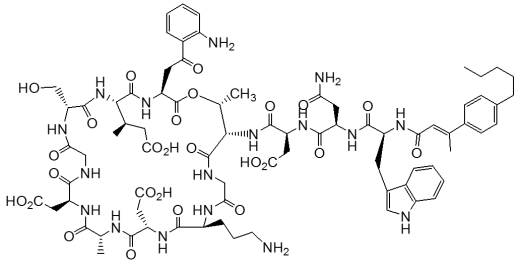
Compound



Mechanism of Action

- Disruption of membrane potential

Stage

- Phase 3

In vitro Microbiology

C. difficile	MIC_{90} = 0.5µg/mL; includes NAP1 isolates
Selectivity	No activity against enteric Gram-negative including bacteroides *spp.* Minimal vs. G(+) gut flora
Cidality	Rapid killing of vegetative cells (>3log in 24 hrs); includes NAP1 isolates
Resistance (*C. difficile*)	Low resistance incidence

Pharmacokinetics

- Low oral bioavailability < 1% (healthy rats and dogs)

Phase 2 Efficacy

- Similar cure rates to vancomycin
- Lower recurrence rates vs. vancomycin; 250 mg BID dose statistically superior

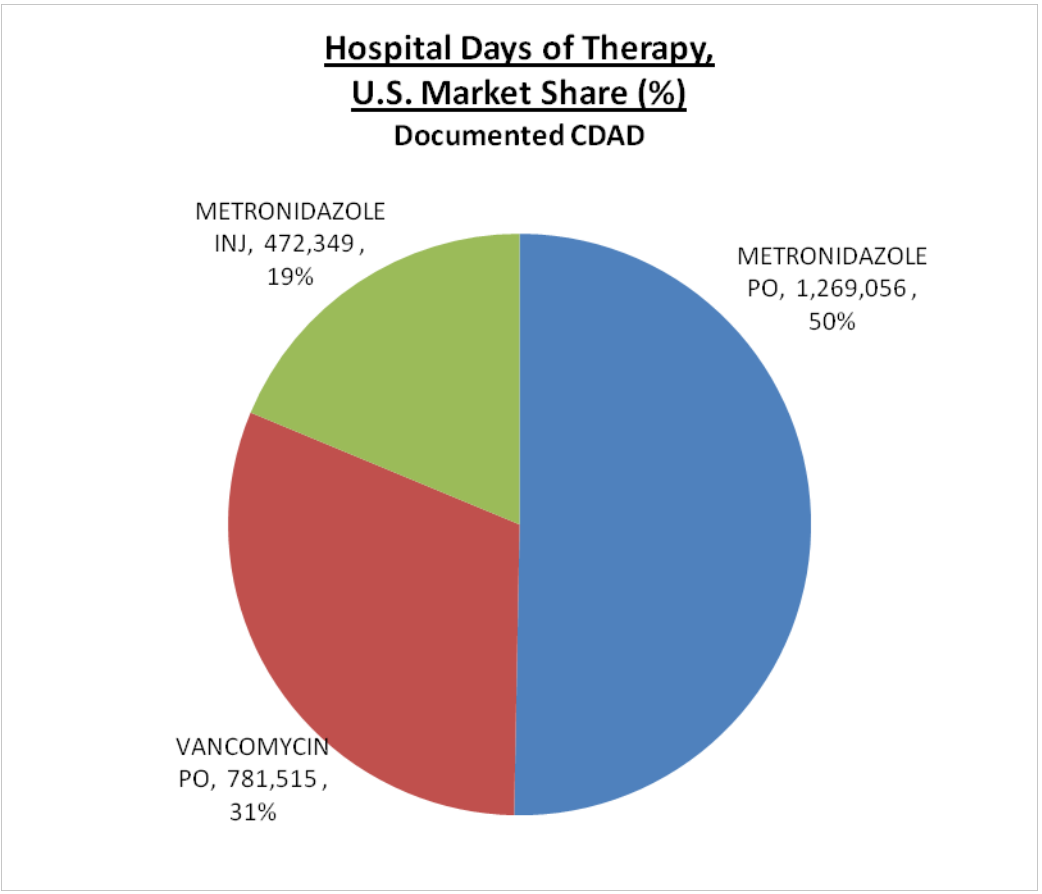
Commercial Outlook

- Growing CDAD market merits new agents
- Disease severity and recurrence rates are increasing
- Estimate global peak annual sales, in the range of $400-500 million, assuming clinical and regulatory success

IP Protection

- Current patent protection expected until Dec 2020 (at least)
- Additional patent protection being sought until 2029 (at least)

Market Landscape for CDAD Treatments



Unmet Medical Need

- Increasing incidence
- Significant mortality
- Hypervirulent NAP-1 strains
- Recurrence concerns* with older therapies

New Market Entry

- Optimer's DIFICID® (fidaxomicin) tablets launched (July 18, 2011):
  - first new approved agent for treatment of CDAD in > 25 years
  - superior to oral vancomycin in sustained clinical response

Pie chart source: 2010 AMR data

* Recurrence is seen in the aftermath of 25% of initial treatments of CDI, L1-1305 – 2010 ICAAC Abstract: Randomized Controlled Trial (RCT) of Fidaxomicin (FDX) Versus Vancomycin (VAN) in Treatment of Recurrent *Clostridium difficile* Infection (CDI).

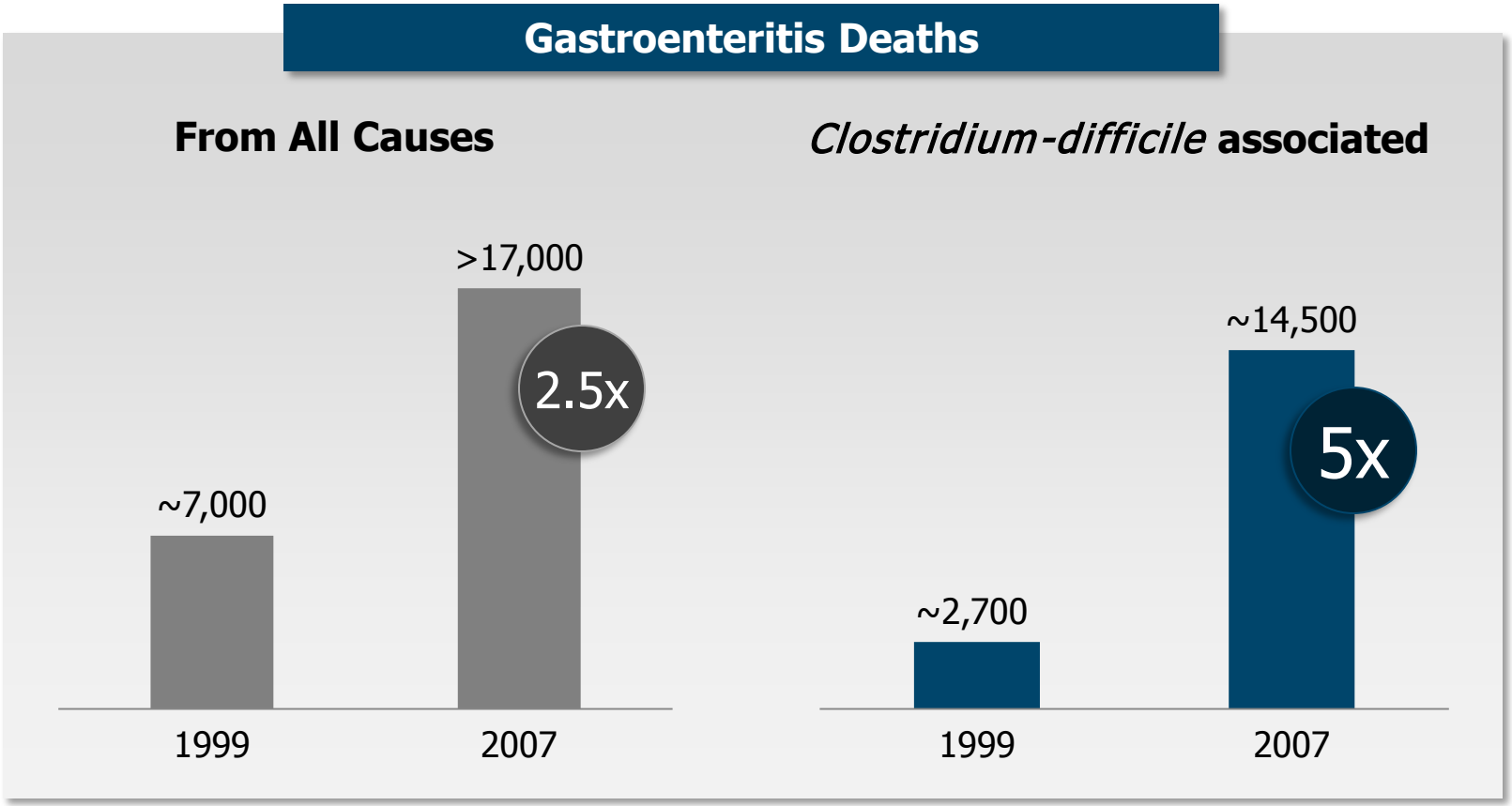
CDAD: A Large Market Opportunity

- Analysis of CDAD market opportunity supports our decision to invest in Phase 3 program
  - Large/growing global market
    - US total days of treatment ~10 million/year (as of 2010): about 50% in-patient
  - We have rights to CB-315 globally (Cubist-discovered compound): no royalties to pay
  - CDAD opportunity requires only 2 Phase 3 trials in this one indication—total external Ph 3 spend estimated at $57 Million
- CB-315 could offer a new therapeutic option
  - Phase 2 results: Recurrence rate for 250 mg dose of CB-315: ~50% improvement compared with oral vancomycin*
  - Differentiated mechanism of action: Would help position CB-315 as a choice for patients whose CDAD recurs with initial therapy

*Recurrence rates in '315 Phase 2 trial: 250 mg '315: 17.2%; Oral vancomycin: 35.5%

CDAD – A Common Serious Disease

- The CDC reports a greater than 5-fold increase in deaths associated with *C. difficile* in the U.S. between 1999 and 2007

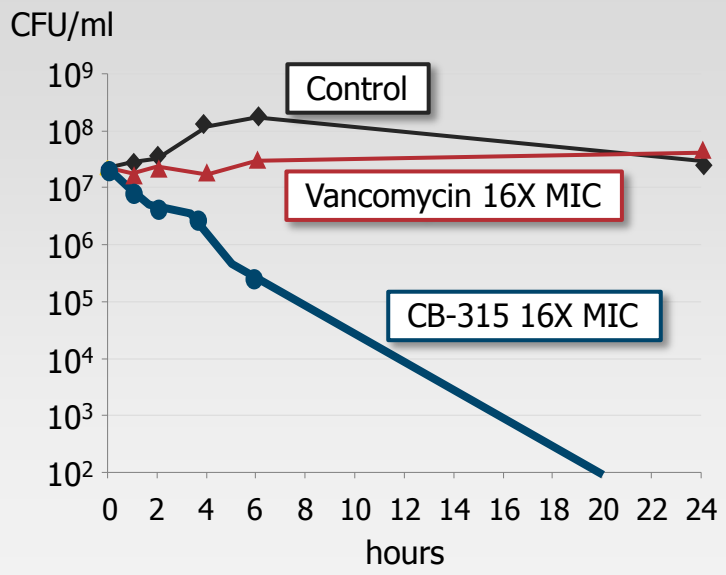


Source: CDC news release/presentation at International Conference on Emerging Infectious Diseases, March 14, 2012

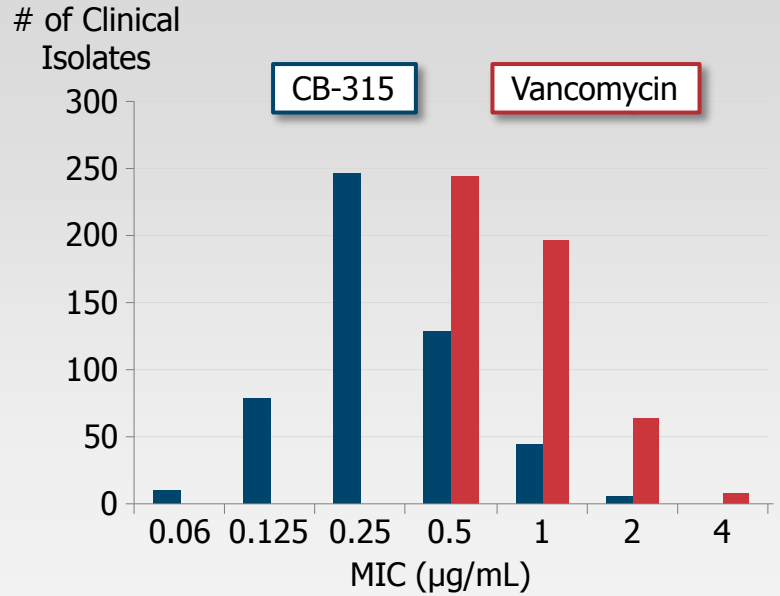
CB-315: Ideal Profile for CDAD

- A novel, orally-administered lipopeptide that has demonstrated potency and cidality against *C. difficile*
- Stays in the GI tract, little systemic exposure
- Minimal impact on normal bowel flora

In vitro Cidality vs. *C. difficile*



In vitro Potency vs. *C. difficile*

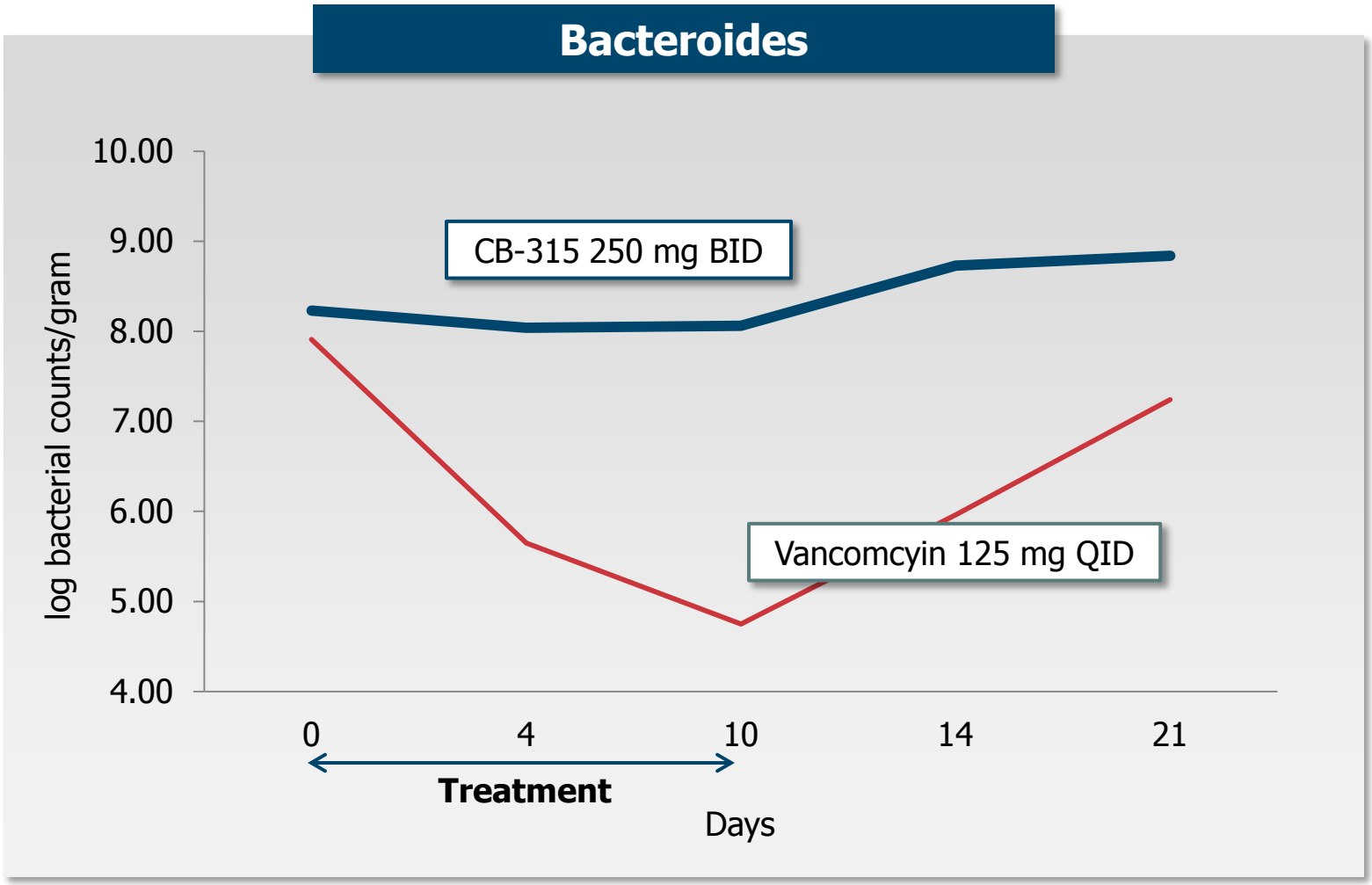


Importantly, CB-315 Reduces Recurrences

MITT Population	Phase 2		Conclusion
	Vancomycin	CB-315 250 mg	
Cure Rates	89% (59/66)	87% (58/67)	**Strong cure rate**
Recurrence Rates	36% (21/59)	17% (10/58)	**Reduced recurrence rate**

53% reduction (P<0.035)

Minimal Effects on Bowel Flora vs. Vancomycin



CB-315 Has a Favorable Safety Profile

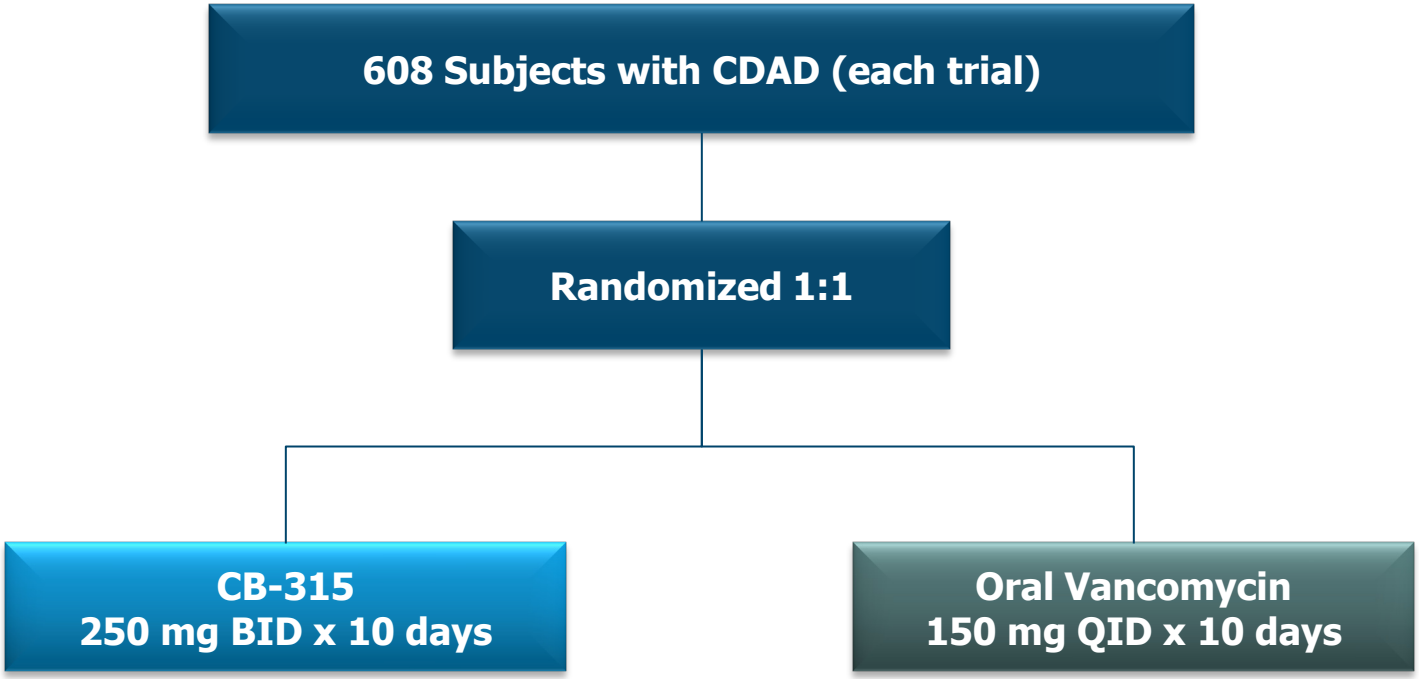
Safety Profile

- Phase 2 results showed no concerning safety signals for either CB-315 dose group
- No concerns with GI bleeding, leukopenia, CPK or LFT elevations



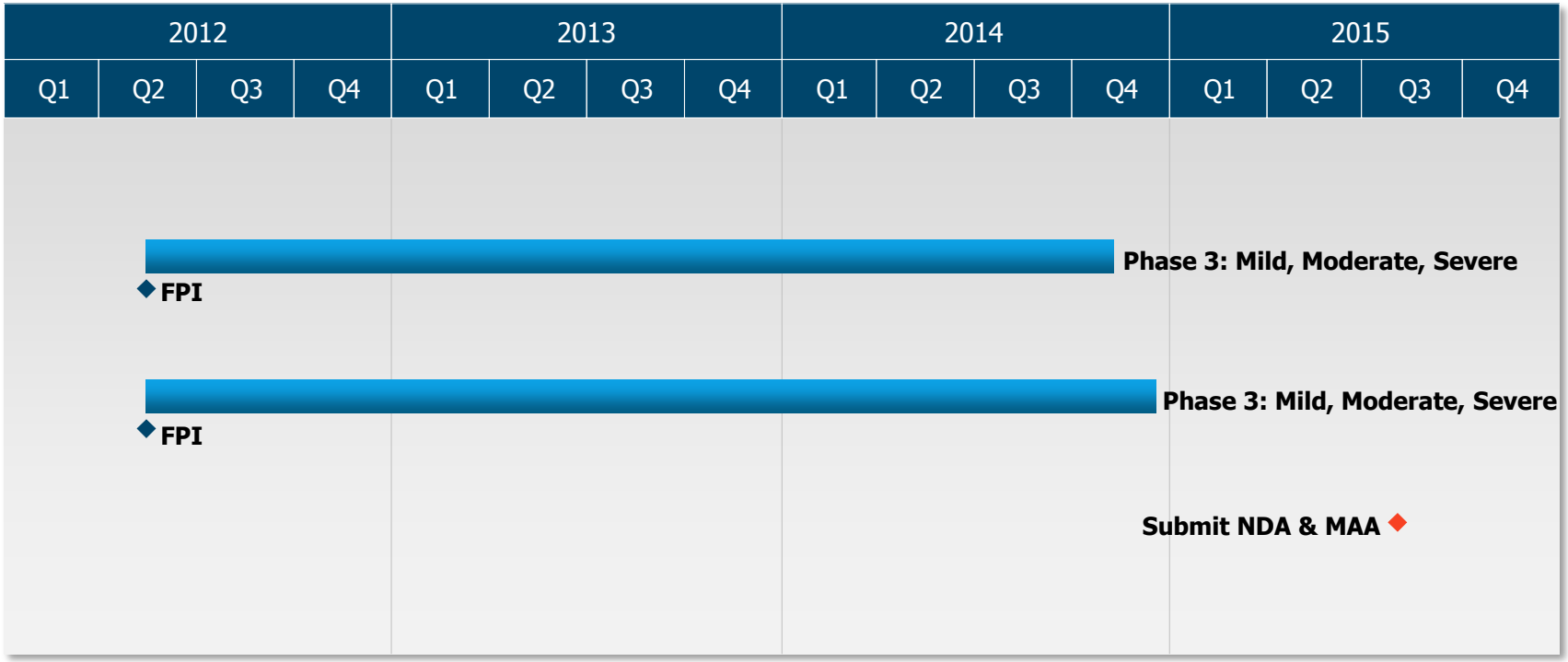
Phase 3 Study in CDAD Starting

- Two Phase 3, randomized, active controlled, double blind, international multi-center studies



CB-315 Program Targeting an NDA in 2015

Development Timeline



CB-315 – Advancing the Treatment of CDAD

- Large unmet medical need
- Ideal preclinical profile: Potent, cidal
- Phase 2 met high bar to reduce recurrences + minimal disruption of bowel flora
- Phase 3 trials starting; Targeting NDA in 2015

Clostridium difficile-associated diarrhea (CDAD) Competitive Landscape (1 of 2)

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Marketed Products

	Vancocin®	Flagyl® / Metronidazole	DIFICID®
Company	Viropharma/Generics	Pfizer/Generic	Optimer/Cubist
Class	Glycopeptide	Nitroimidazoles	Macrolide
Dosing, form	TID / QID, oral	TID, oral and IV	BID, oral
Indications	Clostridium difficile-associated diarrhea	Various anaerobic bacterial infections including trichomoniasis and amebiasis*	Clostridium difficile-associated diarrhea
Status	Market Generics approved 4/11/2012	Market	Market (Launched July 2011 in US)

Information is as of July 3, 2012

*Metronidazole is not FDA approved for Clostridium *difficile*-associated diarrhea but is recommended in the 2010 SHEA guidelines.

Clostridium difficile-associated diarrhea (CDAD) Competitive Landscape (2 of 2)

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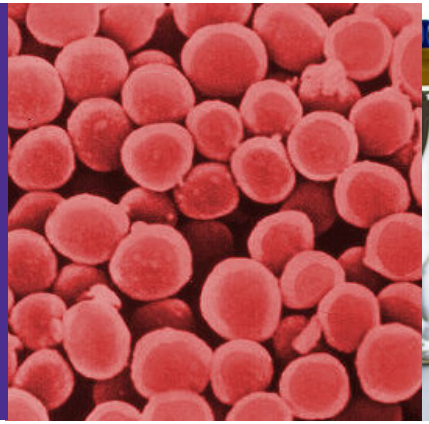
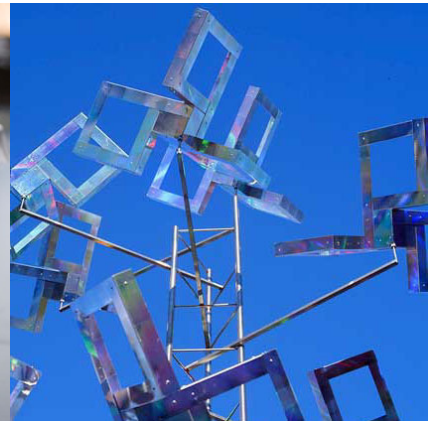
Known Compounds in Development

	CB-183,315	MK-3415A	ACAM-CDIFF	Cadazolid	LFF-571	VP-20621
Company	Cubist	Merck	Sanofi	Actelion	Novartis	Viropharma
Stage	Phase 3	Phase 3	Phase 2	Phase 2	Phase 2	Phase 2
Class	Lipopeptide	Monoclonal antibodies (mABs)	Toxoid Vaccine	Unknown	Semi-synthetic thiopeptide	Spores of non-toxigenic C. difficile strain
Dosing form	oral	IV	IM	oral	oral	oral
Anticipated Indication	Treatment of Clostridium difficile-associated diarrhea (CDAD)	Adjunctive treatment of Clostridium difficile-associated diarrhea (CDAD)	Prevention of Clostridium difficile-associated diarrhea (CDAD)	Treatment of Clostridium difficile-associated diarrhea (CDAD)	Treatment of Clostridium difficile-associated diarrhea (CDAD)	Prevention of recurrence of Clostridium difficile-associated diarrhea (CDAD)

Information is as of April 18, 2012 based on public information

CUBIST
PHARMACEUTICALS





Cubist Pharmaceuticals

The Shape of Cures to Come™

CB-5945

In development for treatment of opioid-induced constipation in adults taking opioid therapy for chronic non-cancer pain

CB-5945 Overview

Compound

- Structure not yet disclosed publicly

Mechanism of Action

- Peripherally-acting μ opioid receptor antagonist

Stage

- Phase 3 expected to commence by YE12

In Vitro Pharmacology

μ Opioid Receptor Binding*	K_i = 0.36 nM
μ Opioid Receptor Antagonist Potency*	K_B = 0.29 nM

* **human cloned receptors**

Pharmacokinetics

- Good PK profile in humans with rapid and almost complete absorption; low variability in PK parameters
- High degree of peripheral selectivity at low dose

Phase 2 Efficacy

- Demonstrated significant improvement in bowel function

Commercial Outlook

- Currently no FDA-approved drugs to treat Opioid-Induced Constipation (OIC) in patients with chronic non-cancer pain
- OIC is the most common adverse effect occurring with chronic opioid use persisting throughout duration of opioid therapy
- >6 million on chronic opioid therapy for 90+ days
- Estimate potential peak year sales of $1 B, assuming clinical success and approval with a competitive label

IP Protection

- U.S. Patent through May 2025 (Composition of matter)
- Pending patent protection for methods of treatment/use (filed September 2010)

CB-5945 Has A Validated MOA for the Treatment of OIC

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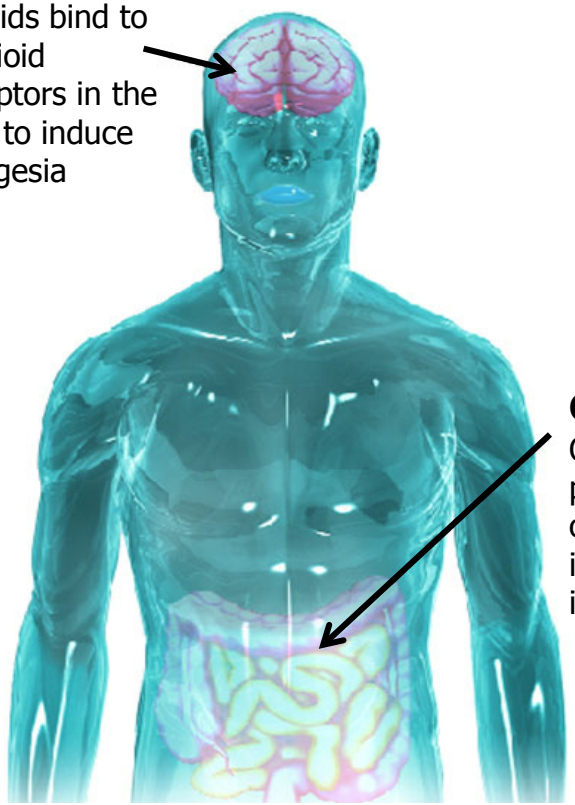
Opioid Receptor Binding

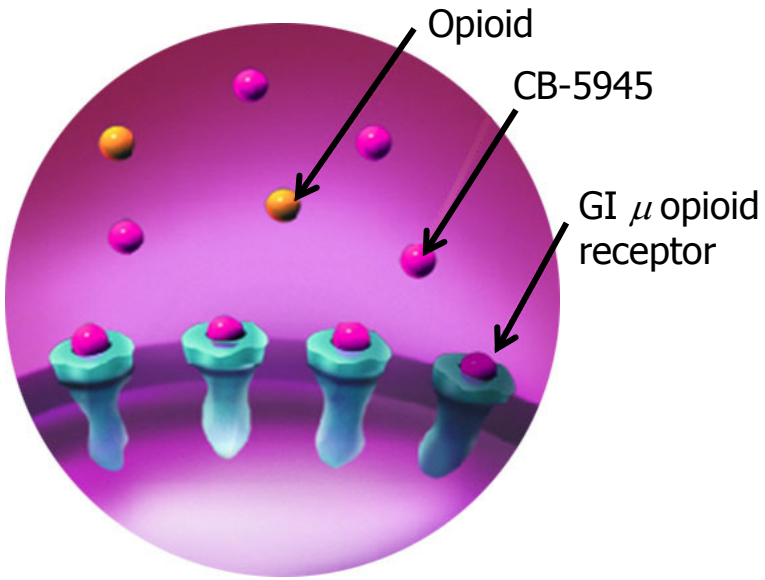
CNS
Opioids bind to μ opioid receptors in the CNS to induce analgesia



GI Tract
Opioids bind to peripheral μ opioid receptors in the GI tract, impairing motility

CB-5945 Advantage

- High affinity & potency at μ opioid receptor
- Peripherally acting
- No compromise to CNS-mediated analgesia



Chronic Noncancer Pain (CNCP) Affects Many Patients…

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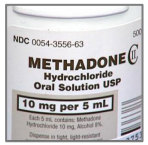
Chronic Noncancer Pain

- 1 of 5 adults report moderate to severe continuous or intermittent CNCP
  - Most common CNCP types
    - Back pain, osteoarthritis, fibromyalgia, headache, neuropathy
  - ~ 70 % of patients with CNCP have had their pain condition for > 5 years

Extensive Use of Opioids

- 6.4 million patients/year receive opioids for > 90 days
  - Average treatment duration = 236 days
  - Average morphine equivalent total daily dose may exceed 200 mg



Source: Sullivan MD, et al. *Pain* 2008;138:440-449; Manchikanti L, et al. *Pain Physician* 2009;12:259-267; Chou R, et al. *J Pain* 2009;10:113-130; Chapman C. *Journal of Pain* 2010;11(9):807-829; Irving G. *Journal of Pain* 2011;12(2):175-184; Camilleri M. *Am J Gastroenterol 2011;*106(5):835-42; Evidence based characterization of the US opioid market, IMS, December 2010.

Opioid-Induced Constipation (OIC): A Common Adverse Effect that Degrades Quality of Life

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#1 Side Effect

- Constipation is the most common side effect of opioid management of chronic non-cancer pain
  - Affecting up to 80% of patients
  - Persisting for the duration of opioid therapy

Degrades Quality of Life

- In surveys of patients on opioid therapy for chronic noncancer pain, those *with* OIC vs. those *without* report significant impairment on their daily lives




Source: Moore RA, et al. *Arthritis Research Ther*. 2005;7:R1046-51; Allan L, et al. *Br Med J*. 2001;322:1134-5; Kalso E, et al. *Pain* 2004;112:372-80; Tuteja AK, et al. *Neurogastronenterol Motil* 2010 Apr;22(4):424-30; Camilleri M. *Am J Gatroenterol. 2011;* 106(5):835-42. Olesen AE, et al. *Adv Ther* 2011 Apr;28(4):279-94; Bell TJ, et al. *Pain Med*. 2009;10:35-42; Bell TJ, et a. J Opioid Management. 2009;5(3):137-144; Penning-van Beest, et al. *J Med Econ*. 2010;13:129-135.

Current Treatment Options are Limited and Often Ineffective

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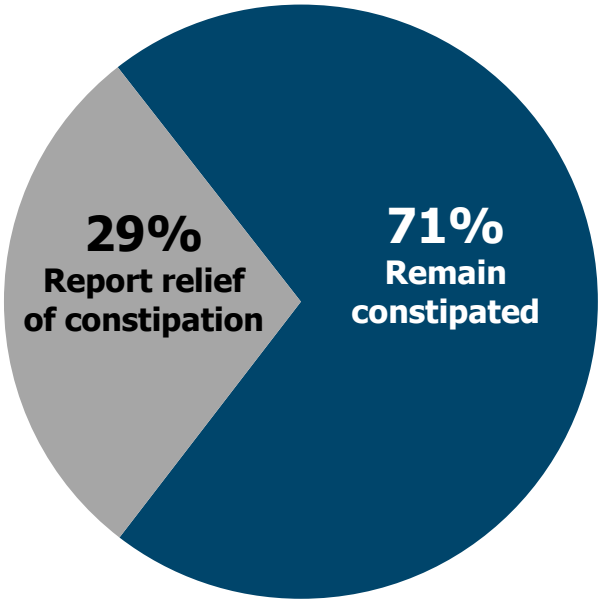
Patients on Laxatives

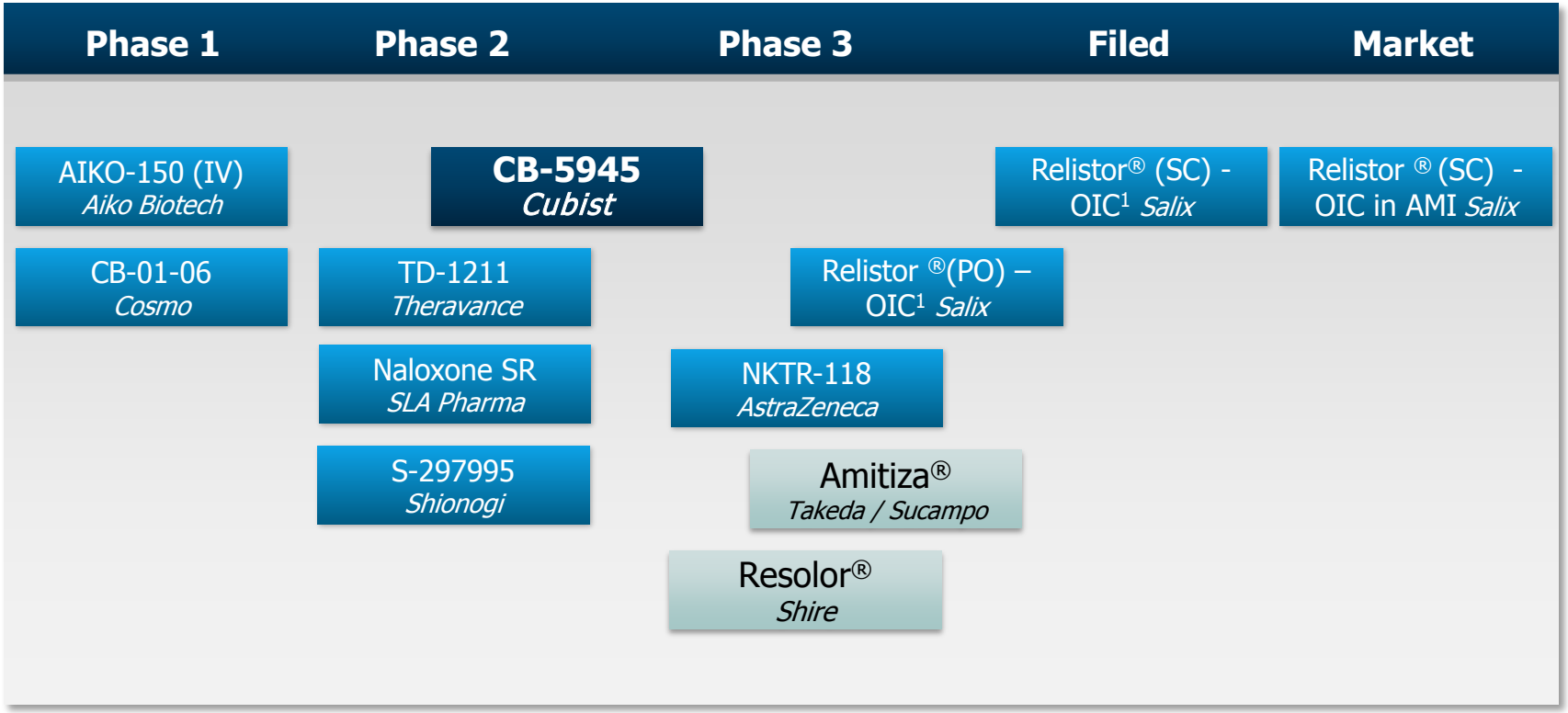


Laxatives Ineffective For Most OIC patients

- The majority of patients with opioid induced constipation use laxatives
  - Highly unpredictable and associated with significant side effects
- Despite laxative therapy, majority of patients remain constipated

Source: Benyamin R, et al. *Pain Physician* 2008;11:S105-S120; Dennison C, et al. *Pharmacoeconomics* 2008;23:461-76; Camilerri M. *Am J Gatroenterol. 2011;* 106(5):835-42; PROBE II survey, conducted in March 2007 by GlaxoSmithKline.

Competitive Space Highlights Large Unmet Need



Note: All compounds except Amitiza and Resolor are peripherally acting μ opioid receptor antagonists

CB-5945 has the potential to be the best in class

Relistor (SC) is approved for OIC in patients with Advanced Medical Illness; SC form is filed for OIC in chronic non-cancer pain patients;
Complete Response received requesting additional clinical data July 27, 2012; PO form completed Phase 3 study in Dec. 2011., anticipated sNDA filing mid 2012.
Amitiza (CIC-2 chloride channel activator) is approved for chronic constipation and IBS-C in women; Phase 3 OIC topline results reported Feb 2012, sNDA filed July 26, 2012.
Resolor (5-HT4 agonist) is approved ex-US for chronic constipation in women; Phase 3 OIC study is ongoing

CB-5945 Commercial Rationale

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- Chronic non-cancer pain (CNCP) is common
- Long-term opioid use will remain the gold standard
  - Majority of patients will experience persistent GI effects, of which constipation is the most common and bothersome
  - GI side effects negatively impact patient quality of life and can result in sub-optimal pain control
- Treatment pattern is established, but lacking
  - No FDA or EMA approved monotherapy to treat OIC in CNCP

CB-5945 Phase 2 Summary

- Studies 45CL242 and 45CL243 achieved the primary endpoint for the CB-5945 0.25 mg dose
  - *Improvements in SBM frequency and SBM responder rates were clinically meaningful and statistically significant*
  - Trends in other OIC symptoms favored CB-5945
  - Clear dose response observed
  - CB-5945 0.25 mg BID dose demonstrates the most favorable benefit-to-risk profile
- CB-5945 was well tolerated
  - Low and comparable incidence of treatment-emergent adverse events (TEAEs) compared with placebo *with highly favorable GI AE profile*
  - Most TEAEs were of mild severity
  - SAEs occurred ≥ 3 weeks after last dose of study medication and in patients at high risk and with pre-existing disease
  - No evidence of central opioid withdrawal or reversal of opioid analgesia
- Data support Phase 3 development of CB-5945 0.25 mg dosed twice daily
- End-of-Phase 2 FDA meeting successfully completed
- Expect to initiate Phase 3 trials in 2012

High Potential for Differentiation Based on Ph 2 Efficacy and GI Tolerability Profile

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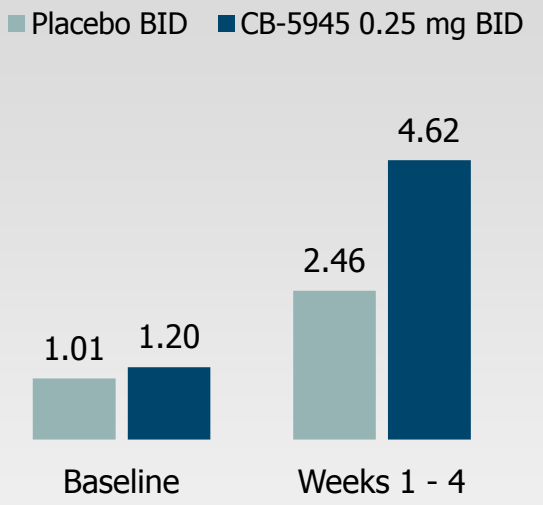
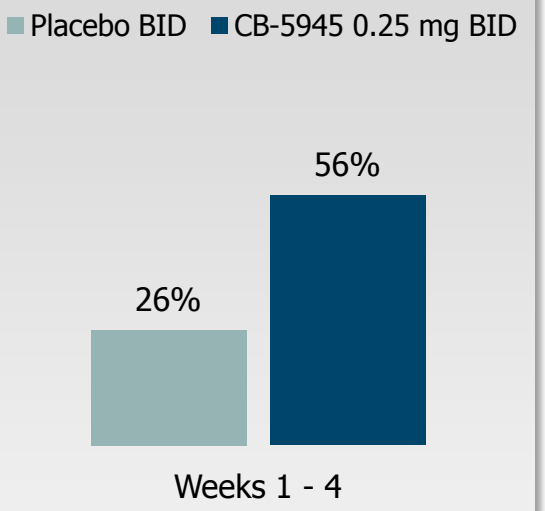
Mean Weekly SBMs



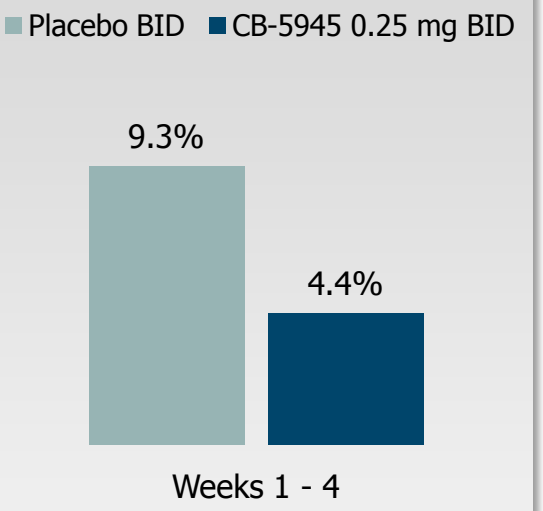
Statistically significant and clinically meaningful mean treatment difference compared with placebo (1.98; P <0.001)

Overall SBM Responders



Statistically significant and clinically meaningful difference (P =0.005)

Patients with ≥ 1 GI AE



Clinically meaningful improvement in SBM frequency and responders with a highly favorable GI AE profile

Source: Study 45CL242; N = 43 for placebo; N = 45 for CB-5945 0.25 mg BID.

CB-5945 Competitive Landscape

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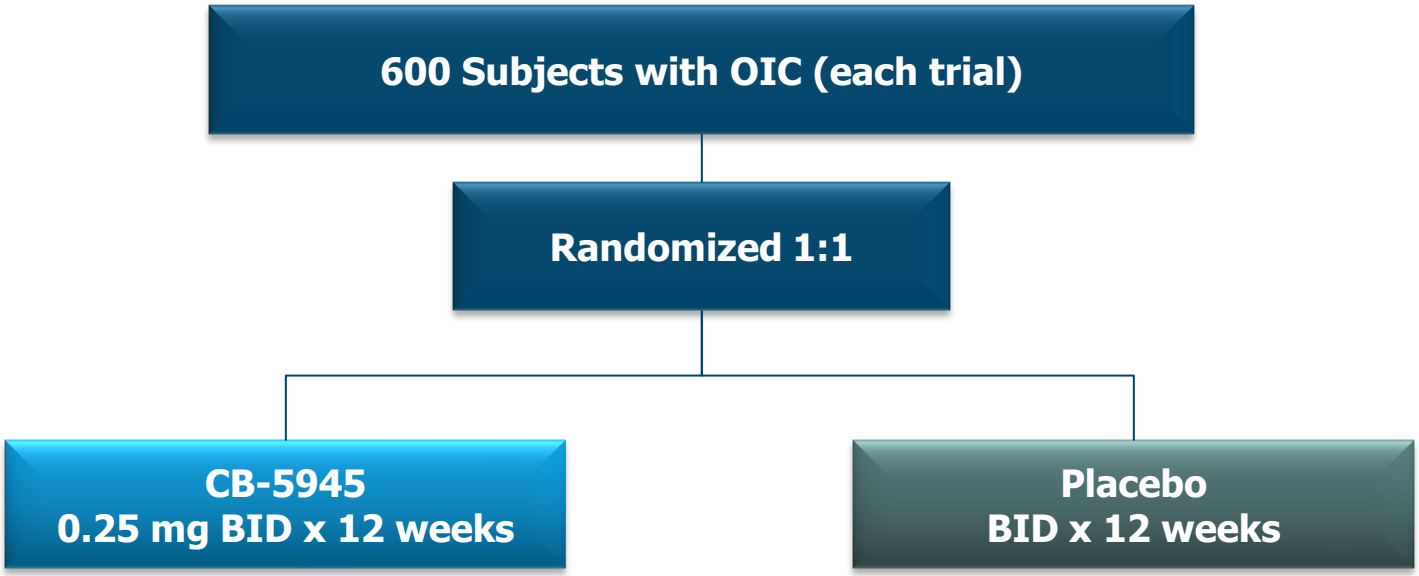
Compound	Company	ROA	Mechanism of Action	OIC Development Stage	Comment
Relistor® (methylnaltrexone)	Progenics/Salix	SC	PAM-OR antagonist	Market	OIC in palliative care (advanced medical illness)
Resolor® (prucalopride)	Shire/Movetis	PO	`5-HT4 receptor agonist	Phase 3	Marketed ex-US for Chronic Idiopathic Constipation (CIC) in women; Phase 3 in OIC ongoing; no US studies to date
Relistor® (methylnaltrexone)	Progenics/Salix	SC	PAM-OR antagonist	Filed	OIC in non-cancer pain (Received complete response letter requesting additional clinical data - July 27,2012)
Relistor® (methylnaltrexone)	Progenics/Salix	PO	PAM-OR antagonist	Phase 3	Positive Phase 3 results (1 study with primary endpoint not consistent with chronic use) announced Dec 2011 (press release; clinicaltrials.gov) Anticipated *sNDA* filing 3Q12
Amitiza® (lubiprostone)	Sucampo/Takeda	PO	CIC-2 chloride channel activator	Phase 3	Marketed for CIC & Irritable Bowel Syndrome with Constipation (IBS-C). Sucampo said two of three Phase 3 studies conducted in opioid-induced bowel dysfunction met primary end point; sNDA filed July 26, 2012
Naloxegol	Nektar/AZ	PO	PAM-OR antagonist	Phase 3	Initiated 1Q11/NDA filing expected mid 2013
CB-5945	Cubist	PO	PAM-OR antagonist	Phase 2 complete	EOP2 Dec 2011; First patient for Phase 3 in 2012
TD-1211	Theravance	PO	PAM-OR antagonist	Phase 2b	Phase 2 single-blind safety and Phase 2 b study completed; positive topline Phase 2 results announced July 10, 2012
Nalcol (Naloxone SR)	SLA Pharma	PO	PAM-OR antagonist	Phase 2 complete	Clinically and statistically significant Phase 2 Results announced May 14, 2012
S-297995	Shionogi	PO	PAM-OR antagonist	Phase 2	Phase 2 efficacy trial anticipated completion 3Q12

Information is as July 27, 2012

Phase 3 Clinical Program in OIC Expected to Start by End of 2012

- Three Phase 3, randomized, double blind, placebo controlled efficacy studies

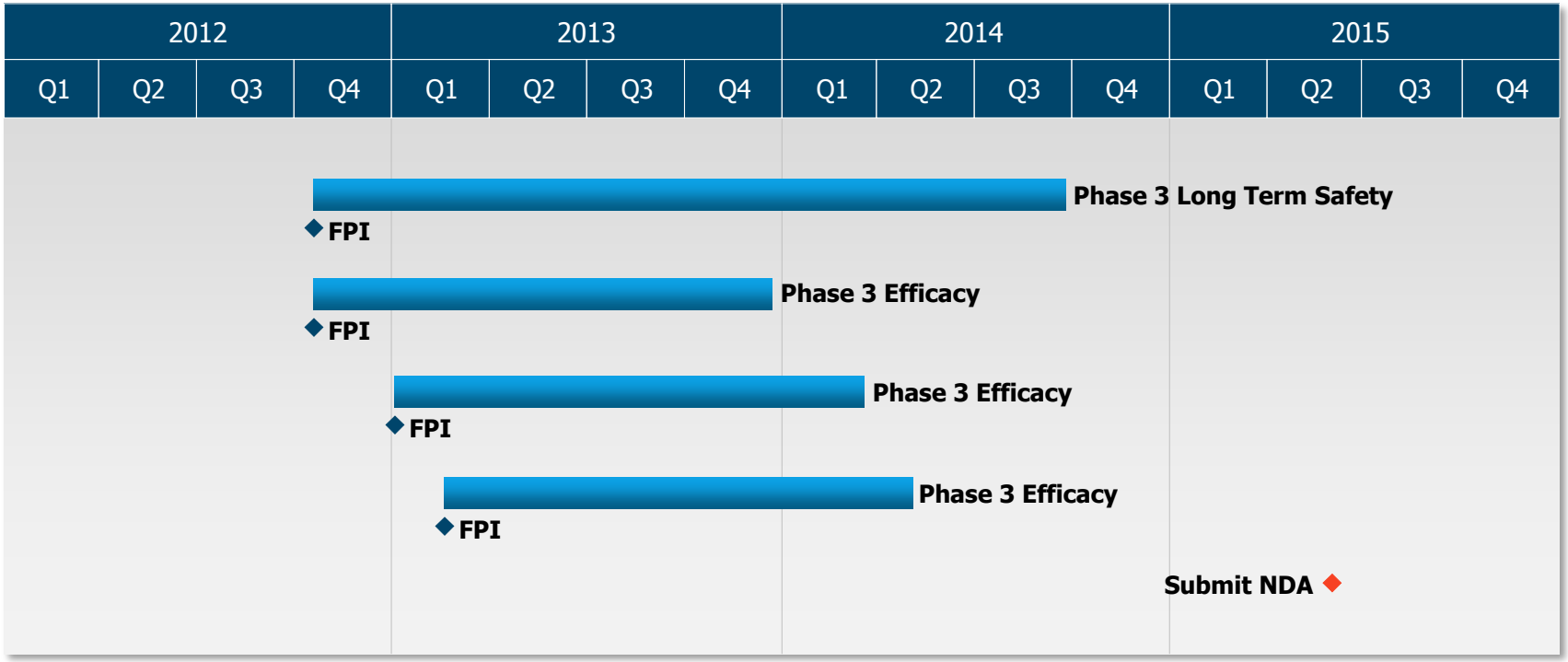


- Phase 3, randomized, double blind, placebo controlled long term safety study
  - 1,400 OIC subjects per study
  - Randomization 1:1
  - 52 weeks treatment



CB-5945 Program Targeting an NDA in 2015

Development Timeline



CB-5945 has the Potential to be Best in Class for the Treatment of OIC in CNCP

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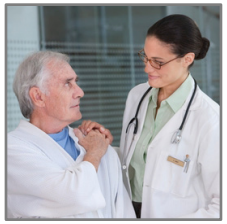
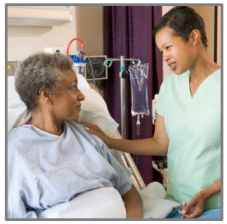
Large Unmet Medical Need

- Opioid therapy is the foundation for managing chronic noncancer pain (CNCP) and use continues to increase
- OIC is common, persistent, and significantly lowers quality of life in patients with CNCP
- Laxatives are often ineffective and associated with limiting side effects

Differentiated Product – Advancing

- Robust phase 3 program strategically designed to maximize potential for differentiation, clinical, and regulatory success while minimizing risk
  - on target to initiate 2H 2012





Potential Differentiation

CB-5945: Ph 2 data suggests Best in Class GI Tolerability Profile

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- GI AE event rate at doses reported to be associated with statistically significant efficacy

	CB-5945	Relistor (PO)*		Relistor (SC)	NKTR-118	TD-1211		
	0.25mg BID (n=45)	300 mg QD (n=201)	450 mg QD (n=200)	12mg QD (n=150)	25mg QD (n=30)	5mg QD (n=16)	10mg QD (n=53)	15 mg QD (n=52)
Change from baseline in mean weekly SBMs	+ 3.4	+2.4	+2.4	+3.1	+3.6	+3.2	+3.4	+3.7
Abdominal pain	2%	9%	11%	21%	40%	50%	17%	19%
Diarrhea	0%	7%	8%	6%	13%	6%	11%	8%
Nausea	2%	6%		9%	13%	19%	15%	6%
Vomiting	2%	Not reported		1%	13%	25%	2%	0%

Note: Data compiled from non-comparative Phase 2 studies, except for Relistor (Phase 3).
*Includes abdominal pain and abdominal pain upper.

Phase 3 Development Strategy

CUBIST PHARMACEUTICALS

- Develop CB-5945 as a long-term treatment for chronic OIC
- Primary treatment strategy: restoration of normal bowel motility
- Design program to support potential for
  - Clinically meaningful differentiation from competitors
    - GI tolerability profile
    - Symptom improvement
    - Durability of response
  - Broadest indication and/or most inclusive label

NKTR-118 (Naloxegol) Phase 2 Top Line Results

CUBIST PHARMACEUTICALS

Clinical Data

Phase 2 study in OIC patients

- 208 patients; 4 week treatment period

Primary Efficacy

Change from baseline in mean weekly SBM frequency at 1 week

PBO	5mg	PBO	25mg	PBO	50mg
+1.8	+2.6	+1.9	+3.6*	+1.9	+4.4*

* Statistically significant

GI Tolerability

% of patients experiencing	PBO (n=32)	5mg (n=33)	PBO (n=27)	25mg (n=30)	PBO (n=37)	50mg (n=35)
Abdominal pain [a]	3%	21%	11%	40%	5%	46%
Diarrhea	16%	15%	4%	13%	5%	31%
Nausea	3%	15%	19%	13%	8%	20%
Vomiting	6%	0%	4%	13%	5%	11%

[a] Includes abdominal pain and abdominal pain upper

Information as of May, 2012

Sources: clintrials.gov; "NKTR-118 Significantly Reverses Opioid-Induced Constipation,", 20th AAPM Annual Clinical Meeting (October, 2009); The American College of Gastroenterology Annual Meeting, Oct 23-28, 2009 by Webster L, et al.

TD-1211 Phase 2 Studies Top Line Results

CUBIST PHARMACEUTICALS

Clinical Data

Phase 2 study in CNCP patients with OIC (Study 0074)

- 69 patients, 2 week treatment period

Efficacy

Change from baseline in mean weekly SBM frequency over2 weeks

PBO	0.25mg	0.75mg	2mg	5mg	10mg
+1.6	+1.4	+0.9	+0.9	+3.2*	+4.9*

* Lower 95% CI l< 1 (proof of concept)

Clinical Data

Phase 2b study in CNCP patients with OIC (Study 0084)

- 217 patients, 5 week treatment period (efficacy assessed Ws 2 – 5)

Efficacy

Change from baseline in mean weekly SBM frequency over 4 weeks (weeks 2 – 5 of treatment; first 4 days of each cohort received 5mg dosing)

PBO	5mg	10mg	15mg
+1.9	+2.7	+3.4*	+3.7*

* Statistically significant

GI Tolerability

% of Patients Experiencing	PBO (n=14)	0.25mg (n=8)	0.75mg (n=8)	2mg (n=8)	5mg (n=16)	10mg (n=16)
Abdominal pain[a]	7%	0%	38%	25%	50%	75%
Diarrhea	7%	0%	0%	13%	6%	31%
Nausea	0%	13%	25%	25%	19%	50%
Vomiting	0%	0%	0%	38%	25%	19%

[a] Includes abdominal pain and abdominal pain upper

GI Tolerability

% of Patients Experiencing	PBO (n=54)	5mg (n=56)	10mg (n=53)	15mg (n=52)
Abdominal pain[a]	13%	16%	17%	19%
Diarrhea	0%	7%	11%	8%
Nausea	4%	7%	15%	6%
Vomiting	2%	7%	2%	0%

[a] Includes abdominal pain and abdominal pain upper

Information as of July 2012

Sources: clintrials.gov; Theravance press release, October 21, 2010; Theravance press release and investor presentation, July 10, 2012

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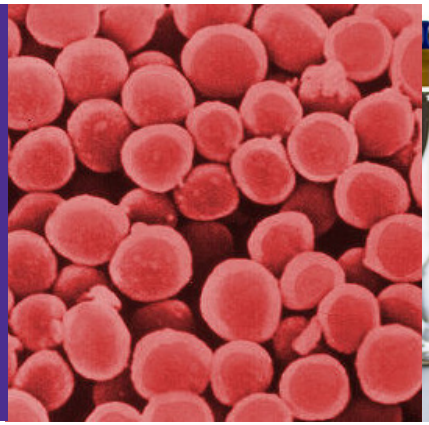

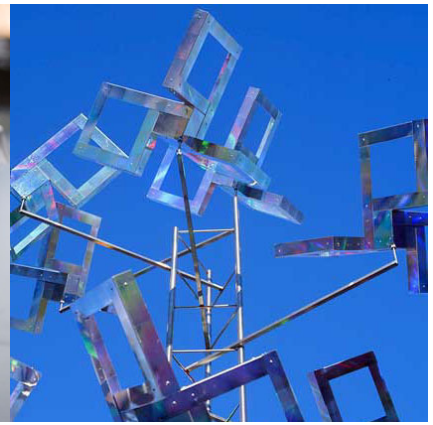

Cubist Pharmaceuticals

The Shape of Cures to Come™

CB-625

Initial development for treatment of post-surgical pain

CB-625 Overview

CUBIST PHARMACEUTICALS

Compound

- Structure not yet publicly disclosed.

Mechanism of Action

- Antagonist of the human TRPA-1 ion channel

Stage

- Phase 1

In vitro Pharmacology

Human TRPA1 channel	IC_{50} 93nM
>100X selective vs. other ion channels	IC_{50} >10μM

In vivo Pharmacology

Analgesic activity in multiple animal pain models	10-30mg/kg

Pharmacokinetics

- Good bioavailability
- Limited potential for drug-drug interactions

Nonclinical Safety

- Well tolerated up to the maximum feasible dose with no adverse effects.
- Non-genotoxic
- At clinically relevant doses/concentrations:
  - No effect on GI motility
  - No effect on the CNS function
  - No evidence of abuse potential
  - No effect on CV system
  - No respiratory depression

Commercial Outlook

- 70 million patients on opioid therapy in U.S.

IP Protection

- U.S. Composition of matter patent through July 2029
- Additional pending patent protection for composition and methods of treatment/ use (filed August 2011)

Large Market Opportunity for Pain Medications

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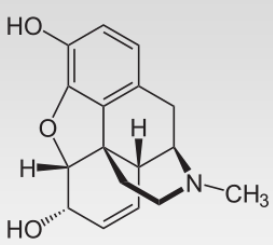
Total US Hospital-Based Analgesic Rx – 2011*

300M days of therapy

Majority of Rx

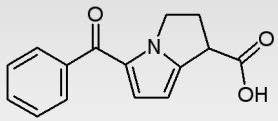
Generic Opiates



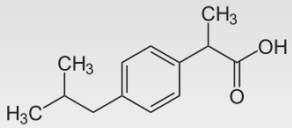
Morphine

Oxycodone

NSAIDs



Ketorolac



Ibuprofen

* Cubist estimate of top 3 opiates and NSAIDs hospital usage, based on IMS data

Current Pain Medications Have Major Drawbacks

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Desired Effects

- ✓ Analgesia
- ✓ Anti-inflammatory

+

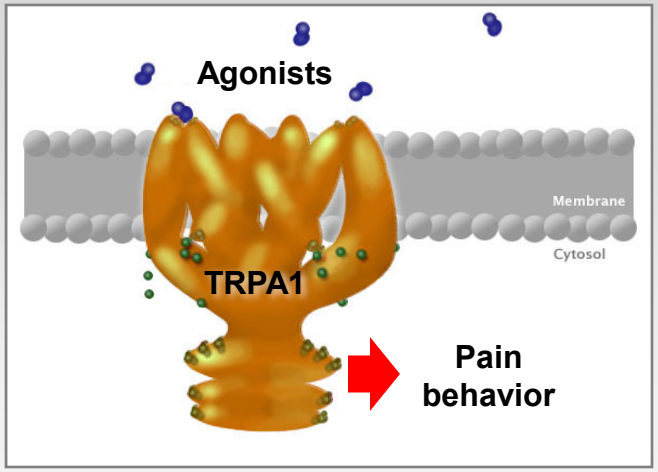
Undesired Effects

- x Respiratory depression
- x Euphoria
- x Constipation
- x GI bleeding

TRPA1 is a Valid Target for Treating Pain

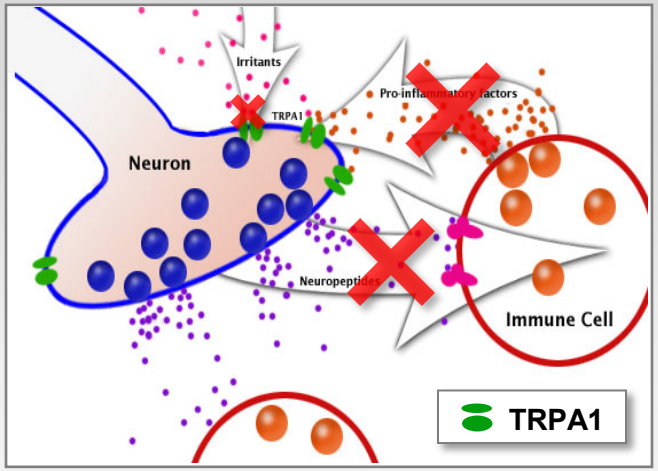
The role of TRPA1:

- An ion channel that serves as a broad irritancy receptor
- Exposure to TRPA1 agonists (e.g. acrolein, formaldehyde, and isocyanates) causes pain behavior



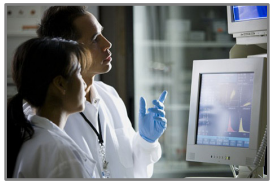
Preventing TRPA1 function:

- Using genetic deletion or a pharmacological inhibitor dramatically reduces pain responses in rodents as well as inflammation
- TRPA1 biology is highly supportive of it being a valid target for treating acute pain and inflammation



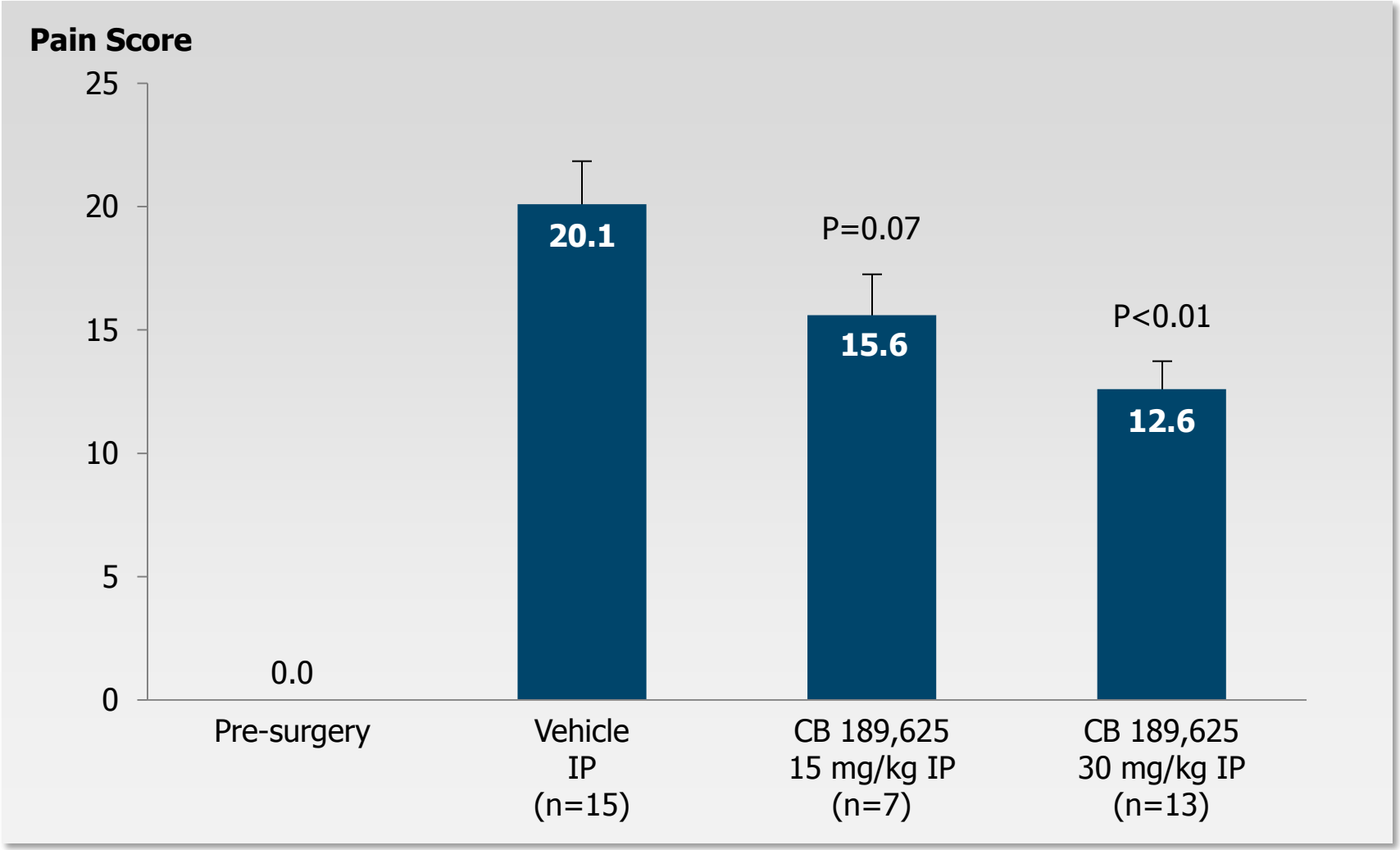
CB-625 is a Promising Clinical Candidate

Required Attribute		CB-625 Property
Potent	→	✓
Selective	→	TRP channels, hERG, etc.
Efficacious	→	Pain & asthma models
Safety	→	14 day tox & safety pharm
IP	→	Composition of matter patents filed


Preclinical efficacy and safety data support advancement into clinical development

CB-625 is Effective in Treating Incision Pain



Source: Brennan Postoperative Pain Rat Model (Efficacy measured 1-2 hours post-dose)

A Novel Treatment for Acute Pain

CUBIST PHARMACEUTICALS

Partnership

- Cubist has partnered very effectively with Hydra Biosciences to discover and then advance an innovative treatment for acute pain into the clinic

Rapid Progress

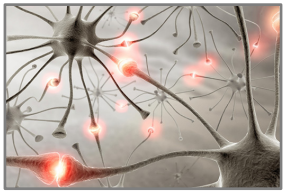
- From collaboration initiation to CTA filing took just over 2 years

Wider Applications

- TRPA1 antagonists, such as CB-625, may also have clinical application in acute inflammatory disorders

Pipeline

- Demonstrates our success in creating a pipeline of innovative, acute care therapies in antibacterials, pain and other indications



Cubist Pharmaceuticals

The Shape of Cures to Come™

Financials

Statements of Income
GAAP (Unaudited)

In thousands, except share and per share data

	Three months ended June 30,		Six months ended June 30,	
	2012	2011	2012	2011
Revenues:				
U.S. CUBICIN product revenues, net	$ 200,180	$ 168,575	$ 384,887	$ 322,291
U.S. ENTEREG product revenues, net	9,706	-	19,148	-
Total U.S. product revenues, net	209,886	168,575	404,035	322,291
International product revenues	11,363	7,747	24,017	16,047
Service revenues	8,665	-	12,329	-
Other revenues	653	516	1,878	1,031
Total revenues, net	230,567	176,838	442,259	339,369
Costs and expenses:				
Cost of product revenues	58,891	38,976	112,843	75,553
Research and development	67,206	41,871	118,378	82,287
Contingent consideration	2,694	81,816	5,523	82,914
Selling, general and administrative	40,255	38,341	84,035	78,505
Total costs and expenses	169,046	201,004	320,779	319,259
Operating income (loss)	61,521	(24,166)	121,480	20,110
Other income (expense), net	(11,273)	(6,961)	(19,786)	(13,768)
Income (loss) before income taxes	50,248	(31,127)	101,694	6,342
Provision (benefit) for income taxes	7,125	(10,512)	25,777	4,372
Net income (loss)	$ 43,123	$ (20,615)	$ 75,917	$ 1,970
Basic earnings (loss) per share	0.68	(0.34)	1.20	0.03
Diluted earnings (loss) per share	0.58 [1]	(0.34)	1.04 [1]	0.03
Shares used in calculating:				
Basic earnings (loss) per share	63,498,953	60,517,553	63,250,165	59,991,068
Diluted earnings (loss) per share	81,166,329	60,517,553	81,001,476	61,828,807

[1] Includes add back of interest expense, debt issuance costs and debt discount amortization on 2.50% notes to income, net of tax effect

Reconciliation of Non-GAAP Proforma Net Income to GAAP Net Income (Loss)

CUBIST PHARMACEUTICALS

(Unaudited)

In thousands, except share and per share data	Three months ended June 30,		Six months ended June 30,	
	2012	2011	2012	2011
GAAP net income (loss)	$ 43,123	$ (20,615)	$ 75,917	$ 1,970
Non-cash debt discount amortization	4,654	4,569	9,481	9,054
Loss on partial extinguishment of 2.25% Notes	3,728	-	3,728	-
ENTEREG intangible asset amortization	4,589	-	9,177	-
ENTEREG inventory step-up	834	-	1,369	-
Expenses related to the acquisition of Adolor	1,448	-	5,037	-
Contingent consideration	2,694	81,816	5,523	82,914
Reversal of reserve for uncertain tax positions	(10,961)	-	(10,961)	-
Non-cash tax adjustment	4,825	(24,228)	21,974	(11,189)
Non-GAAP proforma net income	$ 54,934	$ 41,542	$ 121,245	$ 82,749
Non-GAAP basic earnings per share	$ 0.87	$ 0.69	$ 1.92	$ 1.38
Non-GAAP diluted earnings per share	$ 0.68 [1]	$ 0.53 [1]	$ 1.50 [1]	$ 1.08 [1]
Shares used in calculating:				
Non-GAAP basic earnings per share	63,498,953	60,517,553	63,250,165	59,991,068
Non-GAAP diluted earnings per share	84,076,269	81,961,313	84,231,134	80,802,339

[1] Includes add back of interest expense and debt issuance costs on 2.25% notes and 2.50% notes to income, net of tax effect

2Q12 Calculation of Diluted EPS

GAAP (Unaudited)

(In thousands, except share and per share data)

	Income Available		Common Shares		Per Share
Basic EPS	$ 43,123		63,498,953		$ 0.68
Plus impact of assumed conversions					
Options	-		2,243,221	A	0.66
2.50% Convertible Senior Notes	4,248	B	15,424,155	D	0.58
Diluted EPS	$ 47,371		81,166,329		$ 0.58

Non-GAAP (Unaudited)

(In thousands, except share and per share data)

	Income Available		Common Shares		Per Share
NON-GAAP Basic EPS	$ 54,934		63,498,953		$ 0.87
Plus impact of assumed conversions					
Options	-		2,243,221	A	0.84
2.25% Convertible Subordinated Notes	370	C	2,909,940	D	0.81
2.50% Convertible Senior Notes	2,047	C	15,424,155	D	0.68
Non-GAAP Diluted EPS	$ 57,351		84,076,269		$ 0.68

[A] Number of shares calculated in accordance with GAAP
[B] Add back of interest expense, debt issuance costs and debt discount amortization to income, net of tax effect
[C] Add back of interest expense and debt issuance costs to income, net of tax effect
[D] Weighted average shares issued on full conversion

1H12 Calculation of Diluted EPS

GAAP (Unaudited)

(In thousands, except share and per share data)

	Income Available		Common Shares		Per Share
Basic EPS	$ 75,917		63,250,165		$ 1.20
Plus impact of assumed conversions					
Options	-		2,327,156	A	1.16
2.50% Convertible Senior Notes	8,445	B	15,424,155	D	1.04
Diluted EPS	$ 84,362		81,001,476		$ 1.04

Non-GAAP (Unaudited)

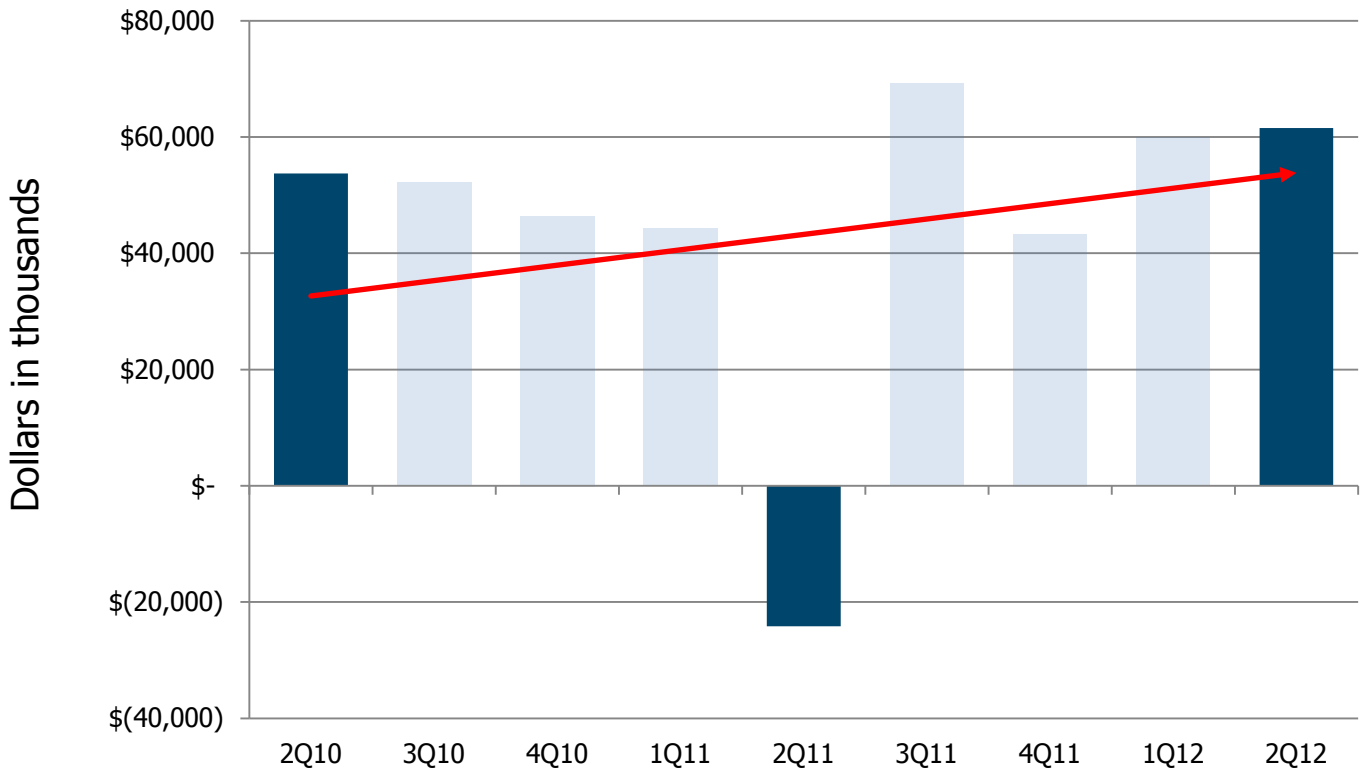
(In thousands, except share and per share data)

	Income Available		Common Shares		Per Share
NON-GAAP Basic EPS	$ 121,245		63,250,165		$ 1.92
Plus impact of assumed conversions					
Options	-		2,327,156	A	1.85
2.25% Convertible Subordinated Notes	819	C	3,229,658	D	1.77
2.50% Convertible Senior Notes	4,087	C	15,424,155	D	1.50
Non-GAAP Diluted EPS	$ 126,151		84,231,134		$ 1.50

[A] Number of shares calculated in accordance with GAAP
[B] Add back of interest expense, debt issuance costs and debt discount amortization to income, net of tax effect
[C] Add back of interest expense and debt issuance costs to income, net of tax effect
[D] Weighted average shares issued on full conversion

Cubist Quarterly Operating Income
GAAP (Unaudited)

2Q12 total operating income of $61.5M

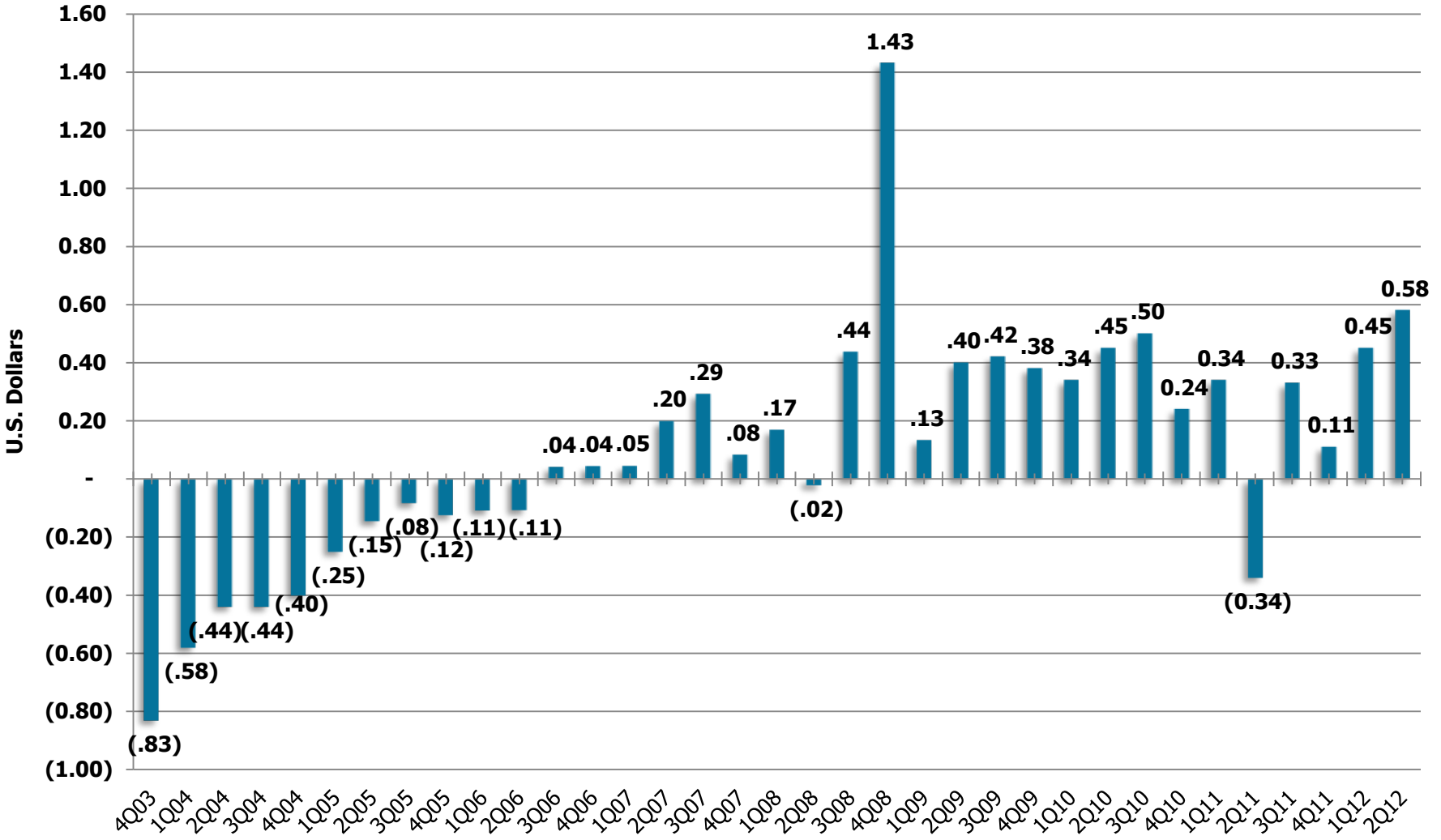


GAAP Diluted Quarterly EPS

Since CUBICIN Launch

CUBIST PHARMACEUTICALS

GAAP (Unaudited)



2012 Cubist Tax Rate

- The Company's effective tax rate for the quarter ending June 30, 2012 is 14.2%
- The second quarter tax rate was reduced by an $11 million benefit as a result of the reduction of reserves related to the recovery of attributes claimed on amended state tax returns
- The Company is forecasting an effective tax rate of 30.8% for 2012
- Since the federal R&D tax credit provisions have not been extended at this time, the Company's forecasted effective tax rate is higher than it would be if federal R&D tax credit components was extended
- If the federal R&D tax credit provisions are extended, the Company's forecasted effective tax rate for the year would be favorably impacted