

Stratanalysis Document

FDA Warning: Cancer –TNF Drug Link in Children

Stratanalysis
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FDA Warning Cancer-TNF Drug Link

Renewed Safety Review For TNF Blockers

Investigative Evidence on the link between TNF-blockers and Juvenile Cancer

- **Investigation:** In June 2008, the FDA announced that it was investigating the link between TNF blockers and cancer in children and teens
- **Results:** That investigation is now complete, and identifies 48 cases of malignant cancers in children and teens and 147 cases of leukemia in all patients (including adults) taking TNF blockers. Eleven children and teens died of lymphoma or complications of treatment; 26 of the 30 deaths among leukemia patients were linked to TNF blockers
- **Fallout:** Based on this review, the FDA has asked companies to include strengthened warnings about the occurrence of lymphoma and other cancers in children and young adults using these medicines.

- TNF blockers currently available in the market and impacted by the announcement are:
 - *Remicade (infliximab)*
 - *Enbrel (etanercept)*
 - *Humira (adalimumab)*
 - *Cimzia (certolizumab pegol)*
 - *Simponi (golimumab)*

TNF - Blockers

- TNF blockers are used to treat rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis, psoriasis, Crohn's disease, ankylosing spondylitis, etc.
 - These drugs neutralize a protein, tumor necrosis factor alpha, that is overproduced in inflammatory diseases, whose normal function in the body is to fight cancer
- The drugs already carry a black-box warning, but the FDA now requires warning labels to highlight the drugs' possible association with lymphoma and other cancers in children and teens

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Enbrel use in Pediatric JIA

Enbrel in Juvenile Idiopathic Arthritis (JIA)

- ENBREL was first approved for juvenile idiopathic arthritis (JIA) in 1999, and **this is the only FDA-approved use** of ENBREL in the pediatric population
 - The drug is indicated for reducing the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients aged 2 and older
- An Amgen and Wyeth statement says that “*ENBREL continues to offer a favorable benefit-risk relationship for patients with the diseases for which it is indicated to treat, including moderate to severe Juvenile Idiopathic Arthritis (JIA). JIA can be a serious and potentially debilitating condition. Amgen will work with the FDA to update the U.S.*”

Enbrel Pediatric Market in the US

- Post-marketing data estimates that approximately **13,847 pediatric patients** have been treated with ENBREL globally through February 2009
- This is equivalent to approximately **44,600 patient-years of exposure** to ENBREL in the pediatric population

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Market Indicators – Juvenile Idiopathic Arthritis

Prevalence

- As of 2006, overall prevalence of juvenile rheumatoid arthritis was estimated to be 30 - 150 per 100,000 children in the US alone
- In the US and Canada there were an estimated 30,000 to 60,000 children and adolescents with juvenile rheumatoid arthritis in the same year
- Currently, approximately 294,000 children under the age of 18 are affected by pediatric arthritis and rheumatologic conditions

Cost to the Economy

- Juvenile arthritis is one of the most common childhood diseases in the United States
- Ambulatory care visits for pediatric arthritis and rheumatologic conditions averaged 827,000 annually in the US
- Arthritis and related conditions, such as juvenile arthritis, cost the US economy nearly USD 128 BN per year in medical care and indirect expenses, including lost wages and productivity

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Market Indicators – TNF Blockers

Sales

- The TNF blocker market was estimated to be worth USD 10 BN in 2006 and growing
- By 2008, sales of the four approved TNF Blocker brands were USD 16.35 BN with double digit growth rates due to indication expansion and new market entrants
 - Enbrel and Remicade had combined sales of USD 6.5 BN

Growth

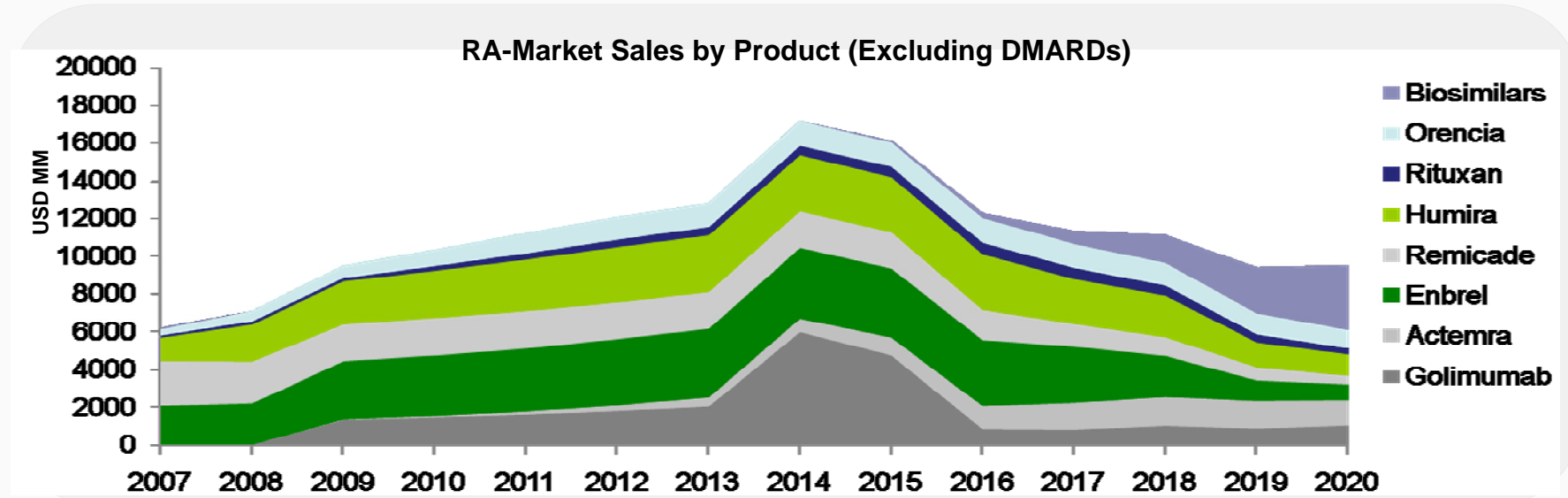
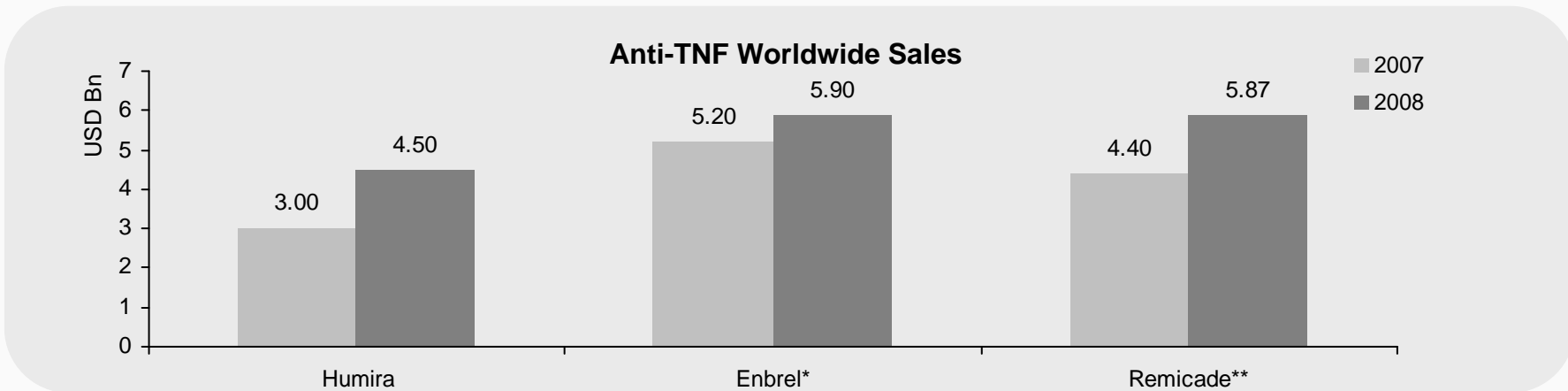
- Abbott's Humira recorded sales growth of 48% in 2008, over the previous year

Pipeline

- Amgen/ Wyeth and Centocor/ J&J, the companies behind Enbrel and Remicade respectively, also have fully human anti-TNF antibodies in their pipeline
- As of 2009, at least 15 TNF Blockers are in human testing and 19 are in the preclinical stage, being evaluated in various indications including ophthalmic use, osteoarthritis, Behcet's disease, organ transplantation, cutaneous sarcoidosis, oral mucositis, atypical dermatitis and sepsis

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TNF Blockers Market (1/2)



Note: *Combined worldwide Enbrel sales of Amgen and Wyeth; **Combined worldwide Remicade sales of J&J and Schering-Plough
 Source: Public sources available on the internet, Stratanalysis viewpoint

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TNF Blockers Market (2/2)

Stratanalysis Viewpoints and Analysis

Market Impact

“Rates for cancer cases with J&J's Remicade were consistently higher compared to expected background rates for lymphomas and all malignancies. Cancer rates for lymphoma were also higher for Amgen and Wyeth's Enbrel, but rates for all cancers were similar to background rates.”

- FDA

Sales of Remicade and Enbrel will be most hit

- The FDA did not calculate cancer rates for Abbott's Humira, UCB's Cimzia and J&J's Simponi
 - Humira and Cimzia are not widely used in the pediatric patients
 - Simponi was not approved at the time of analysis
- Anti-TNF's will now be used at a later stage for any disease negatively impacting its sales
- In 2008, manufacturers of anti-TNF drugs were instructed by the FDA to revise their prescription labels including the results of a study which proved that patients on TNF blockers are susceptible to serious fungal infections
- Enhanced focus on patient safety while being treated with anti-TNFs as an outcome of the above mentioned events will severely hit the anti-TNF sales

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Thank You

