Welcomes, introductions and disclaimers

- Hello again, I hope you’re all keeping well.
- It’s been a while since I last spoke to you all, was before Christmas.
- Lots of things have happened since then so I’m going to try and summarise some of the key events and provide some colour on potential implications. Will cover them off in no particular order but have tried to bucket them. Within the raw notes that accompany the podcast, I’ll provide links to sources so that you can do your own reading and draw your own conclusions.
- Again, this is a work in progress so please keep sharing your feedback! Finally, my usual disclaimers apply; my own words/views, it’s really just a bit of fun. In terms of copyright, you can use freely for personal use, but please tell people where you got this information from. If you want to use commercially, contact me and we can discuss how this could happen.

MASSIVE CAVEAT ALERT!

- PFE acquiring HSP for $17 billion...wow!
- Significant uncertainty in relation to the future of several biosimilar programmes.
- All programmes that are being sponsored by PFE, HSP or Celltrion are under the microscope, so please bear this in mind when I talk about read-out dates, approvals and potential launches.
- Things could change massively over the next few weeks!

Clinical

- Data for Remsima in IBD
  - A poster to be presented at ECCO 2015 this month suggests that patients with IBD are more likely to need surgery and be re-admitted to hospital if they’re treated with biosimilar infliximab (here).
A very small study - 14 patients on biosimilar infliximab compared to 22 patients on Remicade - and critically this was not a head-to-head study. Biosimilar infliximab observations took place January to July 2014, and Remicade observations between Dec 2011 to Dec 2013.

Probably wise not to read too much into this study, but it is interesting all the same. Remember Health Canada refused to extrapolate to gastro indications due to issues with the pre-clinical ADCC data for biosimilar infliximab. Looking forward to data from the ongoing CD study for biosimilar infliximab. Should expect to see primary outcomes data in Q1’16.

Data for ABP501 in RA

Amgen announced this week that a Phase III study evaluating the safety and efficacy of its proposed biosimilar version of adalimumab, ABP501, compared with Humira (adalimumab; AbbVie) in patients with moderate-to-severe rheumatoid arthritis (RA) has met its primary and key secondary endpoints (here).

The primary endpoint compared the ACR20 measurements at week 24. According to Amgen’s press release, the ACR20 was within the pre-specified margin for ABP501 compared to adalimumab, showing clinical equivalence. Safety and immunogenicity of ABP501 were also comparable to adalimumab. Key secondary endpoints included ACR50, ACR70 and DAS 28-CRP. Additional information was not provided.

Remember, this is the second data release for ABP501. In October 2014 Amgen released positive data for ABP501 compared to Humira in patients with moderate-to-severe plaque psoriasis (PsO). Could potentially submit this year. If so, could expect approval by Q3 2016 in the US and Q1 2017 in Europe.

In terms of other Amgen programmes, the company has stated that they expect to release primary outcomes data for ABP215 (bevacizumab) in NSCLC during 2015.

Sandoz starts developing biosimilar bevacizumab

Sandoz becomes the latest company to begin clinical development of a biosimilar version of Avastin (here). The Phase I study is being ran in the UK and will evaluate the pharmacokinetics, safety and immunogenicity of GP2019, Avastin-EU, and Avastin-US, when administered intravenously to...
healthy male subjects. Boehringer and Amgen are ahead with programmes in Phase III.

**Regulatory**

- **US**
  - FDA AdCom for Sandoz’s EP2006 (filgrastim)
    - FDA AdCom voted 14-0 in favour of approving EP2006 (to be branded as Zarxio), Sandoz’s filgrastim biosimilar for all five indications of Neupogen. Approval based on clinical data in patients with breast cancer (PIONEER) and healthy volunteers.
    - Sandoz only requested approval for EP2006 as a biosimilar to Neupogen, and not an interchangeable product. Switching studies are ongoing that could support this application during 2015.
    - Despite the significance of this event, ongoing litigation between Amgen and Sandoz could prevent this product from being launched for several months, potentially years. Amgen has sued Sandoz for not following the 351(k) statute, Sandoz has replied agreeing with Amgen and essentially saying they don’t have to.
    - Likely to run and run.
  - Hospira’s submission of SB309 (EPO-zeta) to FDA via 351(k)
    - Actually submitted before Christmas, wanted to wait for the holidays to finish before announcing.
    - Submission likely to be based on a lot of the data that supported the EU approval in December 2007, plus some data from Anaemia Management With Epoetin (AiME) programme which completed in Q1’14. Could see an AdCom sometime during H1’15.

- **Europe**
  - Samsung’s SB4 (biosimilar etanercept)
    - Lots of debate on Twitter about this, thanks to all of you who contributed.
    - Only studied in RA, so will be relying on extrapolation to other indications.
    - No data publication before the filing.
    - Biogen Idec will take commercialisation responsibilities in Europe
- Interestingly, to be manufactured by Biogen in Denmark; what no Samsung Biologics?
- Assuming the EMA sticks to average timelines for this biosimilar review (18 months), approval could come in Q3’16.
  - Human insulin
    - Old filing, still under review.
    - Potentially from Biocon.
    - No word from the company either way.
    - Submitted in July 2014, assuming the EMA sticks to average timelines for this biosimilar review (18 months), approval could come in Q4’15, maybe Q1’16.
- **Japan**
  - Eli Lilly/Boehringer Ingelheim’s biosimilar insulin glargine has been approved in Japan ([here](#); Google translator needed!).
  - Brand name will be Insulin glargine BS Note cart "Lily"...still not sure about the BS tag, but that’s just my opinion.
- **RoW**
  - A non-comparable biologic version of rituximab has been approved in Argentina ([here](#)). Product is RTXM83 which comes from mabXience and has been licensed to a number of companies, including Lab Elea in Argentina who have received this approval.
  - Interestingly Polish biotech, Mabion, have also submitted its biosimilar version of rituximab to ANVISA.
  - I’ve also heard rumours of a non-comparable biologic version of trastuzumab being approved in the Dominican Republic. More news if I find it.

**Pricing**

- **Remsima pricing in Canada**
  - Priced at a 35 percent discount in Canada, aligned with similar discounts seen in Europe. Remember the product has not been awarded all indications in Canada. Health Canada decided that the issues found with the in vitro ADCC data prevented them from extrapolating from rheumatology to gastro indications. Might make commercialisation challenging considering some
data I’ve been sent that suggests Remicade’s leading indications in Canada are the gastro ones (i.e. UC/CD); my contact suggests MS = 50% by value.

- As an aside, Celltrion have partnered with Fresenius who will act as a distributor for Remsima in Canada (here).

**Remsima pricing in Norway**

- Another wow moment!
- Orion Pharma has discounted biosimilar infliximab in Norway by 72 percent compared to the previous cost of Remicade (here).
- MSD refused to budge, discounting Remicade by only 3 percent compared with the old price.
- Suggests they’ve given up on Norway and will focus on grandfathering patients on Remicade that are controlled.
- New patients, therefore, become the area where biosimilar infliximab could start to make gains.
- Implications for rest of EU, particularly EU5.
- Merck commented in its 2014 earnings release that it does not expect discounts of this size in EU5 markets, but reference pricing would play a role in bringing costs down.

**Commercial**

- **Exemptia in India**
  - Positioned as a biosimilar of Humira.
  - Approved on the basis of a 120 patient study in the RA setting (here).
  - Pre-clinical data published recently (here).

- **Accofil and Afolia in Europe**
  - Accofil is a biosimilar filgrastim and will be 8th to market
  - Bemfola is a biosimilar FSH (Merck KGaA’s Gonal-f)

- **Market share news**
  - At the end of January, Russian biotech BIOCAD released a statement saying that sales of AcellBia (biosimilar rituximab) had exceeded $155m in 2014, representing more than 80 percent of the Russian market. Biocad’s product became the treatment of choice in Russia after Biocad won a national tender, displacing Roche (here).
According to figures released by Amgen, JCR Pharma’s biosimilar EPO-alfa has obtained a 74 percent market share in Japan (here). Physicians choosing to prescribe the product is given as the main reason. Bucks the trend in Japan which has been a difficult market for generics and biosimilars to penetrate.

Deals and Alliances

- **Reliance Life Sciences/Torrent Pharma**
  - Focused on 3 mAbs; rituximab, cetuximab, adalimumab
  - Reliance currently conducting Indian trials for all three

- **Merck KGaA in-licenses EU rights to Hanwha’s HD203 (etanercept)**
  - Was originally the flagship programme at Merck BioVentures, but returned to Hanwha soon after Amgen announced new patent protection in the US out to 2028. Approved in Korea in November 2014 based on a 294 patient study in RA. Experts I’ve spoken to suggest that if the deal does go through Merck KGaA will need to re-do the PhIII programme as the data wouldn’t be enough to support a EMA filing (here).

- **Pfizer acquires Hospira for $17 billion**
  - The big story of the year so far.
  - Many have dubbed this “Pfizer’s big bet on biosimilars”.
  - They already have a sizeable presence, focused purely on mAbs.
  - Lots of overlap and potential for divestments and programme terminations.
  - As I told an old client of mine yesterday:
    - CT-P13 likely to stay due to status and clinical development activity, although the highly fragmented commercial arrangement in Europe might need to be resolved (can it?).
    - CT-P6 likely to go with Pfizer pushing their trastuzumab forward. CT-P6 has had a troubled development history. Approved in Korea but many people I’ve spoken to have raised concerns about the mBC data (no EU filing!).
  - Will leave it there as there are way too many uncertainties at the moment. When Pfizer was asked on their analyst call yesterday if they expect to hold on to all biosimilars that HSP partnered with Celltrion, they didn’t answer!