

Stratanalysis Document

Vibativ Approved By FDA For Treatment of cSSSI

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Theravance's Vibativ for Gram-positive infections

Approval of Vibativ for Gram-positive Infections

- On 11th Sept 2009, Theravance and Astellas Pharma announced FDA's approval of Vibativ (telavancin) for the treatment of adult patients with complicated skin and skin structure infections (cSSSI)
 - The drug treats Gram-positive bacteria, including both methicillin-resistant (MRSA) and methicillin-susceptible (MSSA) strains of Staphylococcus aureus
- Vibativ is marketed as a once-daily, injectable lipoglycopeptide antibiotic with a dual mechanism of action - inhibiting bacterial cell wall synthesis and disrupting bacterial cell membrane function

Theravance- Astellas Pharma Collaboration

- Theravance entered into a collaboration arrangement with Astellas Pharma in November 2005 for the development and commercialization of Vibativ worldwide except Japan. (In July 2006, the collaboration was expanded to include Japan)
- Terms of the collaboration are as follows:
 - **Theravance:** 1) Development and FDA filings of the drug for the treatment of (i) complicated skin and skin structure infections and (ii) nosocomial pneumonia; 2) Manufacture of ~6 months of first commercial sale stock for launch of the drug in US
 - **Astellas:** All other development, regulatory, manufacturing, sales and marketing activities
 - Theravance will collaborate with Astellas in marketing in the United States for the first 3 years following approval

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Market Analysis – Market and Epidemiology (1/4)

Market

- Globally as of 2007, the hospital antibacterials market accounted for USD 7.9 BN of the total USD 41 BN anti-infectives market
 - A core group of products in this market, accounting for USD 5.6 BN, have managed to maintain a modest growth of 3%
- The attractiveness of this market lies in the resistance issues which will perpetually increase the demand for effective solutions and ensure that the market remains in growth

Epidemiology

- Invasive MRSA infection affects certain populations disproportionately and is no longer confined to intensive care units, acute care hospitals, or any health care institution¹
 - Incidence rates are highest among persons >65 years (127.7 per 100 000), blacks (66.5 per 100 000), and males (37.5 per 100 000)
- Most MRSA infections (58.4%) are community-onset infections, 26.6% are hospital-onset infections, 13.7% are community-associated infections, and 1.3% are unclassified¹
- In 2005, the standardized incidence rate of invasive MRSA in the US was 31.8 per 100 000

Note:¹According to an Active Bacterial Core surveillance system study of epidemiology of US population

Source: MIDAS Sales Data, IMS Health, March 2007, JAMA,, Datamonitor

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Market Analysis – Sales and Growth (2/4)

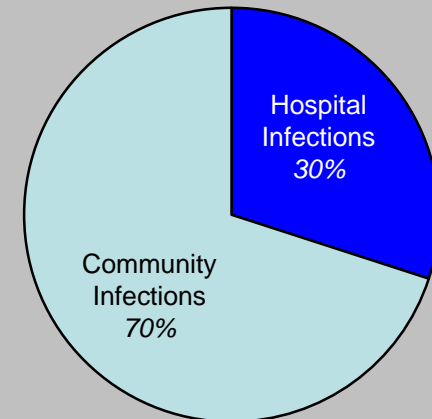
Sales

- CSSSI is a competitive market with new products characteristically reaping high revenues, which stands as an indicator of the hunger for new therapies in this market
 - Cubicin (daptomycin), from Cubist Pharmaceuticals Inc., which the FDA approved for CSSSI in 2003 brought in revenues of USD 433.6 MM in 2008
 - Zyvox (linezolid) from Pfizer had sales of USD 944 MM in 2007, a 21% growth over previous year
- Oritavancin, Elli Lilly's pipeline vancomycin product in IV form was estimated to reap worldwide sales of USD 240 MM by 2013, USD 150MM of that in the US, assuming a 5% share of the fast-expanding IV MRSA market

Growth

- As per CDC data, in 1974, MRSA infections accounted for 2% of the total number of staph infections; in 1995 it was 22%; and in 2004 it had grown to 63%
- The MRSA Days of Therapy (DOT) has been growing at a CAGR of 12% over the 5-year period of 2003-2007 (*refer slide 6 for chart*)

Breakup of Antibacterial Market (USD 26 BN), 2007



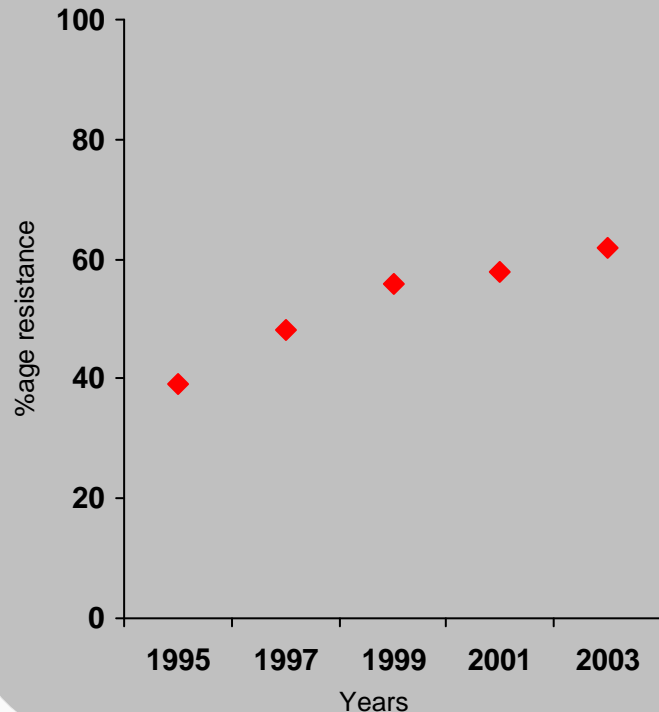
Key pathogens:

Methicillin-resistant Staph. aureus (hospital)
Streptococci (community)
Clostridium difficile (hospital & community)

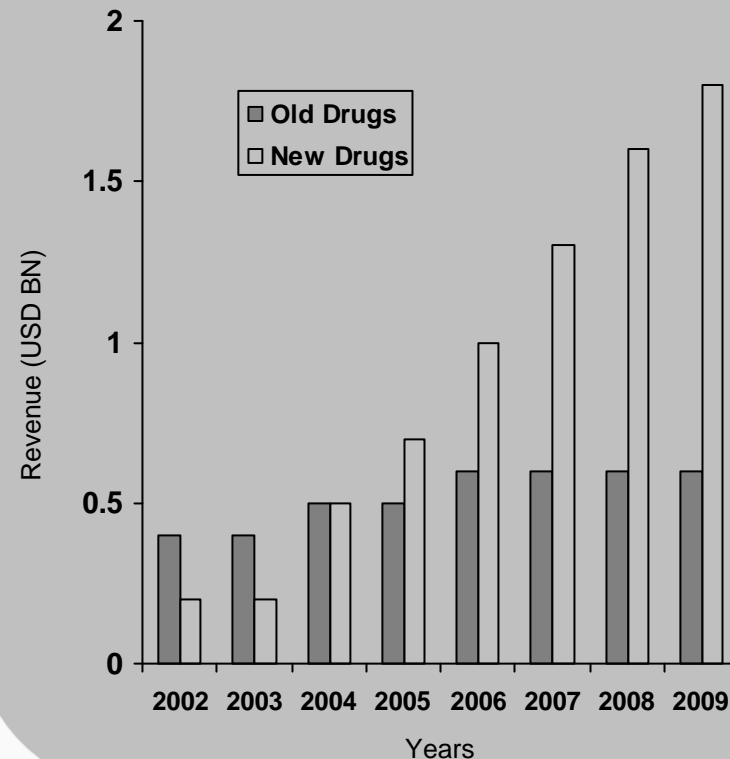
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Market Analysis – Increasing Resistance and New Antibiotics (3/4)

Proportion of *S. Aureus* Nosocomial Infections Resistant to Oxacillin (MRSA) Among ICU Patients, 1995 – 2003



Market for Hospital Anti-MRSA Antibiotics, 2002-2009 (USD BN)

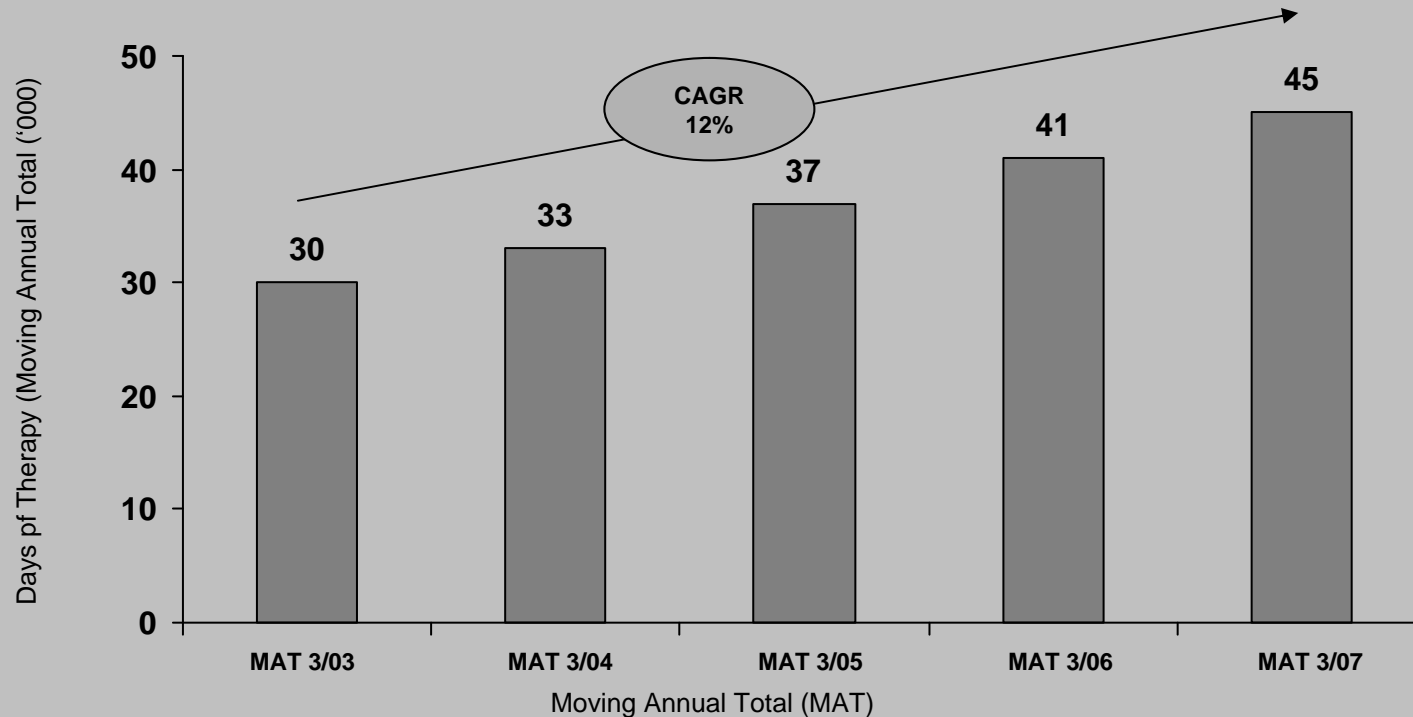


➤ Increasing resistance of the staphylococcus aureus bacterium over the years has created a continuous demand for new antibiotics and therapies in the MRSA market

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Market Analysis – MRSA DOT Growth and Economic Costs (4/4)

MRSA DOT (Days of Therapy) Is Growing Globally – Days of Therapy (Thousands) in Moving Annual Total (MAT), 2003-2007



➤ As per CDC, estimated annual medical costs due to Staph. aureus in the US is ~ USD 5 BN. However, a New York study quoted direct medical costs in the region of USD 34,000 per patient, with overall cost to the city of USD 435 MM

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Competitor Analysis: Current MRSA Drugs (1/2)

- The main competitors of telavancin are vancomycin and linezolid, however, recently there have been observations of rising rates of resistance of the disease towards both these drugs as well as risks associated with treatment failure
- The main advantage of telavancin over vancomycin appears to be a lower frequency of dosage – once daily; Linezolid has an edge over both the drugs in terms of availability of an oral dosage
- Recently, clinicians have been reverting somewhat unsuccessfully to older drugs, such as co-trimoxazole, clindamycin, minocycline, fluoroquinolones and doxycycline

Competitor	Company	Attributes
Vancocin (vancomycin)	Eli Lilly	<ul style="list-style-type: none"> - MRSA resistance to drug seen recently - IV Dosage - Frequent dosing every 6 hrs/ 12 hrs - Occasionally patients experience unacceptable side effects
Zyvox (linezolid)	Pfizer	<ul style="list-style-type: none"> - Already exhibiting resistance - Oral dosage available
Cubicin (daptomycin)	Cubist and Novartis	<ul style="list-style-type: none"> - Shows limited tissue penetration - Requires patient monitoring - Dosed once daily
Tygacil (tigecycline)	Wyeth	<ul style="list-style-type: none"> - Good empiric activity apart from pseudomonas aeruginosa
Zeven (dalbavancin)	Pfizer	<ul style="list-style-type: none"> - Available once weekly - Limited patent coverage left

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Competitor Analysis: Telavancin Vs Vancomycin – ATLAS I, II (2/2)

End Points	Telavancin	Vancomycin	Comments
Therapeutic Response	88.6%	86.2%	Telavancin has a marginally better therapeutic response than vancomycin in population with cSSIs
Therapeutic Response (MRSA)	89.9%	84.7%	Telavancin shows better therapeutic response than vancomycin in population subset with MRSA
Total Adverse Events	79%	72%	Telavancin shows higher rates of overall and serious adverse events than vancomycin, events being nausea, vomiting, foamy urine, etc.
Serious Adverse Events	7%	4%	
Taste Disturbance	33%	7%	Apart from Pruritus, where vancomycin displays significantly higher rates of occurrence than telavancin, the latter has higher chances of adverse events such as vomiting, nausea, taste disturbance, foamy urine, etc.
Nausea	27%	15%	
Vomiting	14%	7%	
Foamy Urine	13%	3%	
Pruritus	6%	13%	
Resistance	Low resistance, effective against MRSA and MSSA	Observed resistance (Vancomycin Resistant-MRSA)	Due to novelty, telavancin is more effective in fighting against MRSA compared to vancomycin, where MRSA has started showing resistance
Dosage	Once daily injectable	2 to 4 times daily IV	Better frequency of dosage of telavancin compared to vancomycin
Usage	Adult prescription only	Usage across age group	Telavancin has been approved by FDA for adult usage only

- Telavancin safety information contains warnings, the most significant being as follows: fetal risk, nephrotoxicity (new onset or worsening renal impairment), geriatric use (risk of adverse reactions greater in patients with impaired renal function), infusion related reactions (administered over a period of 60 minutes to reduce the risk of infusion-related reactions)

Source: Journal Watch; BNET; Bio World Today, Peer View

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Stratanalysis Viewpoints

Physician Opinion (Blogs)

"What advantage does Telavancin have over Vancomycin besides once daily and perhaps coverage of VRE¹? And that will be the marketing edge - once daily and less monitoring. But who cares unless it's outpatient? Will it be more cost effective than Linezolid or Daptomycin? If so, I'd consider it for VRE. I do not foresee this drug will become a blockbuster ... nor a workhorse. Perhaps (it would be successful for) institutions with a high rate of VRE, and for those institutions, they should ask themselves, 'How did we get here?' "

Stratanalysis Viewpoints and Analysis

- The deal highlights the merger of core strengths to the benefit of Theravance, a company focused on discovery and development, and Astellas, which has a strong marketing and sales presence across Japan, North America, Europe and Asia
- The main motivator for the MRSA market is the growing resistance of staphylococcus aureus bacterium to antibiotics, leading to the continuous demand for new therapies
 - However, this also means that the **blockbuster status of a new drug cannot continue for long if the bacterium builds resistance around the same**, and newer drugs hit the market to fill the gap
- With annual medical costs soaring to USD 34,000 per patient, MRSA Days of Therapy growing at a CAGR of 12%, and MRSA infections accounting for increasing percentages of the total number of staph infections, the market shows remarkably high opportunities for new therapies, such as telavancin
 - The issue is whether the drug can generate a continuous ROI in the face of growing resistance of the bacterium, and in a market of constant innovative antibiotics

Note: ¹Vancomycin-resistant enterococcus
Source: Stratanalysis Research

Website: www.stratanalysis.com

Phone:
+44 7950 324483

EMAIL:
hari@stratanalysis.com

SKYPE ID: harithrividramji

Thank You

