Biosimilars Landscape in the US

A multi-billion dollar industry in making

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MEHTA PARTNERS

Advisors

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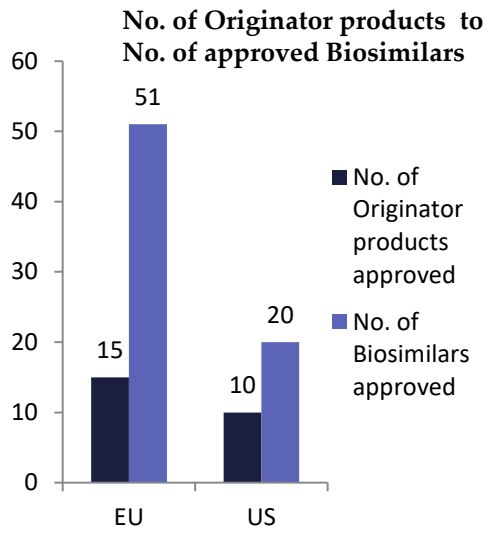
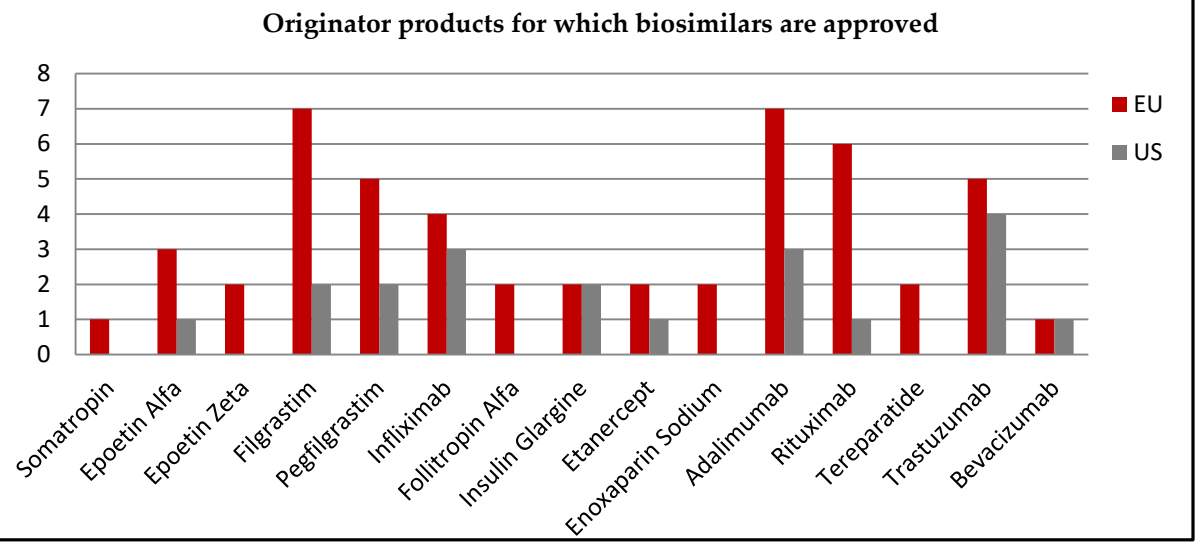
Evolution of Biosimilar Landscape to Date

- Only 15 first wave of biologics losing patent vs 150 generics a generation ago
  - US took the lead with small molecule generics, but now playing catch-up
- Because of complexity, regulators are not ready with the framework
  - This in turn has given an opportunity to the originators to add additional barriers from patent walls to supplying their product
- Therefore, only a few biosimilars have been approved leading to very modest discounting to date
- The question is when, not if, substitution with biosimilars will be a norm
  - US FDA new drug approval pace a big help; 45 approvals in 2017 and nearly 60 in 2018
  - Recent interchangeability guidelines is a positive step favoring biosimilars
- Next wave of biologic patent expiry to experience a normalized landscape
  - Patents for some of the reformulated first wave biologics also expiring then
- Innovator biopharma profits face strong headwinds from biosimilars
  - Over 80% discounting on $500B of most profitable innovator biologics sales could decimate margins in next decade

Source: Company Reports, MP Analysis

Biosimilars Macro Landscape





- Originator biologics sales WW are over $250B, and about one-half from the US
  - By comparison, biosimilars globally account for only $5B in sales, which is likely to triple by 2020 from this low base
  - At least $200B of biologics sales face biosimilar competition, which should amount to $40B in biosimilar sales by 2025—even at 80% discount to the originator's price, as multiple initiatives converge to increase biosimilars marketplace adoption
  - US is likely to be a major contributor to the global biosimilars revenue with ~40 biosimilars already in development, out of which ~20 are nearing approval
- Presently, in EU, 51 biosimilars have been approved for 15 originator products, contributing to about $4.4B of the global biosimilars sales
- By comparison, biosimilars growth has been sluggish in the US with only 18 approved biosimilars for 10 originator products, contributing to just about ~$200m in biosimilars sales
  - Of the 15 approved biosimilars, only 6 are launched for 4 reference products in US and even fewer have achieved any market success

Source: Company Reports, MP Analysis

Current Challenges for Biosimilar Uptake in the US

Regulatory Barriers

- Fluid regulatory landscape leading to high cost and long development timelines
- Unclear substitutability guidelines
- Sourcing of reference products

Legal Barriers

- Patent litigation by originator companies
- Delayed market entry and added cost of development

Manufacturing Complexities

- Reproducibility issues
- Low yield of the product, requiring large manufacturing capacities
- Switch from stainless steel bioreactors to single use bioreactors

Physician Acceptance

- Lack of confidence in switching to biosimilars
- Minimal price difference between bisoimilars and reference drugs
- No health policies that mandate the biosimilar use

Market Place

- Long term contracts of PBMs with originator companies
- Originators slashing down the prices to prevent biosimilar entry
- Originators launching new or alternative strength formulations

Source: Primary research, MP Analysis

US Biosimilars Landscape Today, Outlook Tomorrow (1/2)

- Sales of biosimilars in the US lag, as was the case during initial period in Europe and during the initial period of small molecule generic uptake
- The US marketing and payor landscape compounds these challenges
- However, pace of change to accelerate biosimilar approvals, and to simplify acceptance in the marketplace is gaining momentum
  - Dr. Gottlieb and his successor at the FDA has a number of initiatives, from in silico models to correlate PK-PD responses, to accepting clinical data using non-US originator made products, to developing critical quality attributes to reduce the number of lots of the reference product required, to data sharing agreements with foreign regulators, etc
  - These ongoing range of refinements aim to provide overall clarity of the FDA protocol to approve biosimilars, though this is likely to take another year or so
  - FDA has been open to innovative approaches for establishing biosimilarity for eg. Last year, Coherus' pegfilgrastim got the approval based on its analytical and phase I clinical trial data; such innovative approaches will reduce the development cost as well as the timelines
  - Currently, the time to biosimilars review and approval by the US FDA has reduced to 7-9 months, as compared to 18-24 months in 2014
- Market acceptance will take longer to unfold due to a range of inefficiencies embedded in the 'capitalism as practiced by the regulated industry' structure
  - First wave of biologic originators are playing this structure to the hilt and locking in payor groups with long term contracts with highly discounted prices that the initial group of biosimilar companies have not even had a chance to match or exceed
  - The US Government (regulators, policy-makers and judiciaries) will need to rule on how best to balance the societal needs with the current bias towards market forces, even when these forces are compromised by a range of regulatory barriers

Source: Company Reports, MP Analysis

US Biosimilars Landscape Today, Outlook Tomorrow (2/2)

- With adoption of biosimilars, additional 1.2m patients will have access to biologics, which is currently denied due to high cost
- Payor groups are increasingly taking initiatives to overcome these inefficiencies, where a potential silver lining of giving preference to biosimilars seems to be evolving, almost akin to substitution
  - Approval of next set of biosimilar molecules from the first wave of monoclonal antibodies is likely to trigger a more intensive move in this direction
  - Biosimilar marketers will need to discount their prices well in excess of 60% of the originator price for this effort to achieve a sufficient critical mass
- Competition will only grow even though only a half a dozen companies can be expected to take a lions share of each molecule sales in most major markets
  - Globally, from ~40 companies in 2015, the number of companies that have expanded their biosimilar investments has increased to ~70 in 2018
- Many other companies, who could benefit from creating a sizable biosimilar vertical, still seem to be concerned that status quo will continue and the opportunity will remain constrained, while continuing to require substantial initial investments
  - Smaller companies in biosimilar space inherently face constraints, from amounts they can invest, to number of molecules they can develop
  - Larger companies, many who originated some of the biologics and are now deploying their experiences, and depreciated manufacturing capacity to develop and market the biosimilars of biologics they did not develop, and are still exploring how they can crack open this $40B+ opportunity ($200B originator value at 80% discount) globally
- Pricing strategy and value management are an increasingly important requirement with global price declines and rising competition

Source: Company Reports, MP Analysis

The Tide is About to Turn in Favor of Biosimilars as Politicians, Regulators, Payors & Patients Alike Address the Barriers

- With 15+ biologics facing patent expiry by 2020, and ~25 more in the coming decade, ~$200+B biologics sales underpin the first wave of biosimilar opportunity, which is forecasted to approach $500B around 2030
- These high priced biologics contribute as much as one-half of healthcare inflation even as only a small fraction of eligible patients can afford these treatments globally
- Proof of equivalence from a number of marketed biosimilars points to substitutability, already being partly practiced by a range of countries and payors
- Recently FDA has finalized interchangeability guidelines favoring the biosimilar manufacturers by -
  - Allowing interchangeable designated products to be substitutable at pharmacy level without the intervention of the prescribers
  - Giving more flexibility to use of global or non-US comparator reference product
  - Clear guidelines to design switch studies where the primary endpoint would be to assess PK/PD rather than focus on efficacy, which in turn will reduce the cost and timeline of clinical trials
  - In parallel, preclinical and clinical requirements are being streamlined to reduce development costs closer to $40m from earlier $120m, which in turn should cut time to approval in half to ~3-years from the 6 – 10 years to-date
- Discounts are rising from 30% to 60%, and high innovative biologics prices ease the path to 80% discounts while still achieving attractive operating margins
- Innovators in many markets are resorting to predatory, preemptive discounting approaching 90% to delay market share loss to biosimilars
- Acceleration of biosimilars adoption is expected to treat some multiple of currently treated patient populations in developed countries, and many more in emerging countries, while at the same time lowering healthcare costs, and thereby fostering next wave of innovations

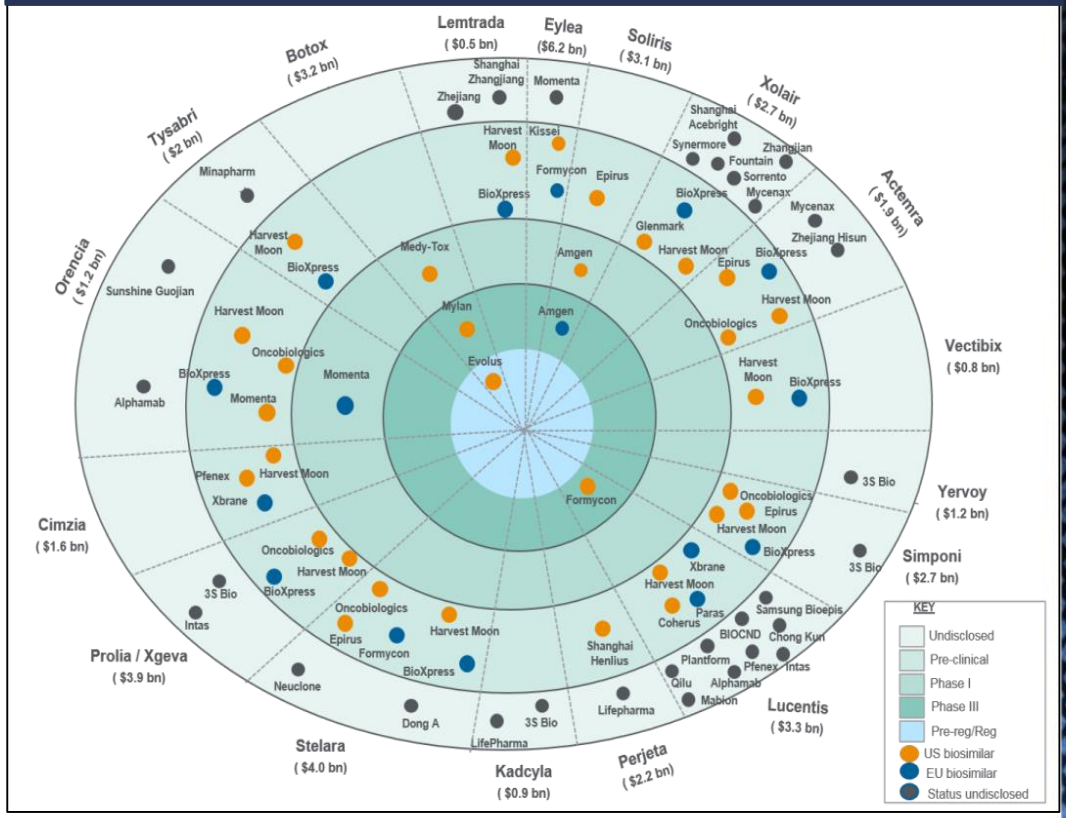
Source: Company Reports, MP Analysis

Growing Biosimilar Opportunities for the US Market

Not too Late for the Early Wave but Just in Time for the Next Wave

Competitive Landscape – Early Wave Biosimilars in US				
Biologics	**Marketed**	**Approved**	**Pending Approval**	**Phase III**
Etanercept	-	1	-	1
Filgrastim	2		3	1
Pegfilgrastim	2	-	2	-
Epoetin Alfa/Zeta	-	1	-	-
Rituximab	-	1	2	2
Trastuzumab	-	4	1	1
Adalimumab	-	3	1	4
Bevacizumab	-	1	1	2
Infliximab	2	1	1	-
Total	6	12	11	11

Competitive Landscape – Next Wave Biosimilars



Source: Company Reports, MP Analysis, www.centerforbiosimilars.com

More Companies are Likely to Join the Race for the Next Wave of Biosimilars

- As the regulatory guidelines get clearer and the substitutability becomes a norm, high competitive intensity is expected for the US market with at least half a dozen companies developing a broader portfolio
  - MNCs working on biosimilars are quiet and will only emerge once their products are in the late phase of development
- Ready and "unlimited" access to capital in China ensures that a number of Chinese companies will strive for global biosimilar leadership
- South Korean companies, led by Celltrion and Samsung, are still searching for a global strategy, anchored around their vast manufacturing and development infrastructure; so far they have relied on their western partners for clinical development
- This competitive landscape, combined with near term market uncertainty, calls for consolidation to reduce duplication of efforts
  - Create a JV/partnership to achieve Top-5 leadership, to be enhanced by consolidating from a position of strength

Source: Company Reports, MP Analysis

Over the Next Decade, Biosimilars will Mimic the Small Molecule Generics

- Next decade will witness at least a couple of dozens of biologics going off-patent, giving an opportunity to launch 3-5 molecules per year
- Cost of development: Low-double digit millions
- Development requirements: In vitro characterization, BA/BE studies with a small clinical safety study
- Timeline of development: ~2 years
- Competition: Extremely high competition with >10 cos for most of the biosimilars
- Market Penetration: >90%
- Discounts to originator: >80%

Source: Company Reports, MP Analysis

Partnering Opportunities

With about 3 decades of diverse experience and integrated perspective in domestic and global BioPharma industry, MP Group has capabilities to support your team in the following key areas –

- **Identify unique and creative domestic and global investment opportunities**
- **Deep-dive assessment of specific opportunities**
- **Assessment and monitoring current investment portfolio (equity/non-equity)**
- **Market and product portfolio due diligence**
- **Technical due diligence of the target investment opportunity**
- **Commercial and technical feasibility studies**

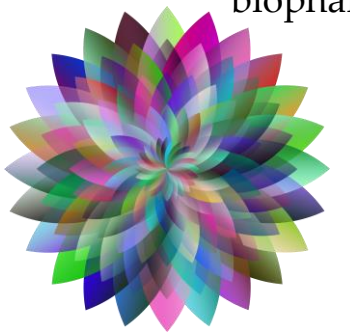
Who We Are

GLOBAL EXPERIENCE

Integrated global perspective anchored around 29 years of biopharmaceutical experience

OUR TEAM

Small and nimble—with industry experience, financial knowhow, scientific expertise and a dash of common sense



BUILDING RELATIONSHIPS

With a worldwide network and lasting friendships, we have built a community of business leaders and science experts to inform our work

WELL GROUNDED

Our globally integrated analysis has identified opportunities early—from NCEs to biosimilars, generics to specialty pharma—which we have helped implement, broadening global growth choices for senior managements

GROWTH AT A FAIR VALUE

As an extension of the management team, we help cross-fertilize actionable ideas

MP THINKS GLOBALLY, ACTS LOCALLY

MP Team's Global Network

Deep roots at every level of Indian Biopharma

	No of Companies* Retained MPA from 'Top 10' group	No of mid-cap, small companies worked/ well-connected with
Global Pharma (US/Eu)	4/10	100+
Indian	8/10	~100
Japan	3/10	70+
ROW	n/a	~100

- ✓ Retained by senior managements from across the globe
- ✓ Also robust connections with – API, CRAM, CRO, Biotech/Biosimilar, PE, VC and angle investors companies in all geographies
- ✓ Good access to ~all medical specialists, bureaucrats, academia

* At top management level

LANDMARK DEALS IN INDIA CONCEPTUALISED AND EXECUTED BY MP TEAM

1st NCE licensed-out from India (Dr. Reddy's balaglitazone out-licensed to Novo Nordisk)

1st Indian company acquiring major unit in the USA (Sun Pharma acquires Caraco Pharma)

Largest pharma deal of India Daiichi Sankyo acquires Ranbaxy

1st Indian Company making alliance with an MNC for NCE manufacturing (JV between Altana and Zydus Cadila to manufacture 'on patent' pantoprazole)

1st Indian company investing in US Biotech (GVK Bio acquires Aragen Biosciences in the US)

Major deal where an MNC partner buy-outs its Indian partner (Astra Zeneca buys out Astra-IDL, A Hinduja Group Company)

Largest divestment by MNC in India (Brand divestment of Solvay to Indoco Remedies and Alembic Pharma)

1st strategic entry by an Indian company in Japan through brand acquisitions (Sun Pharma acquired 14 long listed products from Novartis, Japan)

First Indian co investing in innovation with direct MNC link (Piramal acquired Hoechst R&D center)

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