WHERE NEXT FOR BIOSIMILARS?

Dr Duncan Emerton
Senior Director, Syndicated Insights & Analysis
FirstView (a division of FirstWord Pharma)
E: duncan.emerton@firstword-pharma.com
T: +44 20 7665 9251
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AGENDA…

- INTRODUCTIONS…
- SOME INITIAL THOUGHTS…
- RECENT DEVELOPMENTS…
- MARKET DYNAMICS, CRITICAL UNCERTAINTIES…
- WHERE NEXT FOR BIOSIMILARS…?
- Q&A…
YOUR PRESENTER...

Dr Duncan Emerton; Senior Director, FirstWord

• Over 15 years industry experience, 7 of which have been focused on biosimilars.
• Previous roles include R&D, sales, marketing, medical affairs, business analysis and strategic consulting.
• Prior to joining FirstView, spent 9 years at Datamonitor, final role was Director and Biosimilars Practice Lead within the healthcare consulting team.
• Extensively published and quoted on the subject of biosimilars, and regularly presents at conferences.
• Editor-in-Chief, The Biosimilarz Blog! (www.biosimilarz.com)
KEY SOURCES OF INFORMATION...

Recently published FirstView reports, plus personal experience

Biosimilar Index: Tracking the Biosimilar Development Landscape

The Future of Biosimilars: Mapping Critical Uncertainties and the Impact of Future Events

Sources: FirstView
A QUICK NOTE ABOUT TERMINOLOGY…

Biosimilars vs. Non-Comparable Biologics

• For the purposes of presentation, a product will be deemed to be a biosimilar if it is being, or has been, **developed via a rigorous comparability exercise versus an approved reference medicinal product (RMP) that has been laid down as part of national biosimilar guidelines (e.g. EMA, FDA, etc.).**

• Within the presentation, reference will be made to non-comparable biologics (NCBs, sometimes called intended copies or copy biologics). These are products that have not been studied comparatively, and are unlikely to be approved and launched in Western EU, the US, Japan and other markets where a rigorous comparability pathway exists.

Sources: FirstView
AGENDA…

INTRODUCTIONS…

SOME INITIAL THOUGHTS…

RECENT DEVELOPMENTS…

MARKET DYNAMICS, CRITICAL UNCERTAINTIES…

WHERE NEXT FOR BIOSIMILARS…?

Q&A…
WHAT’S DRIVING THE INTEREST IN BIOSIMILARS?

“There’s gold in them there hills!”

“There’s gold in them there hills biologic brands!”

“Hmmm, it’s a lot more difficult than we first thought!”
AGENDA…

INTRODUCTIONS…

SOME INITIAL THOUGHTS…

RECENT DEVELOPMENTS…

MARKET DYNAMICS, CRITICAL UNCERTAINTIES…

WHERE NEXT FOR BIOSIMILARS…?

Q&A…
KEY MARKET MILESTONES, H1 2014

Clinical

06/14: EULAR 2014 SPECIAL! Data presented for Epirus Biopharma’s BOW-015 (infliximab; here); Celltrion’s CT-P13 (here), Pfizer’s PF-06438179 (infliximab; here) and PF-05280586 (rituximab; here); Amgen’s ABP501 (adalimumab; here); Sandoz’s GP2017 (adalimumab; here) and Hanwha Chemical’s HD203 (etanercept; here)

05/14: Pfizer completes Phase I/II PK/PD study of PF-05280586 in RA patients (here)

05/14: Samsung Bioepsis initiates Phase III eBC study of SB3 (trastuzumab) in Europe (here)

05/14: Coherus initiates Phase III psoriasis study for CHS-0214, a proposed biosimilar of etanercept (here)

04/14: Coherus initiates Phase III RA study for CHS-0214, a proposed biosimilar of etanercept (here)

04/14: Sandoz updates clinical status of Phase III FL study for GP2013 (biosimilar rituximab (here)

03/14: mabXience initiates Phase I study for its biosimilar version of bevacizumab in CRC patients (here)

03/14: Celltrion initiates a Phase III study of CT-P6 in eBC patients, readout expected H2 2017 (here)

03/14: Celltrion initiates a Phase III safety/efficacy study for CT-P13 in Crohn’s disease (here)

02/14: Amgen initiates an open label safety study for ABP501 (biosimilar adalimumab) in Europe (here)

01/14: Amgen increases recruitment target for Phase III study of ABP980 (biosimilar trastuzumab) in eBC from 588 to 808 patients (here)

Sources: FirstView Biosimilars Index (as of 1 June 2014)
KEY MARKET MILESTONES, H1 2014

**Regulatory**

05/14: Russia’s Biocad announces Russian approval of biosimilar rituximab (AcellBia; BCD-021) ([here](#))

03/14: Sandoz receives Japanese approval for Filgrastim BS Injection 75 µg/150 µg/ 300 µg Syringe ([here](#))

03/14: Italian Medicines Agency announces plans to revise current biosimilar position statement ([here](#))

03/14: Sandoz receives Japanese approval for Filgrastim BS Injection 75 µg/150 µg/ 300 µg Syringe ([here](#))

01/14: Biocon confirms intention to launch CANMAb (biosimilar trastuzumab) in 150mg and 440mg presentations ([here](#))

01/14: Celltrion and Hospira receives Health Canada approval for Inflectra and Remsima (both biosimilar versions of Remicade) ([here](#), [here](#))

01/14: Celltrion and Hospira receives Health Canada approval for Inflectra and Remsima (both biosimilar versions of Remicade) ([here](#), [here](#))

01/14: Celltrion confirms Korean MFDS approval of Herzuma (biosimilar trastuzumab) as a treatment for eBC, mBC and mGC ([here](#))

04/14: EMA publishes second draft biosimilar insulin guideline for consultation, consultation ends 31 July 2014 ([here](#))

04/14: CADTH releases Common Drug Review Procedure and Submission Guidelines for Subsequent Entry Biologics in Canada ([here](#))

04/14: Finox Biotech receives EC approval for its biosimilar version of follitropin-alfa, brand name Bemfola ([here](#))

03/14: Finox AG confirms a positive CHMP endorsement for its Bemfola (biosimilar follitropin-alfa) as a treatment for infertility ([here](#))

01/14: Celltrion confirms Korean MFDS approval of Herzuma (biosimilar trastuzumab) as a treatment for eBC, mBC and mGC ([here](#))

01/14: Celltrion confirms Korean MFDS approval of Herzuma (biosimilar trastuzumab) as a treatment for eBC, mBC and mGC ([here](#))

Sources: FirstView Biosimilars Index (as of 1 June 2014)
KEY MARKET MILESTONES, H1 2014

Commercial

03/14: Celltrion partners with Mundipharma, Kern Pharma and Biogaran on biosimilar infliximab in Europe (here)

03/14: CRO inVentiv Health teams up with Australia’s Proteomics International to expand its biologics characterization services (here)

02/14: Alvogen announces the launch of Inflectra (biosimilar infliximab; CT-P13) into Central and Eastern Europe (here)

02/14: Merck and Samsung Bioepis enter collaboration agreement to develop and commercialize insulin glargine candidate for diabetes (here)

01/14: Ranbaxy licenses Indian marketing rights for BOW-015 (biosimilar infliximab) from Epirus Biopharma (here)

05/14: Millhouse LLC and Pharmstandard acquire 50% and 20% stakes, respectively, in Russia’s Biocad (here)

05/14: Korea’s Samsung to invest $2bn in biologics, with most going toward biosimilars (here)

04/14: Epirus Biopharmaceuticals agrees to merge with Zalicus Inc., and becomes Epirus Biopharmaceuticals, Inc. (here)

04/14: Lupin and Japan’s Yoshindo partner to develop biosimilars, the first programme will be biosimilar etanercept (here)

Q1 2014

Q2 2014

Sources: FirstView Biosimilars Index (as of 1 June 2014)
**KEY MARKET MILESTONES, H1 2014**

**Other**

**06/14:** Janssen files to dismiss Celltrion’s request for Declaratory Judgement on Remicade patents ([here](#)).

**05/14:** Coherus Biosciences secures $55m Series C financing, money to fund clinical studies ([here](#)).

**05/14:** The Association of the British Pharmaceutical Industry (ABPI) releases the 3rd edition of its biosimilar position statement ([here](#)).

**04/14:** Epirus Biopharmaceuticals closes Series B financing for $36m, confirms new Phase III for BOW-015 and identity of BOW-030 and BOW-050 ([here](#)).

**04/14:** Celltrion seeks declaratory judgement vs. Janssen Biotech in the US over alleged patent extension tactics for Remicade ([here](#)).

**03/14:** Roche sues Celltrion in South Korea over an alleged Herceptin formulation technology patent infringement ([here](#)).

**03/14:** Sandoz announces that Vasant Narasimhan will replace Ameet Mallik as head of biosimilars from 1 April 2014 ([here](#)).

**03/14:** Brazil’s Cristalia receives ANVISA approval to manufacturer trastuzumab, etanercept and somatropin API for the Brazilian market ([here](#)).

**02/14:** Norway unveils near 40 percent discounting for biosimilar infliximab (Remsima, Inflectra) in country-wide biologics tender ([here](#)).

**02/14:** Roche sues Biocon, Mylan and the Drug Controller General of India (DCGI) in relation to the country’s November 2013 approval of biosimilar trastuzumab ([here](#)).

**01/14:** Sanofi sues Eli Lilly in the US over its December 2013 505(b)(2) FDA submission of its proposed insulin glargine copy, LY2963016 ([here](#)).

**Sources:** FirstView Biosimilars Index (as of 1 June 2014)
BIOSIMILAR MARKET DYNAMICS

Key landscape statistics

BIOSIMILAR/NCB PROGRAMS… 387
BIOSIMILAR/NCB COMPANIES… 141
TARGETED REFERENCE PRODUCTS… 40
ACTIVE COUNTRIES… 17
THERAPEUTIC CLASSES… 13

Sources: FirstView Biosimilar Index (as of 1 April 2014)
BIOSIMILAR MARKET DYNAMICS

Approved biosimilars

Sources: FirstView Biosimilar Index (as of 1 June 2014); The Biosimilars Blog! (here); (1) CANMAb approved Nov 2013, but Roche has sued Biocon regarding claims of biosimilarity to Herceptin; (2) Herzuma (trastuzumab) and Remsima (infliximab); (3) Biocad claims AcellBia (rituximab) is a biosimilar.
BIOSIMILAR MARKET DYNAMICS

Landscape dynamics by therapy area

Sources: FirstView Biosimilar Index (as of 1 April 2014)
## BIOSIMILAR MARKET DYNAMICS

*Landscape dynamics by class (1)*

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<td><strong>387</strong></td>
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</table>

*Source: FirstView’s Biosimilar Index (published March 2014, updated April 2014); company reported information*

**Sources:** FirstView Biosimilar Index (as of 1 April 2014)
BIOSIMILAR MARKET DYNAMICS

Landscape dynamics by class (2)

Sources: FirstView Biosimilar Index (as of 1 April 2014)
BIOSIMILAR MARKET DYNAMICS

Landscape dynamics by molecule

Sources: FirstView Biosimilar Index (as of 1 April 2014)
BIOSIMILAR MARKET DYNAMICS

Landscape dynamics by company HQ

Sources: FirstView Biosimilar Index (as of 1 April 2014)
BIOSIMILAR MARKET UNCERTAINTIES…
A complicated web of issues…

Source: FirstView analysis; primary market research (n=12 interviews). Key: API = active pharmaceutical ingredient; CMO = contract manufacturing organisation; EPO = erythropoietin; G-CSFs = filgrastim; IFN = interferon, LCM = lifecycle management; mABs = monoclonal antibodies.

Sources: FirstView Future of Biosimilars (May 2014)
BIOSIMILAR MARKET UNCERTAINTIES…

Clinical

Indication selection remains a critical decision point for developers…

Safety concerns for biosimilars remain, particularly in real world settings…

The race to be the second biosimilar mAb is on, but Amgen seems to have the edge…

- mBC vs. eBC for trastuzumab (Pfizer)?
- Including gastro indications for anti-TNFs (Health Canada?)
- RA vs. NHL for rituximab?

- Real world studies for biosimilar mAbs “will definitely see safety issues”, but this is to be expected (Madsen on NOR-SWITCH)

- Amgen now ahead with trastuzumab and adalimumab, BI for rituximab, Sandoz for etanercept
- First to market benefits?

Sources: FirstView Future of Biosimilars (May 2014)
BIOSIMILAR MARKET UNCERTAINTIES…

Regulatory

Extrapolation no longer guaranteed, unless scientifically justified…

Health Canada refused to grant gastro indications for Remsima and Inflectra citing “differences between SEB and the reference product”

Interchangeability in the US remains a potential game changer, so clear guidance is key…

Clear guidance on interchangeability unlikely, more likely to be vague and maintain need for scientific advice from the regulators (case by case)

Jury still out on whether or not the biosimilar 351(k) pathway will be used in the US…

Patent provisions remain a concern for many developers in the US, so full BLA submissions (tbo-filgrastim) could be the way forward (Remsima?)

The naming debate rages on, but how critical is this to the market’s evolution (brand vs. Gx)…?

US likely to push for having different INNs, with EU sticking to its current system (Japan different already)

Impact on global PCV systems?

Sources: FirstView Future of Biosimilars (May 2014)
BIOSIMILAR MARKET UNCERTAINTIES...

Legal

Legal tactics move front and center as the next phase of originator defense kicks in; key focus = IP, but other issues being challenged (claims)...

- Hospira vs. Roche (UK)
- Roche vs. Celltrion (Korea)
- Celltrion vs. Janssen (US)
- Roche vs. Biocon (India)
- Sandoz vs. Amgen (US)
- Who will be up next?

How often, and how hard, originator companies head to the courts in order to defend their turf remains a critical uncertainty...

- More of an issue in the US, but increased activity in other markets cannot be ruled out (as the above examples illustrate)

Sources: FirstView Future of Biosimilars (May 2014)
BIOSIMILAR MARKET UNCERTAINTIES…

Commercial (1)

Price matching continues to be the “elephant in the room” for biosimilar developers…

• A rarely discussed scenario is that the originator matches the price of the biosimilar product (very likely)

Aggressive payers could actually cost the system more money, especially in the US…

• Current rebating in the US market ensures lower prices vs. list price for biologics
• Biosimilar push = rebate trap!

Portfolio management remains critical, but even more so now that current targets are saturated…

• Second wave (big mAbs) saturated, limited opportunity left, so all eyes on third wave (>2020 patent expiry) but selection very challenging

Calculating uptake and profitability of biosimilars remains challenging…

• Using historical uptake rates for biosimilars provides useful benchmarks, but market and class behaviors differ massively

Sources: FirstView Future of Biosimilars (May 2014)
BIOSIMILAR MARKET UNCERTAINTIES…

Commercial (2)

Source: FirstView analysis; primary market research (n=12 interviews).

Ph = physician; Py = Payer; (1) anti-TNF mAb; (2) oncology mAb; (3) renal dialysis setting; (4) oncology setting

Sources: FirstView Future of Biosimilars (May 2014)
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- Q&A...
WHERE NEXT FOR BIOSIMILARS?

The focus is now very much on the commercial issues…

Sources: FirstView Future of Biosimilars (May 2014)
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QUESTIONS, COMMENTS, HECKLING…?

duncan.emerton@firstword-pharma.com
uk.linkedin.com/in/duncanemerton

@fwpharma or @biosimilarz

www.fwreports.com or www.biosimilarz.com