TwoLabs
PHARMA SERVICES

OPPORTUNITIES AND RECENT TRENDS FOR BIOSIMILARS

About Two Labs

Two Labs provides expert, integrated services that eliminate barriers to product launch and provide strategies for continued market viability.

For a free consultation call us at 614-389-4004 or email info@twolabs.com.

OPPORTUNITIES FOR BIOSIMILARS:

Over the last year, biosimilars have seen increasing success in the US market. The number of biosimilars approved has accelerated, product sales for biosimilars are increasing, net prices are being driven down (for both brands and biosimilars), and payers are beginning to prefer biosimilars over brands on their formularies.

ACCELERATING RATE OF APPROVAL:

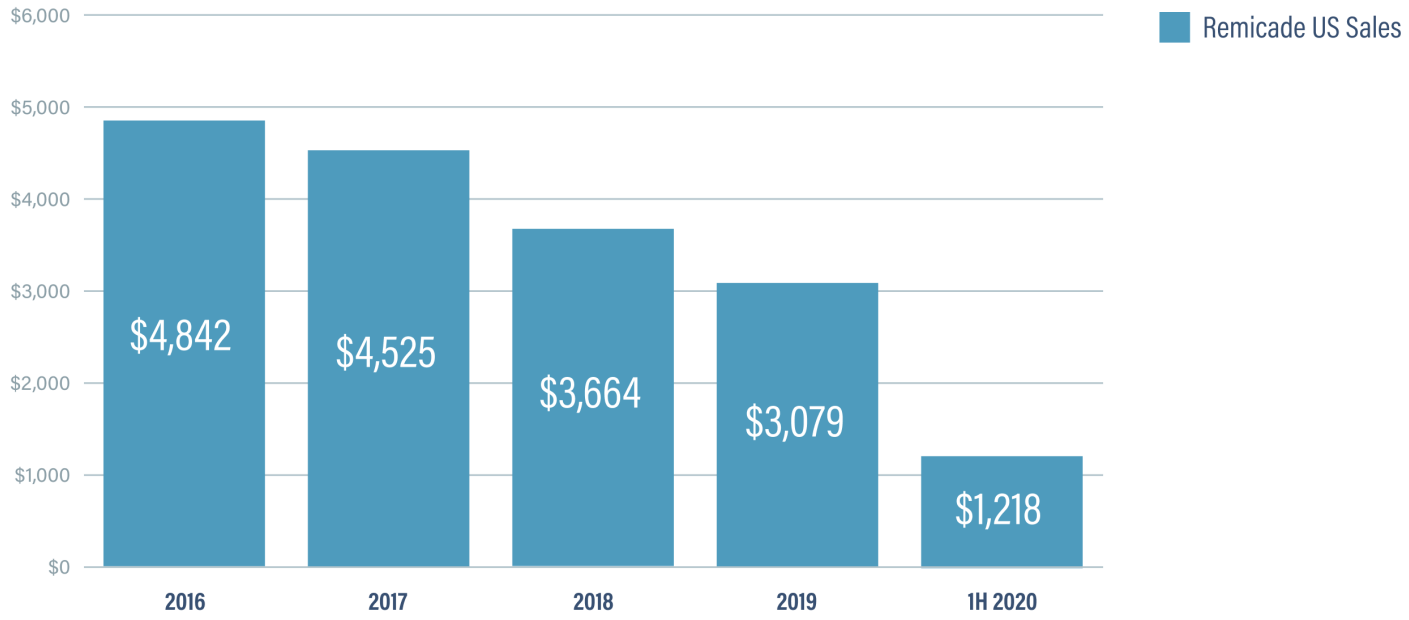
There are currently 23 approved biosimilars in the US and 16 are marketed. Ten of the marketed biosimilars have been approved in 2019 and 2020 alone[i].

This accelerating rate of approval is partially due to the fact that the biosimilar approval pathway is now well established, making it easier to bring biosimilars to market. Additionally, in May of 2019, the FDA issued guidance for interchangeability, which is likely to further improve the uptake of biosimilars because it will allow for substitution for the reference product at the pharmacy counter. For example, Boehringer Ingelheim is now actively seeking interchangeability for its Humira biosimilar, Cytezlo[ii].

PRODUCT SALES:

In recent years, product sales for branded reference products have begun to decline while sales for biosimilars are increasing. For example, Inflectra and Renflexis, two infliximab biosimilars, have been available since 2016. Sales of Remicade have declined 36% since 2016 with most of those losses occurring between 2018 and 2019. Quarterly decline has continued in 2020 with sales totaling $1,218 million in the first half of the year. While this decrease is primarily attributed to biosimilar competition, the negative impact of COVID-19 may have impacted sales due to patients forgoing doctors' office visits (Figure 1[iii]).

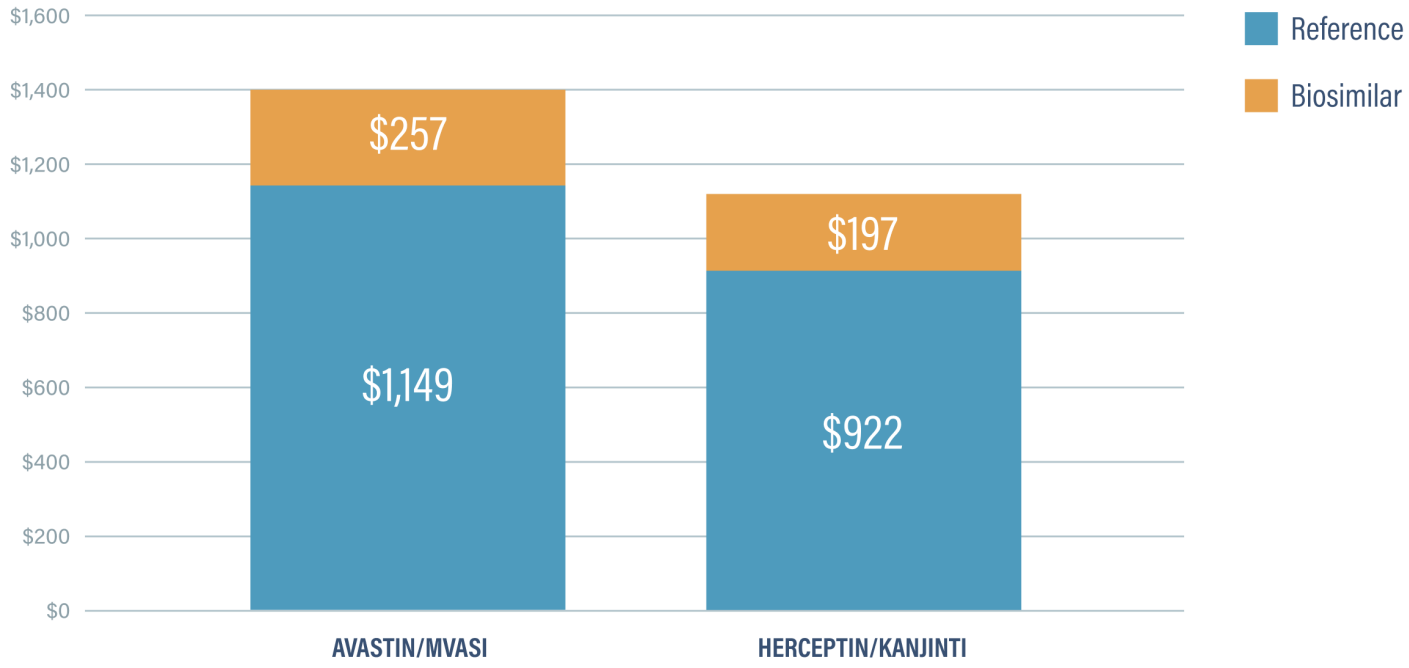
REMICADE US SALES (USD, MILLIONS)



For more recently launched biosimilars, stronger uptake relatively soon after launch has been observed.

For example, Amgen's biosimilars to Avastin and Herceptin, Mvasi and Kanjinti, which launched in July of 2019, have seen significant uptake. By mid-year 2020, Mvasi made up 18% of the Mvasi/Avastin market and Kanjinti comprised 18% of the Kanjinti/Herceptin market (Figure 3[iv]). More recently, Trazimera, Ontruzant, Herzuma, and Ogivri gained market access as additional biosimilars to Herceptin, and Zirabev entered the market as an additional biosimilar to Avastin. It will be important to monitor how this market continues to evolve with multiple biosimilars available.

AVASTIN + HERCEPTIN VS. MVASI + KANJINTI (USD, MILLIONS)



One contributing factor to the success of Mvasi and Kanjinti is that Amgen has approached sales of biosimilars in the same way they would a new branded product, dedicating resources and experience specifically to their biosimilars.

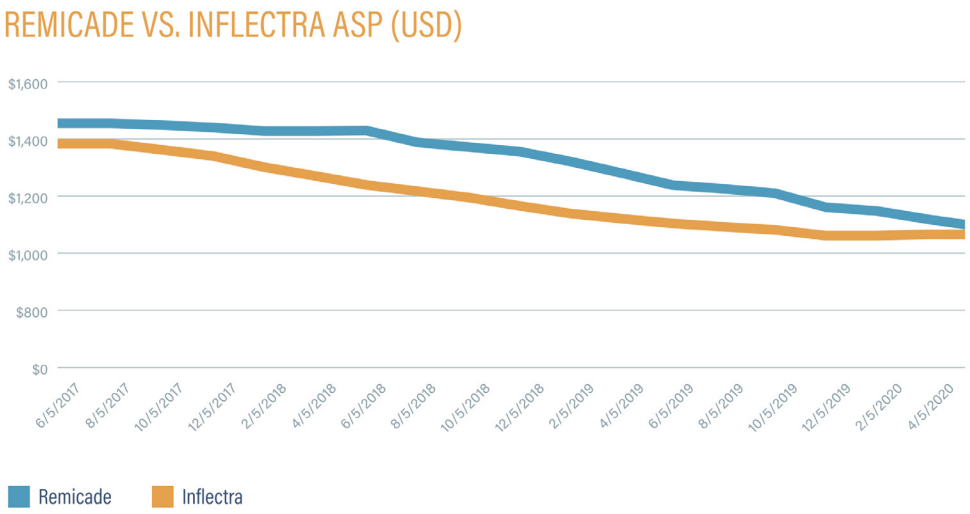
INCREASED COMPETITION:

The market for biosimilar Neulasta exemplifies how the availability of multiple biosimilars for the same reference product can lead to a more competitive market where payers have greater negotiating power. In 2018, the first biosimilar to Neulasta, Fulphila, became available. Although this did not have a significant impact on the market, by 2019, when Udenyca, another biosimilar to Neulasta became available, it achieved meaningful market share. According to estimates by IQVIA, Udenyca comprised approximately 20.5% unit market share in the pegfilgrastim market by the end of 2019[v]. However, in the end of 2019, a third pegfilgrastim biosimilar, Ziextenzo, entered the market. Now that there are four pegfilgrastim options, payers are able to negotiate with manufacturers and choose preferred and non-preferred options. While Express Scripts, a major pharmacy benefit manager, preferred all four pegfilgrastim products in 2020, in August 2020 they announced that in 2021 they would prefer Mylan's Fulphila and Sandoz's Ziextenzo, and Udenyca would move into a non-preferred position[vi].

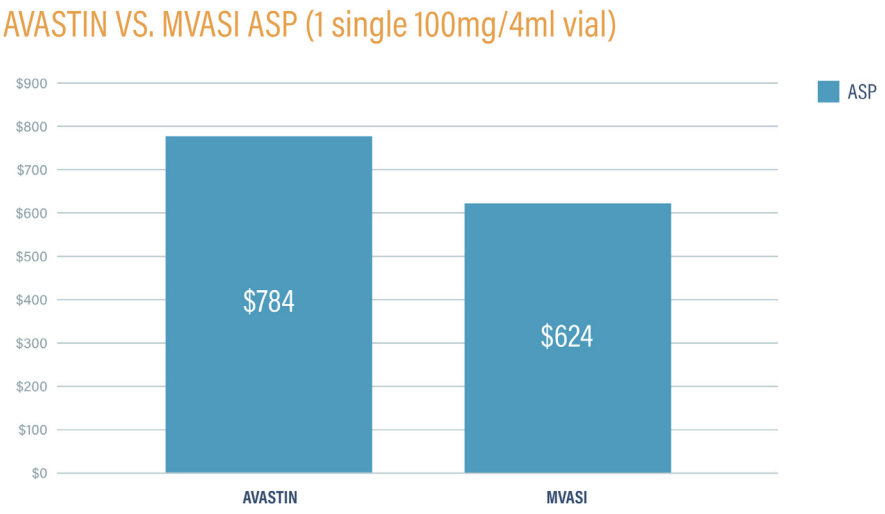
NET PRICES:

In addition to observing sales trends, by looking at average sales prices (ASP), we can gain an idea of how price is evolving in markets where biosimilars are available.

For example, by looking at Remicade and Inflectra ASP since 2017, we observe two interesting trends. First, the ASP gap between Remicade and Inflectra increased between June of 2017 and February of 2019. Then, the differential stabilized and eventually decreased. This shows that while there was initially an increase in net price differential for brand versus biosimilar, today both products have a similar net price. Second, it is notable that the ASP of both products has declined significantly since 2018. Remicade ASP has dropped by 40% and Inflectra has dropped by 41%. (Figure 4). This is evidence that biosimilars are offering attractive discounts and at the same time are pushing branded manufacturers to reduce their price in an effort to maintain market share.



We observe a similar trend in oncology where the ASP for Mvasi is 20% below Avastin (Figure 5[viii]).



PAYER ACCESS:

With attractive net price discounts from biosimilar manufacturers, we are beginning to see payers prefer biosimilars on formularies. For example, in August of 2019, United Healthcare, one of the top insurance companies in the United States and a bellwether that other insurance companies often follow, announced that beginning October 1, 2019, Mvasi and Kanjinti (Amgen biosimilars to Avastin and Herceptin) would be preferred on many formularies and that Genentech's innovator brands would no longer be preferred on formularies. Furthermore, while United Healthcare previously maintained Remicade in a preferred formulary position, they announced that beginning October 1, 2019 Inflectra would be moved into a co-preferred position with Remicade[ix,x]. Likewise, Kaiser, a high control integrated delivery network, has chosen to prefer Mvasi and Kanjinti and has succeeded in converting 95% of patients from brand to biosimilar[xi].

PHYSICIAN CONSIDERATIONS:

MORE RECENT STUDIES HAVE SHOWN INCREASED COMFORT WITH PRESCRIBING BIOSIMILARS.

Physicians are becoming increasingly comfortable prescribing biosimilars. In a study published in 2016, only 12% of 1,201 physicians were comfortable with biosimilar extrapolation and 55.2% were concerned about the safety of biosimilars. In a study published in 2017, 66% of 131 rheumatologists surveyed indicated that they were likely or extremely likely to initiate treatment for naïve rheumatoid arthritis patients on a biosimilar. However, there was still a significant unwillingness to switch well controlled patients to a biosimilar with 60% of rheumatologists indicating they were unlikely to do so. It is important to note that at the time of both surveys, Inflectra was the only available biosimilar[xii]. More recent studies have shown increased comfort with prescribing biosimilars. A 2018 study of US community oncologists, hematologists, and practice administrators showed that 65% of clinicians (n=196) had prescribed a biosimilar in the past year and 95% (n=40) were very or somewhat confident that biosimilars are as safe and effective as the reference biologic[xiii]. It will be important to continue to monitor physician familiarity in prescribing biosimilars.

REMAINING CHALLENGES:

Branded manufacturers continue to employ defensive tactics to meet the challenges of biosimilars. For example, something called the 'rebate trap' is making it difficult for biosimilars to gain access to PBM formularies. "The rebate trap refers to the situation in which drug makers condition rebates on greater sales volume, which PBMs often accomplish with formulary placement and other tactics. PBMs and plans profit from the spread between drug list prices and rebated prices.[xiv]"

Another tactic employed by branded manufacturers is to develop new formulations/devices not offered by the biosimilar manufacturers. For example, Amgen has developed the Neulasta OnPro device, which automatically delivers Neulasta the day after chemotherapy administration so that patients can remain at home and avoid a follow up visit with their physician the day after chemotherapy to receive Neulasta[xv]. This device is not available for Neulasta biosimilars and helps Amgen to maintain a competitive edge.

In addition, originator products may be indicated for conditions under orphan exclusivity, blocking biosimilars from getting approved for the full label of the originator product. For instance, Avastin has orphan drug designation for the treatment of patients with platinum-sensitive recurrent epithelial ovarian cancer until 2023, an indication that Mvasi and Zirabev currently do not have in their labels[xvi,xvii]. Recently launching in combination with Tecentriq in advanced hepatocellular carcinoma in May 2020 further shields Avastin from biosimilar competitors fully adopting its label.

Furthermore, branded manufacturers are continuing to extend patents and therefore we are still a few years off from seeing biosimilars to top selling rheumatology drugs, Humira and Enbrel.

In addition to defensive tactics being employed by branded manufacturers, there are still practice economic incentives for providers to prescribe brands over biosimilars. Because reimbursement is based off a product's ASP and the ASP for the reference product is typically higher than that of the biosimilar, providers ultimately are reimbursed more when they prescribe the branded reference product[xviii].

CONCLUSIONS:

Biosimilars are beginning to make headway in the US market. The availability of cheaper biosimilar options is requiring manufacturers of reference products to provide increased discounts, driving net prices down. Future research should consider the level of physician familiarity in prescribing biosimilars. As physicians become more comfortable prescribing biosimilars, we may see increases in biosimilar uptake. In addition, it will be important to track the biosimilars market as patents continue to expire, and especially to monitor the market in 2023 when biosimilars of top selling brand, Humira, become available.

i Biosimilar Product Information. https://www.fda.gov/drugs/biosimilars/biosimilar-product-information [Accessed August 18, 2020]

ii Boehringer Ingleheim starts clinical study on interchangeability between its adalimumab biosimilar candidate and U.S.-formulated Humira. https://www.boehringer-ingelheim.us/press-release/boehringer-ingelheim-starts-clinical-study-interchangeability-between-its-adalimumab [Accessed August 5, 2020]

iii J&J SEC Filings

iv Amgen and Genentech SEC Filings

v https://www.biospace.com/article/releases/coherus-biosciences-reports-fourth-quarter-and-full-year-2019-financial-results/

vi https://www.bigmoleculewatch.com/2020/08/26/coherus-neulasta-biosimilar-loses-preferred-status-at-express-scripts/

vii PriceRx, Remicade and Inflectra, https://pricerx.medispan.com [Accessed August 18, 2020]

viii PriceRx, Avastin and Mvasi, https://pricerx.medispan.com [Accessed August 18, 2020]

ix United Healthcare Will Prefer Amgen's Anticancer Biosimilars Beginning in October. https://www.centerforbiosimilars.com/news/unitedhealthcare-will-prefer-amgens-anticancer-biosimilars-beginning-in-october [Accessed August 12, 2020]

x United Places Biosimilar Inflectra On Preferred Tier with Remicade. https://insidehealthpolicy.com/inside-drug-pricing-daily-news/united-places-biosimilar-inflectra-preferred-tier-remicade [Accessed August 12, 2020]

xi How Did Kaiser Permanente Reach 95%+ Utilization of Biosimilar Heceptin and Avastin so Quickly? https://biosimilarsrr.com/2019/11/07/how-did-kaiser-permanente-reach-95-utilization-of-biosimilar-herceptin-and-avastin-so-quickly/ [Accessed August 12, 2020]

xii Leonard E, Wascovich M, Oskouei S, Gurz P, Carpenter D. Factors Affecting Health Care Provider Knowledge and Acceptance of Biosimilar Medicines: A Systematic Review. J Manag Care Spec Pharm. 2019 Jan;25(1):102-112. doi.org/10.18553/jmcp.2019.25.1.102 [Accessed August 20, 2020]

xiii https://www.journalofclinicalpathways.com/article/community-oncologists-perception-and-acceptance-biosimilars-oncology

xiv https://www.neulasta.com/onpro

xv https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=20103178

xvi https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/mvasi/mvasi_pi_hcp_english.pdf

xvii http://labeling.pfizer.com/ShowLabeling.aspx?id=11860

xviii https://www.centerforbiosimilars.com/conferences/specialty-therapies-and-biosimilars-conference/cms-paymendt-policy-plays-role-in-biosimilar-uptake

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