Pharmaceuticals

Biosimilars – Slow US offtake not a concern

Biosimilars offtake in US has been perceived to be lower despite the fact 15 biosimilars have been approved by FDA till end CY18 with three more approvals in first four months of current calendar. This is in sharp contrast to an extremely supportive macro in which biosimilars by definition would be helpful in lowering out of pocket costs for consumers. However, we reckon that such a perception built around biosimilars has been on basis of a few data points which primarily include lackluster performance of two Remicade biosimilars. We believe it would be inaccurate to extrapolate the ongoing low penetration of biosimilars as a template which can be then extended to all upcoming launches. Indeed, one can argue that ramp up of Basaglar, a biosimilar to Sanofi's Lantus from 20% to 25% in prescription volumes and 300bps rise to ~19% in value share over a span of less than a year is a solid counter example to the prevailing perception. Moreover, of the 20-odd approved biosimilars, about half of them have not yet been launched as in several cases, innovators have entered in to settlement agreement with some of the oncology and immunology biosimilar manufacturers which precludes their launches before agreed timelines. Another interesting nuance can be seen with launch of Neulasta biosimilars which, within a year of launch, have captured over ~25% prescription volume share of the syringe market; albeit, innovator still accounts for ~60% volumes due to shift to follow-on auto injector kit. In a sense, we believe there is just not enough history of biosimilar sales available, unlike in small molecules, which can be used to conclude a definite lack of progress. Albeit concerns will be raised on Adalimumab (about 6 players have settled) and Pegfilgrastim (at least 4 in pipeline) and it remains to be seen how market share is divvied up basis price discounting to get formulary coverage.

Remicade biosimilars not a template to judge US progress

Remicade biosimilars despite being at least 2-3 years in the market and supported by marketing firepower of Pfizer and Merck have had a volume and value share of just 6% each as per data till February 2019 ; such is the strong defence mounted by innovator which still accounts for over 90% of prescriptions. This lack of penetration has been one of the key reason for perceived lack of biosimilar progress in US. However, the contrast with Neupogen could not be more illuminating as oncology biosimilars now control ~80% of the syringe market even though Amgen still has over 40% of total Filgrastim prescription volume through vials, which does not have biosimilar presence. (except Granix).

Looking at biosimilar off take from a therapy perspective we believe that oncology as a therapy is more acute and pliable to faster biosimilar penetration with high growth of new patients which can be put on biosimilars; on the other hand, physicians in inflammation or immunology which have chronic and large stable populations with slower intake of fresh volumes may refrain from switching to biosimilars which do not, as yet, have built a database of responses from an immunogenicity and efficacy perspective outside of clinical trials. In this regard, biosimilars would behave more like branded drugs in small molecules and their absorption would depend on formulary coverage, pricing, payor contracting; in other words, those first off the block would enjoy the longest runway for growth. In this note, we look at the existing US biosimilar landscape and potential launches in the next 2-3 years. Within our coverage universe, Biocon is at the forefront of biosimilar development buttressed by partnership with Sandoz in addition to Mylan; albeit stock is fully valued at 30x FY21 PE despite doubling of EPS over FY19-21E.

Research Analyst: Bhavesh Gandhi ✉ bhavesh.gandhi@yessecuritiesltd.in
Head of Research: Amar Ambani ✉ amar.ambani@yessecuritiesltd.in

US biosimilars: Indvidual dynamics at play

A look at the 3 key biosimilars of Infliximab (Remicade), Filgrastim (Neupogen) and Pegfilgrastim (Neulasta) shows each molecule has its own dynamics; even with just this data set, apart from Remicade, other two biosimilars have made a difference to respective market which convices us about the long runway ahead.

Neulasta: Innovator Amgen, to ward off the biosimilar challenge has moved about 2/3rd of the volume market to follow-on brand Onpro which has a dosing advantage of being injected at home vs. syringe which requires visit to the physician office. Albeit, Biocon/Mylan and Coherus biosimilars have captured 25% of the syringe prescription market in a short period of time, with Mylan launching Fulphila at a 33% discount to the wholesale acquisition cost of innovator brand. Additionally, since biosimilar syringes are cheaper than Onpro kit, there exists a possibility of shift from the latter to the former, thereby expanding biosimilar market.

Neupogen: Unlike Neulasta where innovator orchestrated a shift to a follow-on brand, Neupogen, or Filgrastim has seen a larger impact of biosimilars. Since competition has largely been restricted to the syringes market, Neupogen still has ~30% share of the total prescriber volume but Zarxio, the Sandoz biosimilar has a ~40% value share of the total filgrastim market with another 22% held by Teva biosimilar Granix.

Remicade: Despite two biosimilars on market for 2-3 years, Remicade has hold on to its own with more than 90% share each of the volume and sales. In terms of pricing, biosimilars have been launched at a 20-35% discount to the innovator brand, though given the vagaries of US distribution system, the net price to insurers is not known and depends on the extent of rebates on offer. Looking at ongoing biosimilar commentary, we reckon treatment of rebates and their size will play an important role in the absorption of biosimilars.

Pfizer earnings commentary bullish on oncology biosimilars

Pfizer garnered an approval for Trastuzumab in March 2019 and in its Q4 CY18 earnings call, company remains optimistic on progress of its oncology biosimilars. It expressed hope that the experience in oncology biosimilars is likely to be different from those in the inflammation and immunology space as the latter are of a longer duration and hence more susceptible to strong defence tactics adopted by innovators. Such commentary augurs well for Trastuzumab biosimilars; Biocon/Mylan, by virtue of a settlement with Roche and early FDA approval would be the first off the block, probably in H2 CY19, in our view.

Angela Hwang- Group President, Pfizer Biopharmaceuticals Group: "What we're also seeing are differences in the EU and in the U.S. So in the EU, we see a very rapid uptake and actually great acceptance of biosimilars. And if I just use infliximab molecule as an example, the infliximab biosimilars are about 65% of the total molecule. We see a market that, I think, is evolving and developing in the U.S. and I think that our experience with infliximab in the U.S. really is not a great analogy for what might be to come with our new oncology biosimilars. Just because they're very different dynamics in the inflammation and immunology (I&I) space compared to the oncology space. However, we see different dynamics in the oncology space, and that is because oncology drugs are shorter in duration of therapy. So that allows new patients to turn over faster. And it will make it easier for the physicians to initiate new patients on oncology biosimilars. And we believe that this will enable customers to benefit from the cost savings that they can derive from biosimilars much more quickly than what you might see in the I&I space where the duration of therapy is very long. It's a long chronic disease. So we are excited about the upcoming launches of our oncology biosimilars".

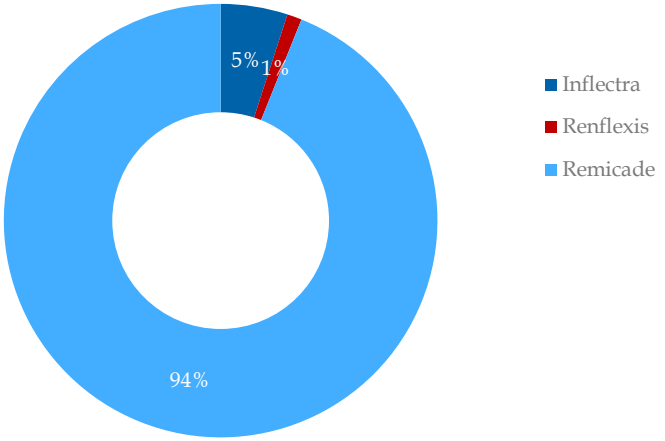
Source: Company, YES Sec – Research

Exhibit 1: FDA approved biosimilars and status

Reference biologic	Biosimilar	Drug name	Company	Approval date	Indication	Status
Herceptin	Trastuzumab	Trazimera	Pfizer	March 2019	Oncology	Unknown
Herceptin	Trastuzumab	Ontruzant	Samsung Bioepis/ Merck	January 2019	Oncology	Unknown
Herceptin	Trastuzumab	Herzuma	Celltrion	December 2018	Oncology	Early in CY20 after launch of Truxima
Herceptin	Trastuzumab	Ogivri	Biocon/ Mylan	December 2017	Oncology	Mylan will launch as per settlement with Roche; timeline undisclosed
Neulasta	Pegfilgrastim	Fulphila	Biocon/ Mylan	June 2018	Oncology	Launched
Neulasta	Pegfilgrastim	Udencya	Coherus	November 2018	Oncology	Launched
Humira	Adalimumab	Hyrimoz	Sandoz	October 2018	Rheumatoid arthritis, chronic plaque psoriasis	US entry not before Sep 2023 as per settlement with AbbVie
Humira	Adalimumab	Cyltezo	Boehringer Ingelheim	August 2017	Rheumatoid arthritis, chronic plaque psoriasis	In litigation with AbbVie over latter's patent position
Humira	Adalimumab	Amjevita	Amgen	September 2016	Rheumatoid arthritis, chronic plaque psoriasis	Settled for Jan 2023 launch
Remicade	Infliximab	Renflexis	Samsung Bioepis/ Merck	May 2017	Rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, and ankylosing spondylitis	Launched
Remicade	Infliximab	Inflectra	Pfizer/ Celltrion	April 2016	Rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, and ankylosing spondylitis	Launched
Neupogen	Filgrastim	Nivestym	Pfizer	July 2018	Oncology	Launched
Neupogen	Filgrastim	Zarxio	Sandoz	March 2015	Oncology	Launched
Enbrel	Etanercept	Erelzi	Sandoz	August 2016	severe rheumatoid arthritis, plaque psoriasis	In litigation with Amgen
Rituxan	Rituximab	Truxima	Teva/ Celltrion	November 2018	Oncology	Launch in H2 CY19; Teva has settled with Roche
Epogen	Epoetin alfa	Retacrit	Pfizer	May 2018	Anemia due to kidney failure, chemotherapy, HIV	Launched
Avastin	Bevacizumab	Mvasi	Amgen/ Allergan	September 2017	Oncology	Avastin will soon be off patent; biosimilar launch expected in H2 CY19

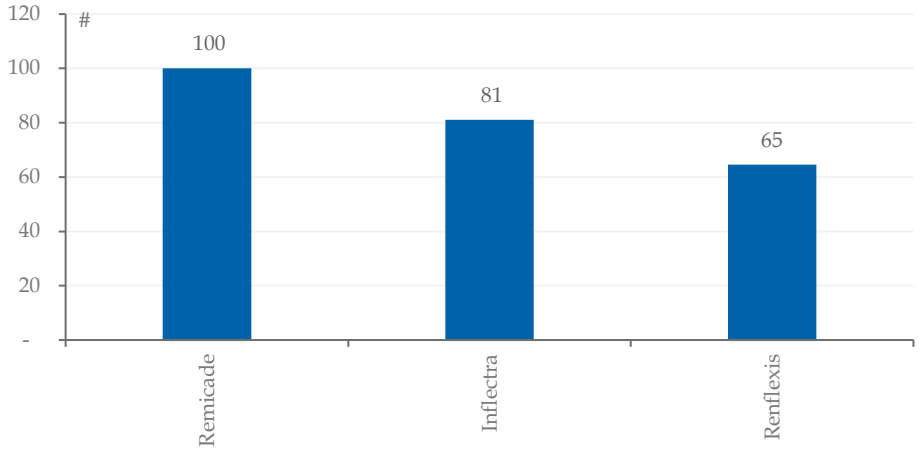
Source: Companies, YES Sec – Research

Exhibit 2: Remicade: Biosimilars have failed to make a dent



Source: YES Sec – Research, Bloomberg Symphony

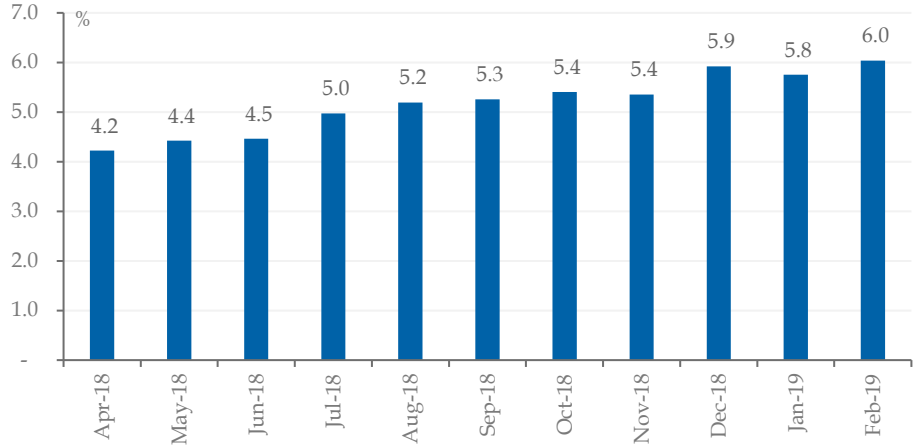
Exhibit 3: Remicade biosimilars at 20-35%* discount



Source: Company, YES Sec - Research, Bloomberg

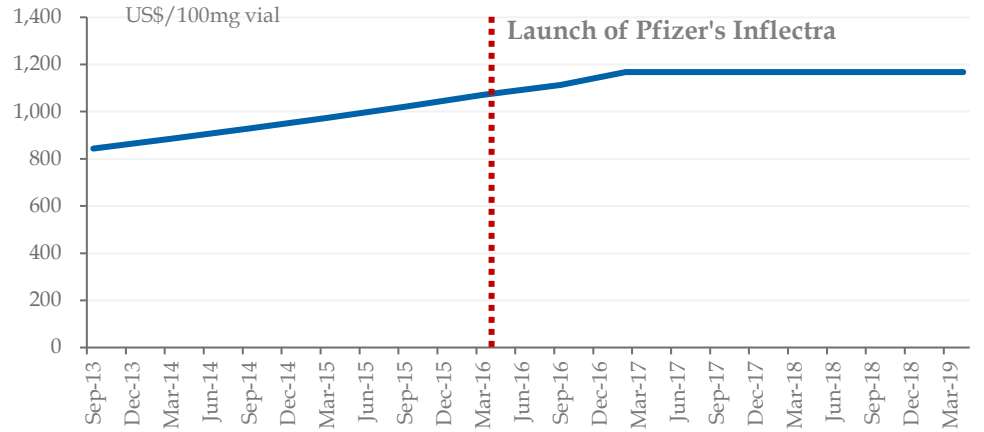
*Based on as reported WAC, Bloomberg Symphony data till February 2019

Exhibit 4: Inflectra (Remicade biosim) volume share at 6%



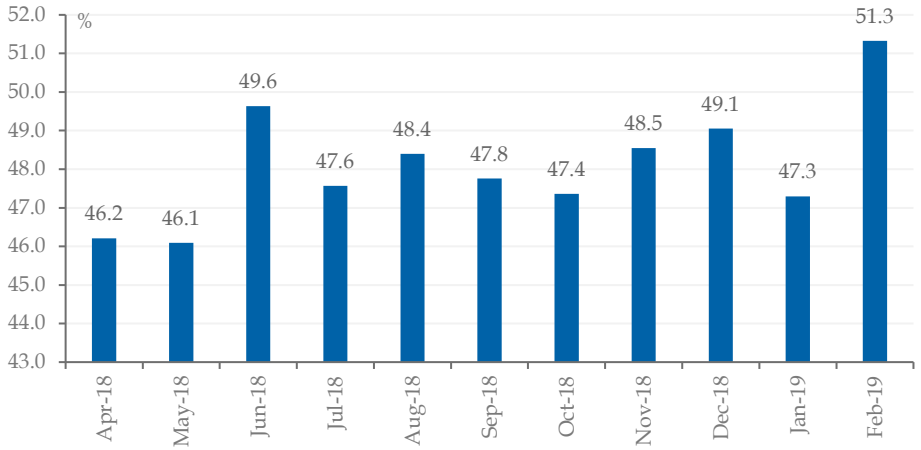
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 5: Remicade WAC trend



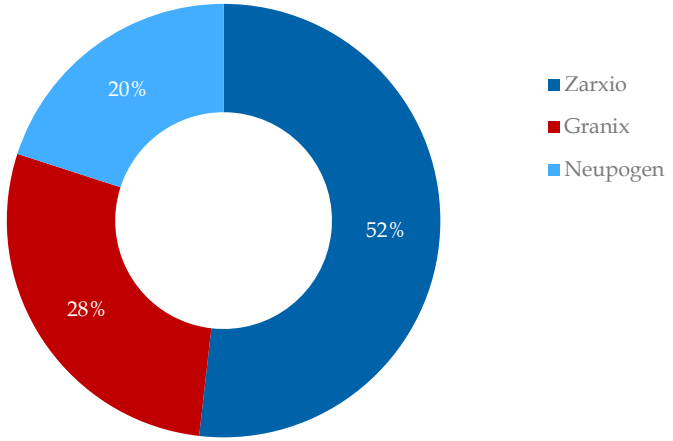
Source: Company, YES Sec - Research, Bloomberg

Exhibit 6: Zarxio has over 50% share in Neupogen syringes



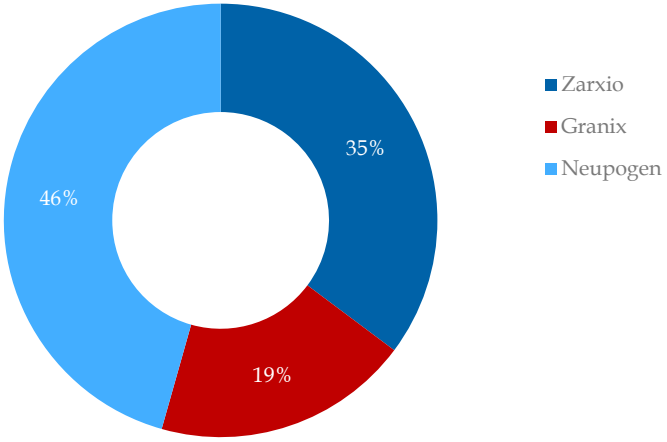
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 8: Filgrastim syringe Rx market break up



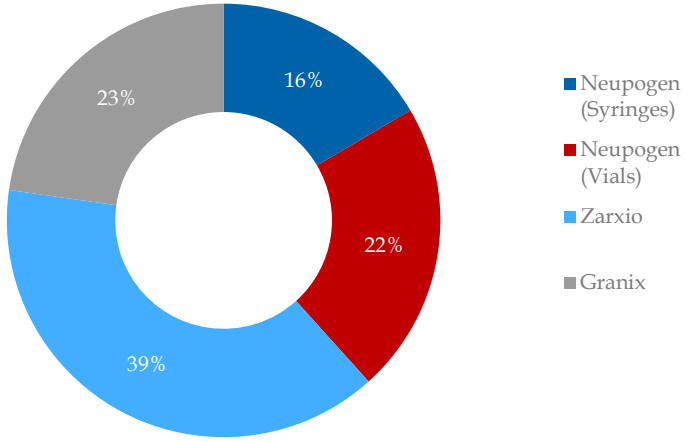
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 7: Neupogen still commands over 40% Rx due to vials



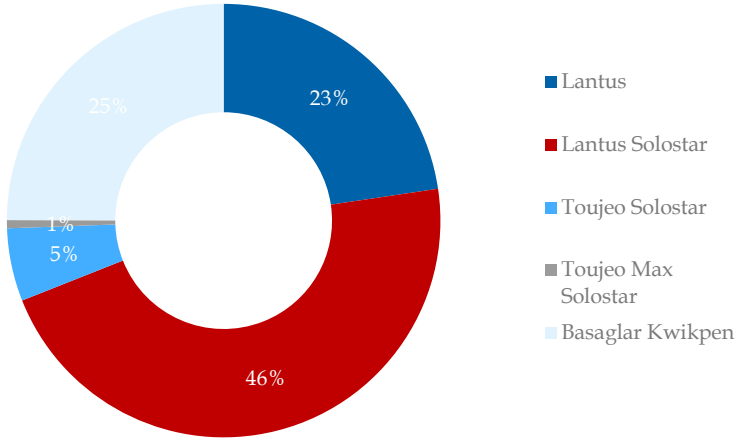
Source: YES Sec – Research, Bloomberg Symphony
Note: Bloomberg Symphony data till February 2019

Exhibit 9: Zarxio dominates Filgrastim US$ sales



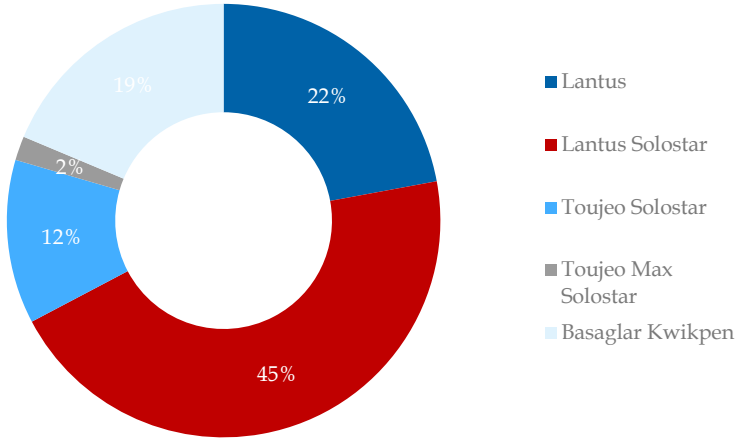
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 10: Basaglar: 25% share in Insulin Glargine volume…



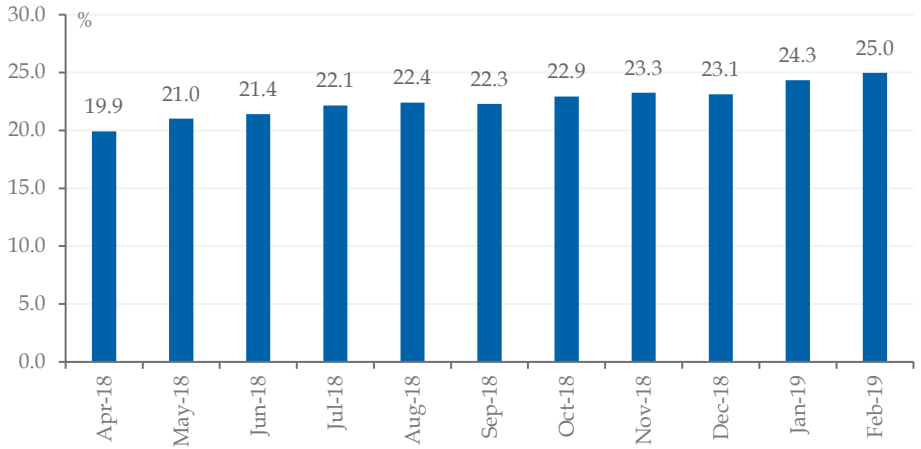
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 12: …and a ~20% share by value



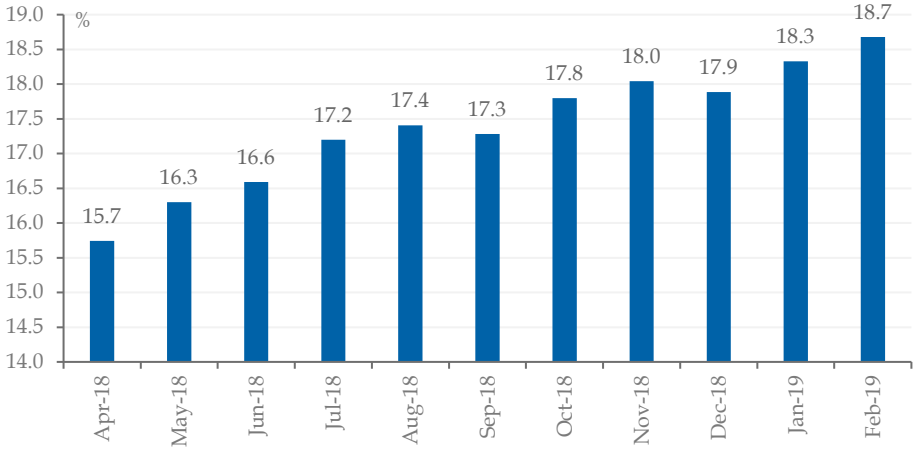
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 11: Basaglar added ~5ppts Rx share in less than 1 year



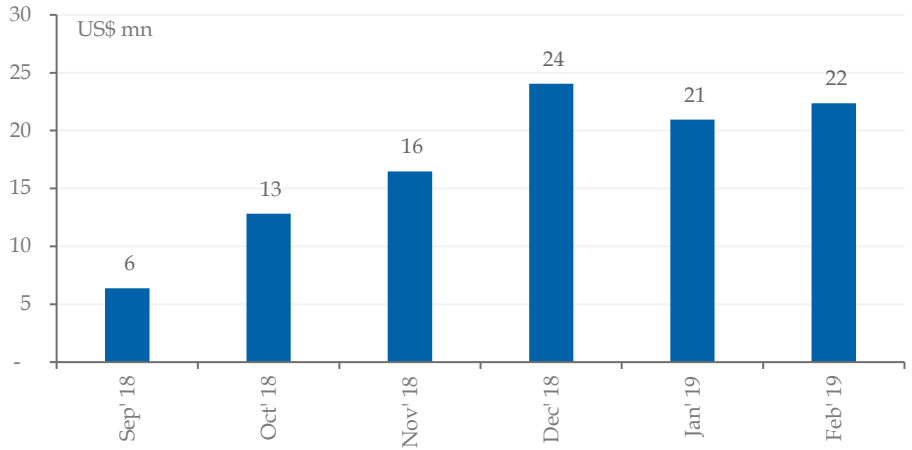
Source: YES Sec – Research, Bloomberg Symphony
Note: Bloomberg Symphony data till February 2019

Exhibit 13: Basaglar: trend in value market share



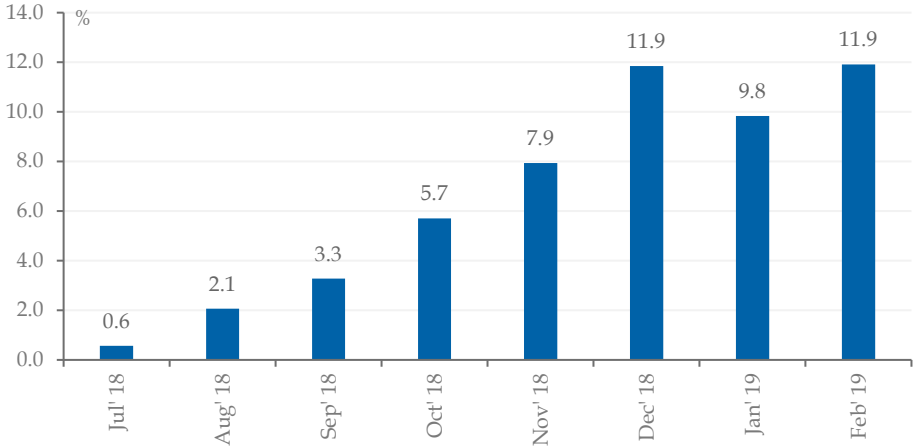
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 14: Fulphila (Neulasta biosim) sales trend



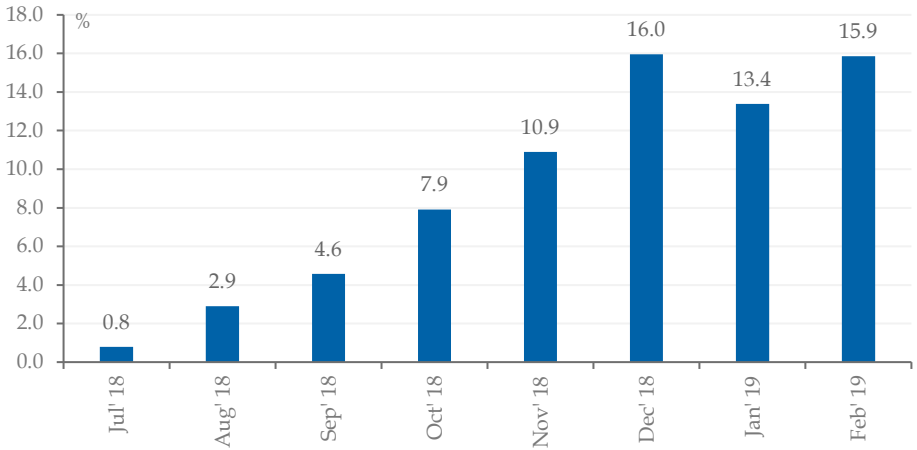
Source: YES Sec – Research, Bloomberg Symphony

Exhibit 15: Fulphila has 12% syringe market by value



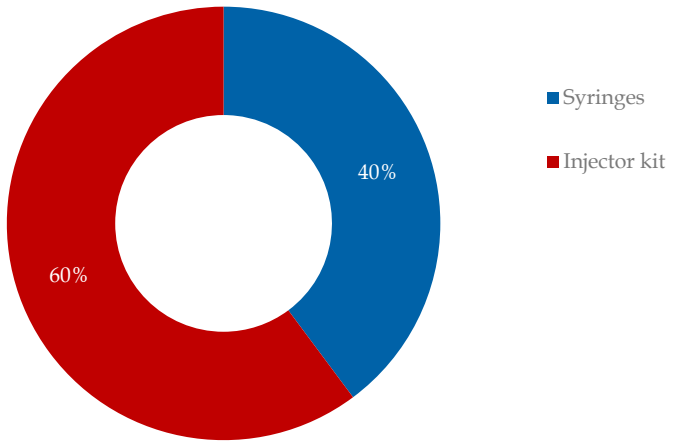
Source: YES Sec – Research, Bloomberg Symphony
Note: Bloomberg Symphony data till February 2019

Exhibit 16: Fulphila: 16% Pegfilgrastim syringe Rx volume



Source: YES Sec – Research, Bloomberg Symphony

Exhibit 17: Pegfilgrastim: ~60% market shifted to injector kit



Source: YES Sec – Research, Bloomberg Symphony

Exhibit 18: Upcoming biosimilars pipeline in US

Filing	Reference biologic	Reference indication	Company	Comments
Pegfilgrastim	Neulasta	Oncology	Sandoz	Resubmitted BLA to FDA in April 2019 after receipt of CRL in June 2016
			Fresenius Kabi	In partnership with Dr Reddys'; two phase I studies met their primary endpoints.
			Pfizer	In Phase 1 studies
			Cadila	Will file in Q1 CY20
Rituximab	Rituxan	Oncology	Sandoz	Received CRL in May 2018; for now, won't pursue any further
			Fresenius Kabi	2nd biosimilar partnership with Dr Reddys'
			Pfizer	In Phase 3 studies
			Amgen/Allergan	Announced positive Phase 1/3 trials in Jan 2019
Adalimumab	Humira	Rheumatoid Arthritis, chronic plaque psoriasis, Crohn's disease	Coherus	Phase 3 studies in Psoriasis completed; already settled with AbbVie for Dec 2023 launch
			Celltrion	Phase 1/3 trials to be completed by 2020
			Fresenius Kabi	Settled with AbbVie for Sep 2023 launch
			Pfizer	Settled with AbbVie for 2023 launch
			Momenta	Settled with AbbVie for 2023 launch
Etanercept	Enbrel	Rheumatoid Arthritis, chronic plaque psoriasis, Crohn's disease	Coherus	Phase 3 clinical studies in psoriasis and Rheumatoid Arthritis completed
			Lupin/Mylan	Mylan to commercialize in markets outside US
Ranibizumab	Lucentis	Age-related macular degeneration, macular edema, diabetic retinopathy	Coherus	Preclinical development
Aflibercept	Eylea	Wet age-related macular degeneration	Coherus	Preclinical development
			Momenta/Mylan	In clinical studies
Bevacizumab	Avastin	Oncology	Pfizer	In Phase 3 studies
			Mylan/Biocon	Global Phase 3 study ongoing
Insulin Glargine	Lantus	Diabetes	Mylan/Biocon	Under FDA review
Insulin Aspart	Novolog	Diabetes	Mylan/Biocon	Global Phase I completed
Insulin Lispro	Humalog	Diabetes	Mylan/Biocon	Preclinical
Recombinant Human Insulin		Diabetes	Biocon	Under active development for US; partnered with Lab Pisa of Mexico

Source: Companies, YES Sec – Research

RECOMMENDATION PARAMETERS FOR FUNDAMENTAL REPORTS

Analysts assign ratings to the stocks according to the expected upside/downside relative to the current market price and the estimated target price. Depending on the expected returns, the recommendations are categorized as mentioned below. The performance horizon is 12 to 18 months unless specified and the target price is defined as the analysts' valuation for a stock. No benchmark is applicable to the ratings mentioned in this report.

BUY > 15%

ADD 5% to 15%

HOLD -15% to +5%

SELL > - 15%

NOT RATED

UNDER REVIEW

POSITIVE: Positive is rating given to stocks we like but yet to be formally included in our coverage universe.

NEGATIVE: Negative is rating given to stocks yet to be formally included in our coverage universe, but we find valuations expensive vis-a-vis fundamentals.

NEUTRAL: Neutral rating is given to stocks that are not under our formal coverage yet, but we find current valuation fairly representing fundamentals.

ABOUT YES SECURITIES (INDIA) LIMITED

YES SECURITIES (INDIA) LIMITED (''YSL'') was incorporated on 14th March 2013 as a wholly owned subsidiary of YES BANK LIMITED. YSL does not have any other associates. YSL is a SEBI registered stock broker holding membership of NSE and BSE. YSL is also a SEBI registered Category I Merchant Banker, Investment Adviser and a Research Analyst. YSL offers, inter alia, trading/investment in equity and other financial products along with various value added services. We hereby declare that there are no disciplinary actions taken against YSL by SEBI/Stock Exchanges.

DISCLAIMER

Investments in securities market are subject to market risks, read all the related documents carefully before investing.

The information and opinions in this report have been prepared by YSL and are subject to change without any notice. The report and information contained herein are strictly confidential and meant solely for the intended recipient and may not be altered in any way, transmitted to, copied or redistributed, in part or in whole, to any other person or to the media or reproduced in any form, without prior written consent of YSL.

The information and opinions contained in the research report have been compiled or arrived at from sources believed to be reliable and have not been independently verified and no guarantee, representation of warranty, express or implied, is made as to their accuracy, completeness, authenticity or validity. No information or opinions expressed constitute an offer, or an invitation to make an offer, to buy or sell any securities or any derivative instruments related to such securities. Investments in securities are subject to market risk. The value and return on investment may vary because of changes in interest rates, foreign exchange rates or any other reason. Investors should note that each security's price or value may rise or fall and, accordingly, investors may even receive amounts which are less than originally invested. The investor is advised to take into consideration all risk factors including their own financial condition, suitability to risk return profile and the like, and take independent professional and/or tax advice before investing. Opinions expressed are our current opinions as of the date appearing on this report. Investor should understand that statements regarding future prospects may not materialize and are of general nature which may not be specifically suitable to any particular investor. Past performance may not necessarily be an indicator of future performance. Actual results may differ materially from those set forth in projections.

Technical Analysis reports focus on studying the price movement and trading turnover charts of securities or its derivatives, as opposed to focussing on a company's fundamentals and opinions, as such, may not match with reports published on a company's fundamentals.

YSL, its research analysts, directors, officers, employees and associates accept no liabilities for any loss or damage of any kind arising out of the use of this report. This report is not directed or intended for distribution to, or use by, any person or entity who is a citizen or resident of or located in any locality, state, country or other jurisdiction, where such distribution, publication, availability or use would be contrary to law, regulation or which would subject YSL and associates to any registration or licensing requirement within such jurisdiction. The securities described herein may or may not be eligible for sale in all jurisdictions or to certain category of investors. Persons in whose possession this document may come are required to inform themselves of and to observe such restriction.

DISCLOSURE OF INTEREST

Name of the Research Analyst : Bhavesh Gandhi

The analyst hereby certifies that opinion expressed in this research report accurately reflect his or her personal opinion about the subject securities and no part of his or her compensation was, is or will be directly or indirectly related to the specific recommendation and opinion expressed in this research report.

Sr. No.	Particulars	Yes/No
1	Research Analyst or his/her relative's financial interest in the subject company(ies)	No
2	Research Analyst or his/her relative or YSL's actual/beneficial ownership of 1% or more securities of the subject company(ies) at the end of the month immediately preceding the date of publication of the Research Report	No
3	Research Analyst or his/her relative or YSL has any other material conflict of interest at the time of publication of the Research Report	No
4	Research Analyst has served as an officer, director or employee of the subject company(ies)	No
5	YSL has received compensation or other benefits from the subject company(ies) or third party in connection with this research report	No
6	Broking/Investment Banking/Merchant Banking relationship with the subject company at the time of publication of Research Report	No
7	YSL has managed or co-managed public offering of securities for the subject company in the past twelve months	No
8	Research Analyst or YSL has been engaged in market making activity for the subject company(ies)	No

Since YSL and its associates are engaged in various businesses in the financial services industry, they may have financial interest or may have received compensation for investment banking or merchant banking or brokerage services or for any other product or services of whatsoever nature from the subject company(ies) in the past twelve months or associates of YSL may have managed or co-managed public offering of securities in the past twelve months of the subject company(ies) whose securities are discussed herein.

Associates of YSL may have actual/beneficial ownership of 1% or more and/or other material conflict of interest in the securities discussed herein.

YES SECURITIES (INDIA) LIMITED
Registered Office: Unit No. 602 A, 6th Floor, Tower 1 & 2, Indiabulls Finance Centre, Senapati Bapat Marg, Elphinstone Road, Mumbai – 400013, Maharashtra, India.
Tel: +91-22-71123123 | **Email:** research@yessecuritiesltd.in | **Website:** www.yesinvest.in

CIN: U74992MH2013PLC240971 | SEBI Single Registration No.: NSE, BSE & MCX: INZ000185632 | MERCHANT BANKER: INM000012227 | RESEARCH ANALYST: INH000002376 |INVESTMENT ADVISER: INA000007331| AMFI ARN Code – 94338 |
Details of Compliance Officer: Name: Vaibhav Purohit,
Email id: compliance@yessecuritiesltd.in, Contact No-+91-22-33479208