



Modeling Federal Cost Savings of Follow-on Biologics

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Project Purpose

- Develop a scoring framework for modeling the impact of FOB entry on overall spending for biologics in United States
 - » Determine key scoring levers, through:
 - A literature review
 - Assessment of relevant economic models
- Use key scoring levers as basis for creating a scoring model
 - » Model assumptions based on previous research
 - Tested against biologics market data
 - » Model can be modified to score legislative proposals



Key Levers in FOB Model

- Biologics baseline spending estimate and projected growth rates
 - Legislative / regulatory
 - » Timing of legislation and implementing regulations
 - » FDA review time / regulatory pathway requirements
 - » Patent and other exclusivity considerations
 - Market creation / reaction
 - » Likely FOB entry by product size / market
 - » Market share of FOBs (physician / patient reaction)
 - » Pricing of FOB entrants / innovator response
 - Share of estimated effect that is Federal (versus other payers)
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Biologics Baseline Spending Estimate and Projected Growth Rates

- 2005 IMS: biologic spending at \$31.5 billion
 - » 20% average growth, 2001-2005
- Baseline adjusted to account for share of growth attributable to new products
 - » Assume new products protected over budget window
 - » Calculate share of growth that is price / utilization by pegging to NHE growth rates for pharmaceuticals (7.7% - 8.2% over 2008-2017)
- Reduce baseline by 14% to account for spending on insulin and human growth hormone, which have FOB pathways under FDCA
- Model assumes all off-patent products are fair game
 - » Legislation may adopt a case-by-case approach

Timing of Legislation and Implementing Regulations

- Various legislative proposals make requirements that bear on timing
 - » Regulation promulgation, clinical testing, review timeframes
 - » No guarantees ...
- Relevant precedents should guide modeling
 - » Time between passage of Hatch-Waxman and final regulations (4 years)
 - » FDA review time (CDER) 15.7 months, 75% of BLAs reviewed in 10 months
 - » EMEA review time all drugs: (15.8 months); approved biosimilars (2 years)

Expected Regulatory Pathway Requirements for FOBs

- FOB application requirements will affect timing of FOB market entry
 - » Requirements for proving similarity to reference product
 - » Requirements for proving safety and efficacy
 - Some form of clinical trial
 - » Requirements to prove no patent or exclusivity infringement
- FOB applicants will also have to meet current BLA (and FDCA) requirements
 - » For instance, licensing and inspection of manufacturing facilities
- Model assumes passage of legislation by FY 2008, then:
 - » FDA promulgation of final rules by start of FY 2011
 - » Immediate submission of FOB applications
 - » 2 year review of applications by FDA
 - » 1st FOB entry by beginning of FY 2013



Patent and Other Exclusivity Considerations

- Model assumes 10% of the biologics baseline goes off-patent in a year
 - » Typical patent life ranges are 8-14 years
 - » Based on current share of off-patent biologics in top tier of revenue

 - Other provisions may affect timing
 - » Additional legislated exclusivity
 - » Disclosure of patents
 - » Disclosure of process / trade secrets (constitutionality concerns)
 - » Minimum wait periods for FOB entry

 - Difficult to know exactly how these provisions would affect timing
 - » No assumption on additional legislated exclusivity
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Market Size Distribution for Brand Biologics

- Need to assess likely FOB markets, likely number of entrants
 - » Large revenue biologics more likely to have FOBs, more entrants
 - Similar to dynamics in the small molecule generics market
 - » Production costs would likely inhibit FOB entry into very small markets
- Threshold considerations include production, marketing, other costs
 - » ROI calculations sensitive to assumptions, failure risk
- Model assumes:
 - » 3 FOBs per large revenue off-patent biologic (large revenue: >\$1 billion)
 - » 1 FOB for medium revenue (medium revenue: \$250 million - \$1 billion)
 - » No FOBs for small revenue biologics (small revenue: <\$250 million)

Market Share Attained by FOB Entrants

- Market share attained by FOBs is a function of payer coverage, physician prescribing behavior, consumer demand, and pricing
 - » Strong PBM / managed care financial incentive to switch
 - » Won't happen without physician, patient comfort
 - » State pharmaceutical interchange laws likely won't apply to FOBs
 - » FOBs will need to be marketed, and will face stiff resistance
 - » Physician financial incentives (64% of biologics administered in MD office)
- Generic penetration rate currently around 60%
 - » Model uses this rate with ramp-up
 - » Likely upper bound (Omnitrope's EU share less than 1%)

■ ■ ■ ■ Pricing of FOB Entrants

- Pricing of FOB entrants will be a function of production and testing costs, number of market entrants, and overall market size
 - » Development of biologics is more expensive than small molecules
 - » Clinical trial requirements will augment these costs
 - » Distribution and marketing costs will exceed generics
 - In near term, FOB market entry may be immature, which affects pricing
 - » Single FOB entrant would not have incentive to price significantly lower than innovator
 - » Early EU data show price reductions of 10-25% for classes where FOBs compete
 - Industry analysts do not expect savings to reach generics levels
 - Avalere model assumes FOB pricing after 3 years on market to be:
 - » Large revenue FOBs priced at 70% of brand (with 3 competitors)
 - » Medium revenue FOBs priced at 90% of brand (with 1 competitor)
 - » Brand raises price in 1st year and lowers price thereafter
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Model Summary

- Model calculates the difference between baseline spending projections and spending under FOB policy for cost estimate
 - » Baseline spending calculated using actuals with 20% growth rate
 - » Baseline modified to account for pipeline and exclusion of insulin / HGH
- Assumes first FOBs enter market in FY2013
 - » Passage of legislation, implementation of regulations, submission of FOB application, and FDA approval
- Model incorporates typical patent life and distribution of market size for biologics
 - » 10% of biologics annually become subject to FOB competition
 - » biologics with larger revenues are more likely to have FOB competition
 - 0-3 FOB entrants depending on market size



Model Summary, Continued

- Assumes FOBs reach market saturation over three years
 - » 60% share
 - » 70-90% of innovator price

- Model output using above assumptions:
 - » Estimated Federal savings of \$3.6 billion over 10 years (2008-2017)
 - » No savings estimated from 2008-2012 due to time elapsing for FDA regulation promulgation and review of initial applications



Current Research

- To improve the model, focus on:
 - » *Temporal effect of disruptive innovation (Product revenue)*
 - » Variance in benefit design / coverage (Dataframe analysis)
 - » Legislated exclusivity period (literature)
 - » Market penetration assumptions (above, literature)

■■■ New Technology Will Affect Savings Stream

- Key variable in modeling is the lifespan of branded biotechnology products
- History shows that competition enters the market prior to patent expiry
 - » Erosion of first generation fertility products
 - » Slowed growth of Remicade after introduction of Humira
 - » Dramatic growth in new MS entrants, leveling of market leaders
 - » Reductions in Humulin sales with Lantus entry
- Cannot assume that out-year growth continues unabated
- Currently researching appropriate modeling assumptions

Disruptive Innovation: Case Studies

- Case 1: 2nd generation products
 - » In 2004, 2nd generation products launch from same manufacturers
 - » Within one year, older products' sales go to almost \$0
 - Case 2: Entry of competitors
 - » Product's growth is 65% and 25% in years before competitors launch
 - » Post launch, product's growth goes down to 12%
 - Case 3: Crowded class with many old products
 - » In 2002, new product growth is 90% and it surpasses revenue of older product
 - » Since 2003, new product has doubled revenue, old product's revenue cut in half
 - Case 4: Old-line product sees competition from product with 2nd indication
 - » Older product sees flat sales (~ 2% per year), newer product doubles revenue
 - » Surpasses competitor within 2 years of 2nd indication
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Translation to Modeling Assumption

- Reduction in savings stream will depend on
 - » Probability of new product entry (size of franchise)
 - » Positioning in class (price, volume)
 - » Timing (physician, patient, payer reactions)
 - X percent chance of a Y reduction in savings over Z years
 - » All products studied to date see erosion of 5-80% over 10 years
 - » Looking at larger biotech, perhaps a 10-25% range erosion
 - Easier to apply in product-specific model
 - » Although product-specific model have other liabilities
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Conclusion

- Some federal savings associated with all proposals
- Many unknowns complicate modeling of FOBs
 - » Regulatory variables
 - » Marketplace variables
- Further modeling work is important to fully anticipate the FOB dynamic
 - » *Temporal effect of disruptive innovation (Product revenue)*
 - » Variance in benefit design / coverage (Dataframe analysis)
 - » Legislated exclusivity period (literature)
 - » Market penetration assumptions (above, literature)