ANCHOR REPORT

Korean biopharmaceuticals

NOMURA
EQUITY RESEARCH

Buy Celltrion, Korea's biosimilar leader

Coming of age: generics-centred players flourishing, preparing to go global

Backed by a supportive domestic environment and years of R&D, Korean biopharma companies look ready to blossom overseas.

We see the entry of biosimilars as a game changer for pharmaceutical companies in the coming years. As the 2013/14 expiry of biologics patents nears, we expect heightened investor interest.

We initiate on Celltrion with a BUY. We expect its revenues to be dominated by sales to emerging markets in the near term, with Europe and Japan to follow.

Key analyses in this anchor report include:

- Comparison of pharmaceutical market development in Korea, India and Japan
- Region-by-region examination of market opportunities
- Countering biosimilars with bio-betters: easier said than done
- A look at other Korean industry players

May 30, 2011

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Action: Why global investors should look to invest in Korea

We are bullish on the prospects of biopharmaceutical start-ups in Korea. We think that past developments have successfully steered generics-centred companies toward R&D. Moreover, the Korean government has fostered a highly supportive environment for biotechnology and biopharmaceuticals with initiatives such as the present Bio Vision 2016 and tax incentives. We believe the generics-centred companies are now about to enjoy the fruits of their labours as Korean-born products expand globally and see their investment appeal heightened.

Stock pick: Initiating on Celltrion with a BUY rating

We begin formally covering the Korean biopharmaceutical sector with Celltrion, as we believe it will become the global leader in biosimilars. We do not expect commercial launch in Europe/Japan to happen until 2013/14, but contrary to consensus expectations, we see its sales to emerging markets dominating its revenue in the near term.

Market opportunity: USD80bn worth of biologics coming off patent

Biosimilars are generics of biologics such as monoclonal antibodies and proteins. Biologics worth USD80bn worldwide are projected to go off patent by 2020, of which Herceptin (USD5bn) and Remicade (USD6bn) will go off patent in Europe/Japan in 2012-14. We believe Korean biopharmaceutical companies have a head start to most global competitors in this market.

Great strides in biopharmaceuticals in recent years

Although Korean-born small-molecule R&D has had only mild success to date, biopharmaceuticals have shown solid progress in recent years. LG Life Sciences has plans to submit its slow-release hGH biosimilar in 2011 for EU approval, while Green Cross signed an agreement with ASD Healthcare in 2010 for US distribution of immunoglobulin IVIG and haemophilia treatment. Celltrion has signed distribution agreements with Hospira in the US and Nippon Kayaku in Japan for sales of biosimilars. Smaller companies such as ISU ABXIS and Aprogen have also been active overseas.

Fig. 1: Coverage/rating summary

Stock	Ticker	Rating	Price	Target Price	Upside (%)
Celltrion	068270 KS	BUY	W34,200	W50,000	46.2

Source: Pricing as of 26 May, 2011; local currency

Rating: *See report end for details of Nomura's rating system.*

Anchor themes

The healthcare sector looks attractive, given fundamentals, including high barriers to entry and an ageing population, which should lead to demand growth over the longer term.

Nomura vs consensus

Our analysis indicates that an economic recovery (particularly in the US) should lead to sector outperformance.

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Executive summary

Korean biopharmaceutical sector and Celltrion
We believe that the Korean biopharmaceutical sector, after 20 years of biotechnology investment and government incentives is coming of age. Through a bold combination of tax incentives, regulatory support and government funding, Korean biopharmaceutical companies such as Celltrion, Green Cross and LG Life Sciences are on the cusp of global expansion. In this report, we focus on Celltrion – the global leader in biosimilars.

Celltrion forecast: FY2011 sales of KRW300bn, 35% EPS CAGR in FY2011-15
We forecast FY11 sales of near KRW300bn, mostly from CT-P13 (Remicade biosimilar) and CT-P06 (Herceptin biosimilar) validation batch sales to partners in developed markets. We forecast 26% y-y growth in FY12F, amid the launch of biosimilars in ROW and validation batch sales of CT-P10 (Rituxan) and CT-P05 (Enbrel). We believe that the principal driver over those years as well will be ROW sales. Our forecast suggests more than KRW900bn in FY15F on the back of strong biosimilar sales, resulting in a 35% EPS CAGR for FY2011-15. Since the company does not have a peer globally, our valuation relies on DCF. We calculate a target price of 50,000KRW.

Celltrion's strengths: Quality, Speed, Partnerships, Capacity, Pipeline
In our view, Celltrion will be the global leader in monoclonal antibody biosimilars. Its foremost strength is its commitment to world-class quality; Celltrion consulted with the EMEA from very early on in the development process in 2006. Celltrion has focused on Herceptin and Remicade targeting earlier expansion in the emerging markets, rather than Rituxan, which faces intense competition in the US. We also believe that its network of marketing partners is strong, with Nippon Kayaku in Japan and Hospira in the US/EU, topping the list. By the end of 2012FY, Celltrion is on target to have 140,000L bioreactor capacity. The company's pipeline of nine biosimilars, we believe, is the best in the industry.

Biosimilar revenue growth to be driven by demand in the emerging markets
The story of biosimilar expansion is less about containing cost in developed nations and more about providing access to patients in the emerging markets. We believe that by halving the price of biologics, there will be a pronounced "market creation effect" where increased volume will more than compensate for the decline in price. Our forecast assumes that the patient population using biologics in the emerging world will triple from the current baseline by 2020.

Developed world penetration rate forecast: 10% EU, 30% Japan, 10% US
We believe that the best biosimilar penetration will be in Japan with a peak penetration of 30%, followed by the EU and the US each at 10%. Although Japan is among the most generics-averse nations in the OECD, its 30% copayment for biologics is still unaffordable for most patients. Note that Nippon Kayaku has about 50% market share in oncology generics – arguably Celltrion's best partner in the world. In Europe, we expect slow acceptance, unless government regulations are changed to promote biosimilars. We forecast 10% penetration in US, due to lack of clarity in the biosimilar approval pathway.

Limited effect from innovators' counterstrategies, competitors' biosimilars
We think that the innovators' counterstrategy to Celltrion's biosimilars will have limited impact. Innovators' next-generation biobetters such as TDM-1 (Herceptin biobetter) and GA-101, subcutaneous Herceptin, Simponi, oral small molecules, etc. are likely to counter biosimilar erosion. Among other biosimilars, only Teva-Lonza and Sandoz have the required world-class quality to match Celltrion, though their pipeline, at present, is not as advanced.

Risks/Upsides: Price wars, clinical trial results are top risks, watch FDA guidelines
The foremost risks to our forecast is the possibility of price wars with innovators, poor clinical trial results of biosimilars, protectionist policies in the emerging world, extensive patent litigations, and lukewarm acceptance by doctors/patients. The most significant catalysts to watch for are announcements of US biosimilar guidelines in CY2011, and anticipated approval and launch of biosimilars in Korea and ROW in 1H CY2012.

Primer for global investors on Korea

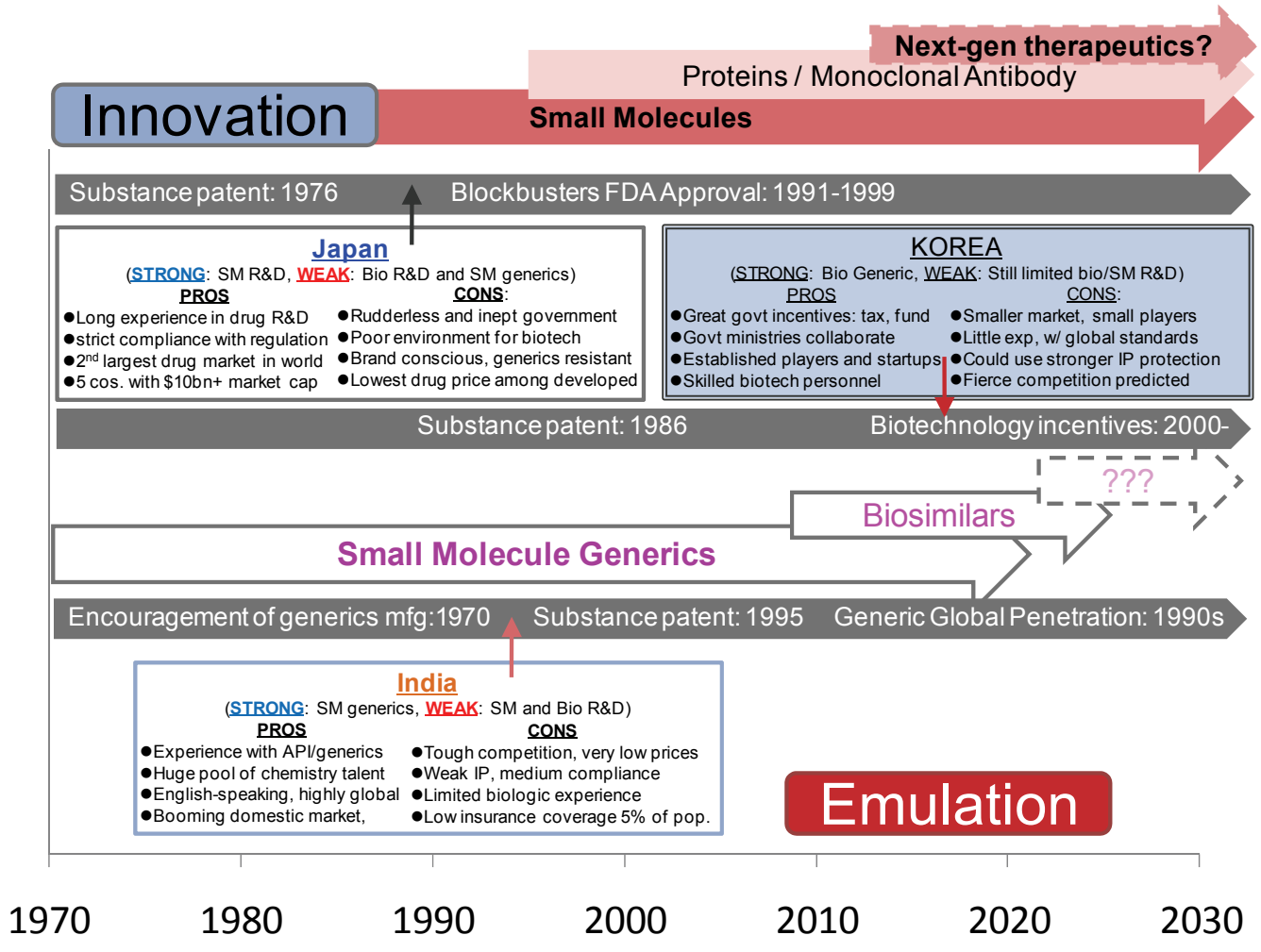
Investment in any pharmaceutical industry requires consideration of the regulatory/legislative environment

The pharmaceutical sector is essentially a passive industry — profound change is only instigated by sweeping reforms of regulation and laws, and in the absence of such reform, the industry tends to run on auto-pilot. Regulated markets such as the pharmaceutical industry have high barriers to entry and high margins, but these also deter competition and inhibit change. In our view, the two most important inflection points historically for pharmaceutical industries in any given country are:

- Introduction of drug and patent regulation
- Demographic/fiscal exigencies from increasing longevity

In our view, investment in the pharmaceutical sector in any country requires consideration of the particular country's position in the global regulatory/legislative environment surrounding pharmaceuticals. In the case of Korea, 20 years have elapsed since the enforcement of product patents in Korea, and it has been 10-plus years since government incentives for the biotech industry were promulgated. We believe the time is now ripe to reap the fruits of 10-20 years of R&D, especially in the Korean biopharmaceutical sector.

Fig. 2: Conceptual diagram of Asian Pharmaceutical Market Development: Korea, India, Japan



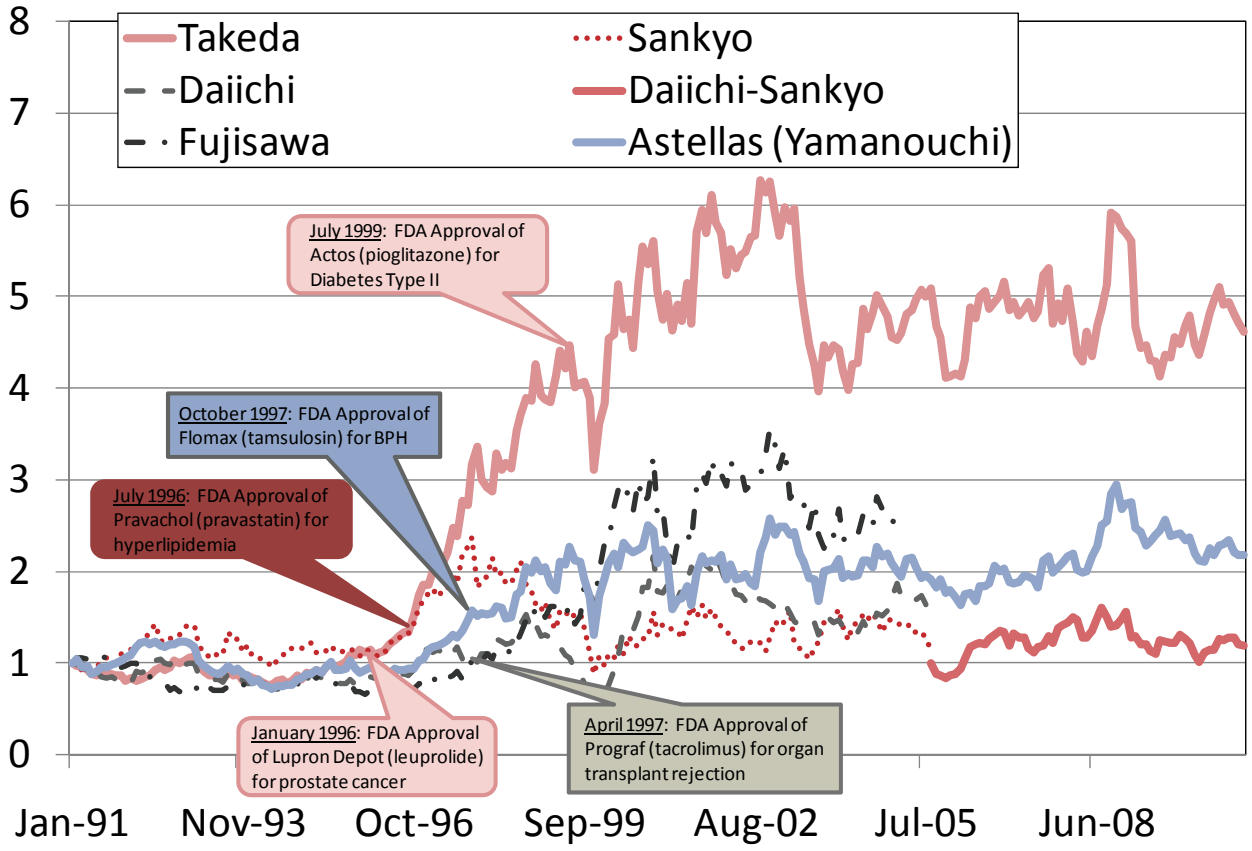
Source: Nomura research

Comparison: Korea, India, and Japan

In order to highlight the importance of regulatory changes, we look at two other Asian countries with pharmaceutical industries that have grown in prominence around the

world: Japan and India. Although there are stark differences among the three nations, the central theme is the same. In all three cases, the pharmaceutical industry was galvanized by a few large regulatory/legislative changes, particularly involving substance patents, an indispensable component for growth in pharmaceuticals. In the case of Japan, the impetus was the enforcement of substance patents in 1976. In India's case, it was both the ratification of the General Agreement on Tariffs and Trade (GATT) treaty in 1995 which enforced patents, and a regulatory change by the FDA to promote generics in 1997. Korea, as we will argue, has been driven by the recognition of substance patents in 1986, and the government's drive for biotech development in 1994.

Fig. 3: Japanese Pharmaceutical Industry: Relative Stock Performance to TOPIX from Jan-91 to Present
Stock price at Jan-1-1990 set at 100

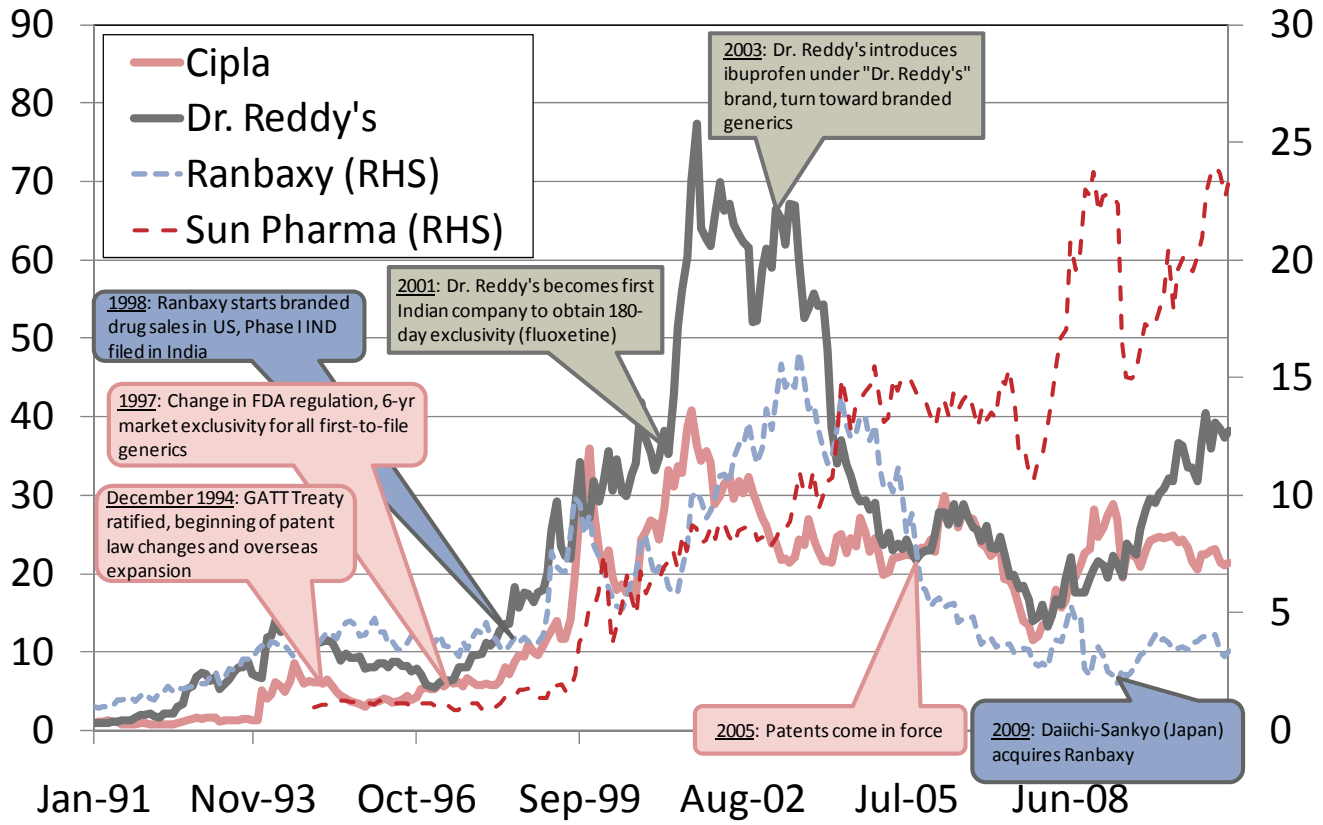


Source: Nomura research, Company data, Bloomberg

Asian Pharma Development Case #1: Japan

The first example is Korea's neighbour to the east, Japan. Until the 1970s, major players in the Japanese pharmaceutical industry were content with a wholesale/import business model. Substance patents were routinely violated since the Japanese courts only recognized manufacturing process patents. Worse, the lack of substance patents inhibited research into new drugs, since innovation was quickly embraced and emulated by rival companies. Realizing the need to galvanize the industry, the Japanese government moved to recognize substance patents in 1976. Thereafter, major pharmaceutical companies focused on innovative research. After nearly 20 years of R&D, the industry entered a golden age with the development and FDA approval of blockbusters such as Pravachol (Daiichi, now Daiichi-Sankyo), Prograf (Yamanouchi, now Astellas), Actos (Takeda), Aricept (Eisai), and Abilify (Otsuka), among many others. Unfortunately, just as the industry was reaching its peak in the 1990s, governments around the globe turned increasingly toward generics. Without guidance from an increasingly splintered government and incapable of realizing the sea change in the global pharma environment, the Japanese industry has largely stagnated in the past decade, we believe.

Fig. 4: Indian Pharmaceutical Industry: Relative stock performance from SENSEX Jan-91 to Present



Source: Nomura research, Company History, Bloomberg

Asian Pharma Development Case #2: India

The second example is India, the global production house of pharmaceuticals. The Indian Patent Act of 1970 drastically weakened patent terms and even allowed for outright government expropriation of patents. Many companies, such as Dr. Reddy's, grew to prominence during this period by supplying developed countries with highly cost-competitive API. There were two triggers that induced dramatic shifts in the 90s:

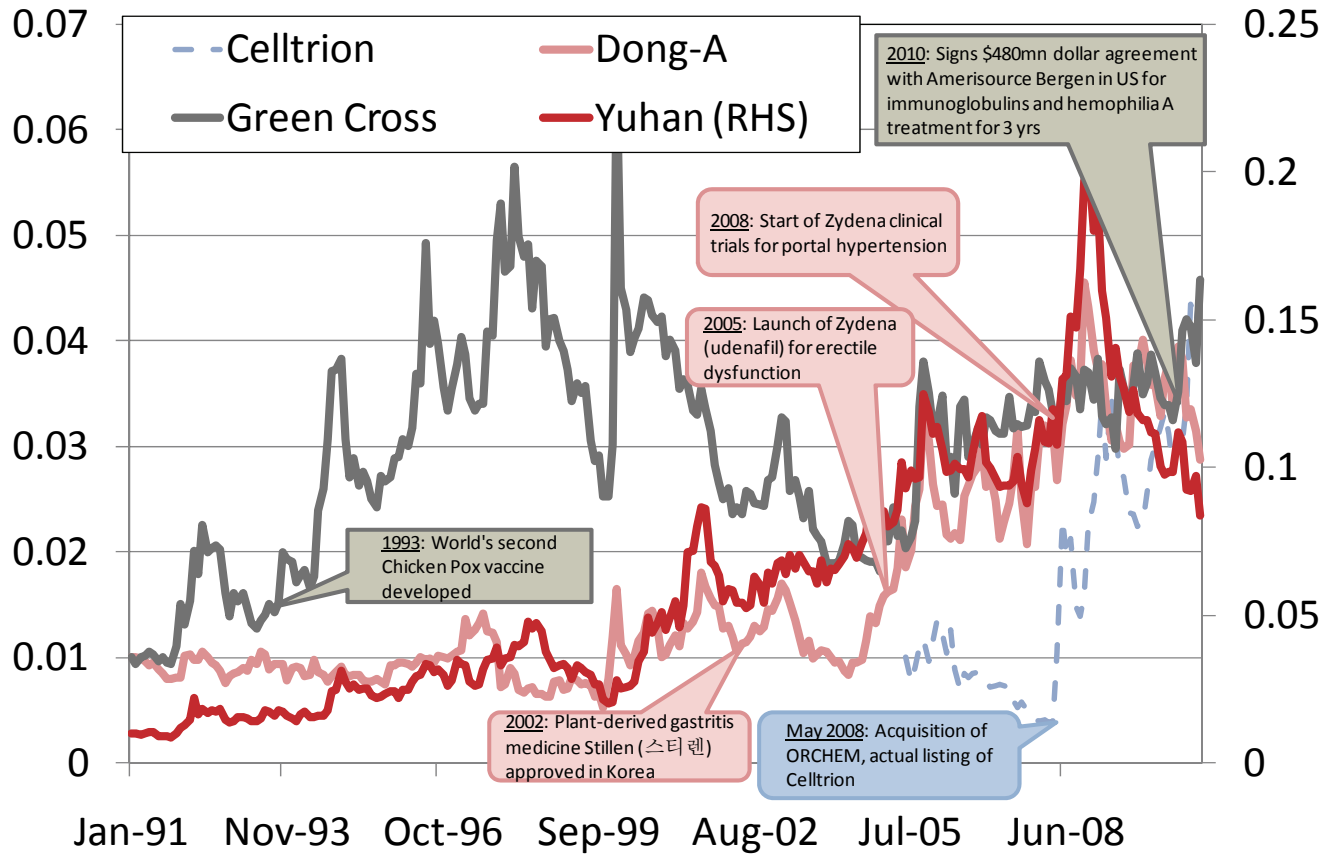
- Ratification of the GATT Treaty in 1994 marked the start of re-imposition of patent rights in India and implied an increasingly competitive domestic environment.
- FDA changed its regulation in 1998 to allow 180-day exclusivity of generic sales to companies who were first to file.

Unlike Japan, where the industry was based on R&D and required 20 years since regulation to see any change, in India the effect was immediate. Buoyed by the global turn toward generics, threatened by the re-imposition of patent rights in India, aided by the large number of English-speaking employees, and supported by the vast army of chemists nurtured through the 80s, India exploded onto the world stage in the late 1990s and early 2000s. Coupled with the recent focus on the burgeoning domestic market, the Indian pharmaceutical industry has continued its high rate of growth until the present day.

Yet, the long shadow cast by the GATT treaty is increasingly being felt in India. As a result of the treaty, patents for drugs that were granted after 1995 are protected as of 2005. The result is a slowly dwindling pipeline of generics. The competitive environment is driving the Indian companies into diverse strategies for growth. It has been only 10 years since the enforcement of substance patent, and more time is required to see if India's turn toward R&D will bear fruit. We note that on 16 May 2011, Glenmark out-licensed its novel monoclonal antibody GBR 500 − a first-in-class VLA-2 antagonist for treatment of Crohn's and other inflammatory diseases − to Sanofi Aventis for upfront payment of USD50mn. This marks the first biopharmaceutical out-licensing deal for an

Indian company. Glenmark could receive over USD600mn in milestone payments in addition to double-digit royalty. Although this is just one out-licensing deal among many failures, we may be witnessing the rise of India's innovation-driven pharmaceuticals.

Fig. 5: Korean Pharmaceutical Industry: Relative stock performance from KOSPI Jan-91 to present



Source: Nomura, company websites, Bloomberg

Regulatory/legislative changes driving innovation in Korea

So where does Korea stand? Like Japan, Korea for many years did not recognize substance patents. This was only recognized in 1987. Since then, the Korean pharmaceutical companies turned increasingly toward R&D in the 90s. Lately, this trend has been reinforced by the following changes.

Driver #1: US/Korea free trade agreement (KORUS-FTA)

The enactment of the free trade agreement between Korean and the US (KORUS-FTA), which was signed in April 2007 and later amended on December 2010, is one turning point. The free trade agreement clearly requires Korean patent terms be extended for any delays in granting patents, mandates a five-year data exclusivity for new pharmaceutical products, and a three-year additional exclusivity for new indications. Although the agreement is still not ratified by either the National Assembly of South Korea or the United States Congress, the free trade agreement clearly benefits innovative companies, and presents the biggest threat to domestic Korean pharmaceutical companies who have largely relied on generics.

Driver #2 and #3: Dual punishment system and price reduction

In addition, Korea has implemented a dual punishment system where both the doctor and the pharmaceutical company can be punished for giving and receiving rebates. Moreover, the Korean government has been actively lowering prices since 2002, when the National Health Insurance Corporation had reported a large deficit of KRW2tr. All of the above points to increased competition in the Korean pharmaceutical sector in the future.

Triple menace driving Korean companies to global expansion and R&D

With the triple menace of strengthened patent laws, rebate punishment, and drug reimbursement cuts, major Korean companies have increasingly strengthened innovation R&D in the past 10 years. Some 20 years since the enforcement of substance patents, Korean companies have successfully developed a variety of drugs as shown in the following table. We note that of the 18 drugs listed in the table, only one (gemifloxacin mesylate, marketed as Factive) has reached US FDA approval, though clinical trials are ongoing in Europe and the US for a number of others. Moreover, with the exception of Stillen, an herbal gastritis drug, which recorded sales of KRW87bn in 2010, the Korean market acceptance of Korean born drugs has been generally limited.

Fig. 6: Innovative Drugs Developed in Korea 1999-2011

Product Name	INN	Indication	KFDA Approval	Company Name
Sunpla	Heptaplatin	Gastric Cancer	Jul-99	SK Chemicals
Chondron	Autologous chondrocyte	Knee Joint	Jan-09	Sew on Cellontech
Easyef	Recombinant Human Epidermal Grow th Factor	Diabetic foot ulcer	May-01	Daew oong
Milican	Chitosan 20 Holmium Nitrate	Liver Cancer	Jul-01	Dong Wha
Q-Roxin	Balofloxacin	Urinary Infection	Dec-01	Choongw ae
Factive	Gemifloxacin Mesylate	Antibiotics	Dec-02	LG Lifesciences
Joins	(Natural Products)	Osteoarthritis	Jul-01	SK Chemicals
Stillen	(Natural Products)	Gastritis	Jun-11	Dong-A
Apitoxin	(Natural Products)	Osteoarthritis	May-03	Guju
Pseudovaccine	Pseudomonas aeruginosa prevention	Vaccine	May-03	CJ Corp
Camtobell	Belotecan	Lung Cancer	Oct-03	Chong Kun Dang
Revanex	Revaprazan	Duodenal Ulcer	Sep-05	Yuhan
Zydena	Udenafil	Erectile Dysfunction	Nov-05	Dong-A
Levovir	Clevudine	Hepatitis B	Nov-06	Bukw ang
Pelubi	Pelubiprofen	Osteoarthritis	Apr-07	Daew on
M-vix	Mirodenafil	Erectile Dysfunction	Jul-07	SK Chemicals
Nortec	Ilaprazole	Duodenal Ulcer	Oct-08	Ilyang
Kanarb	Fimasartan	Hypertension	Sep-10	Boryung

Source: Nomura research

Small Molecule R&D: Development of "me-too" drugs is increasingly difficult

Concerning small-molecule R&D innovation, we believe that the prospect of Korean R&D is somewhat limited. Unlike the 70s-80s when Japanese companies were developing small molecule compounds, global drug development has become exponentially more difficult, particularly with small molecules.

With the exception of some natural product drugs, all of the Korean-born drugs in the table are analogous chemical compounds of existing drugs, otherwise known as "me-too" drugs. Although this strategy offers a lower risk profile compared to completely innovative drugs and can be enormously successful in some cases (e.g. atorvastatin is an improvement on lovastatin, esomeprazole successfully replaced omeprazole), we believe that times and regulations have increasingly turned against market potential of "me-too" drugs in general. In developed countries around the world, "me-too" drugs are increasingly required to show additional and significant benefits compared to the original in order to attain commercial success. Because of dwindling pipelines, large multinational pharmaceutical companies have also been quick to develop "me-too" drugs, implying that "me-too" drugs are being developed well before the original's approval − in some cases upon publication of patent application. Even if some "me-too" drugs demonstrate some advantages over the original, many have failed to gain much traction (e.g. Invega, Effient). Exceptions are possible, but this approach is likely to generate limited returns.

Biopharma: government initiative for biopharmaceutical development

On the other hand, we think R&D in biopharmaceuticals is more promising. As discussed in the next section, the Korean government has been actively promoting the development of biotechnology since the 1980s, marked by events such as the foundation of the Korean Research Institute of Bioscience & Biotechnology (KRIBB) in 1985. The largest impetus was the promotion plan for biotechnology known as 'Biotech 2000' in 1994. This initiative and others have served to create biotechnology start-ups in the early 90s; many of the currently listed biotechnology companies were listed near 2000.

25 years of R&D + 15 years of biotechnology investment = Ripe for investment

After 25 years of incentivizing R&D in pharmaceuticals and 15 years of fostering biotechnology, we believe that the time is ripe to reap the rewards of years of investment. The Korean government has proven admirably effective in promoting biopharmaceutical development. The industry is now at a stage where technology is at a par with leading global players, and global expansion is about to begin – especially with biosimilars. Although the present report focuses on Celltrion, which we believe will be a global leader of biosimilars, other biotechnology companies developing novel antibodies/small molecules are also moving close to phase III clinical trials, where multinational partnership will be needed.

The Korean biopharmaceutical sector

Korean biotechnology promoted by the government

The foundation of the biotechnology sector in Korea can be traced back to the early 1980s when the government began promoting and investing in the biotechnology space. The initiative gained momentum in 1994 when a major promotion plan for biotechnology called 'Biotech 2000' was formulated, which resulted in a 20-fold increase in the size of the industry over the next seven years. In 2000, the Korea Biotechnology Commercialization Center (KBCC) was set up by the government-funded Korea Institute of Industrial Technology (KITECH). KBCC was South Korea's first multi-purpose current Good Manufacturing Practices Contract Manufacturing Organization (cGMP CMO) and it quickly gained critical experience by working with international innovator companies such as Novartis, Pfizer and BMS. The government subsequently handed over the management rights of KBCC to Binex in 2009.

Korean government goal to achieve 22% global market share in biosimilars

The Korean government's multi-pronged approach to promote innovation, drug discovery and biopharmaceuticals was an attempt to motivate the shift from a generic-dominated pharmaceuticals sector to an R&D-based sector. Over the past two decades, proactive government policies towards biotechnology have helped nurture an innovation-driven sector, which is at par with continental peers such as China, Taiwan and India and which continues to catch up to global biotech majors such as the US and Europe. Biotechnology has been identified as one of the country's next generation growth engines and it has been classified into five areas: biomedicines, bio-organs, cell therapy, tissue engineering and bio-chips. Biosimilars, in particular, has been identified as a core growth strategy for the economy and the government would support the financing, marketing and overall business operations of the sector in order to achieve a 22% global market share by 2015. The Ministry of Education, Science and Technology, the Ministry of Knowledge Economy and the Ministry of Welfare will put together their efforts to support global drug development and marketing.

Bio Vision 2016: USD15bn investment in 10 years

A major milestone in the evolution of the sector was achieved in 2006 when the government launched a plan called 'Bio-Vision 2016' with the objective of building a globally competent biotechnology sector that would take South Korea from rank 14 to rank 7 in the global biotechnology space. The total budget outlay for Bio-Vision 2016 is expected to be in excess of USD15bn over a period of 10 years and it aims to primarily restructure government biotechnology programmes, strengthen the scientific infrastructure, globalise the biotech industry and strengthen the regulatory framework. Core strategies for the execution of the plan include the establishment of contract research and contract manufacturing organisations at select clusters within the country. In 2011, the Korean government also launched 'Project Columbus', a promotion scheme that caters specifically to pharmaceutical and medical device companies that are looking to expand into the US market. South Korean companies currently hold a 1.1% market share in the US and the Ministry of Health and Welfare aims to increase this share to 3.4% by 2015. A total of 38 companies comprising 21 pharmaceutical and 17 medical device makers have been selected for Project Columbus. The companies would be eligible to receive marketing, licensing and R&D support from the government.

In March 2011, the National Assembly of South Korea also passed a special law in order to promote and support the pharmaceutical sector through the following measures:

- Establishment of a five-year comprehensive plan to promote and support the pharmaceutical sector.
- Establishment of a promotion and support committee.
- Setting up a pharmaceutical industry development fund.
- Establishment of a certification system for innovative pharmaceutical companies.
- Granting tax benefits, including corporate tax, registration & acquisition tax, property tax.
- Granting priority to innovative companies in government project participation.

Tax incentives: Incheon Free Economic Zone

The government has also been encouraging foreign direct investment into Free Economic Zones (FEZs) through tax incentives and cash grants. FEZs are characterised as industrial complexes, coupled with facilities such as international schools, hospitals and broadcasting stations for the purpose of inviting knowledge industries and high value-added service industries. The Incheon Free Economic Zone hosts some of the largest biopharmaceutical production facilities in South Korea, with the presence of companies such as Celltrion and KBCC. In addition to FEZs, a nationwide promotion policy of bio clusters has resulted in the establishment of four major biotechnology clusters containing 25 regional bio centres that specialise in biopharmaceuticals, biochemistry, bio-agriculture, etc.

Regulatory support: Korean biobetter guidelines expected by the end of 2011

The regulatory environment in Korea has been conducive to the growth of the sector as it has encouraged innovation by providing clear biopharmaceutical guidelines and establishing a streamlined approval process. In order to enhance the international competitiveness of Korean biosimilars, the Korean Food and Drug Administration (KFDA) has worked in cooperation with domestic drug manufacturers and has established a regulatory system that supports early quality management along with non-clinical, clinical, manufacturing and quality management. The regulatory approval pathway for biosimilars was published in July 2009 and it clearly defined a biosimilar product and recommended manufacturing guidelines that were in line with ICH Q5E standards. The government has also held cGMP education sessions in order to impart finer details about biopharmaceutical manufacturing. The KFDA is expected to release biobetter guidelines by the end of 2011. These guidelines would define bio-betters and provide safety and approval standards.

Advantage Korea: Korea has an edge over India in biopharmaceuticals

The core strength of Korean biotechnology companies lies in their high-quality manufacturing facilities, extensive bio-research capabilities, network of global drug development partnerships, availability of a well qualified human resource pool and the country's business friendly government policies. When compared with countries such as India which too has a very well established generics industry, South Korea's early foray into the biotech sector and consistent policies over the decades give it a clear edge. Despite having conquered the global generics space, Indian pharmaceutical companies are still in the process of establishing a foothold in the biotechnology and drug discovery space. The Indian government established the Department of Biotechnology in 1986 and attempted to promote biotechnology but a lack of decisive policies and concentrated efforts to promote the sector, coupled with a frail intellectual property rights system till 2005, resulted in a relatively slow take off for the life sciences sector. Private sector entrepreneurship, however, has helped shape up a competent Contract Research Organization (CRO) industry with the likes of Jubilant Life Sciences and GVK Bio that work with MNCs such as Endo Pharmaceuticals and Pfizer, respectively. While international pharmaceutical majors have partnered extensively with Indian generics companies in order to exploit their low cost and high quality finished dosage products, they have not struck any comparable number of drug discovery partnerships with Indian biotechnology companies.

Korean biotech companies have swiftly and successfully established a strong network of partnerships with domestic as well as international pharmaceutical majors. Genexine has partnered with Dong A to co-develop and co-market a first generation protein and a next-generation antibody fusion protein, while Crystal Genomics has partnered with Astra Zeneca to develop a non-steroidal anti-inflammatory drug. Korea's life sciences sector has evolved to become globally renowned for protein engineering, based on fermentation, cell fusion and gene recombination. South Korea now envisions being a top player in the global biosimilar market by 2020 and the country has proactively adopted strategies to promote the development of biosimilars as well as bio-betters and innovative drugs.

A short introduction to Korean biopharmaceutical companies

ISU Abxis

ISU Abxis is a listed subsidiary of ISU Chemical and is a part of the South Korean conglomerate ISU Group. The company was founded to create innovative antibody therapeutics. The company currently markets Clotinab – a biosimilar of Eli Lilly's ReoPro, thereby becoming the first Korean company to manufacture and market biosimilar monoclonal antibodies. ISU Abxis' antibody therapeutics pipeline includes biosimilar molecules such as ISU302 (Cerezyme) and ISU 103 (Herceptin) and ISU 303 (Fabrazyme). ISU Abxis' novel drug pipeline includes a molecule for Asthma/Sepsis (ISU 201) and a monoclonal antibody for metastatic cancer (ISU 102). Another key biosimilar product in the pipeline is ISU103, an HER2+ biosimilar that is currently in preclinical trials for which the company aims to submit the Investigational New Drug (IND) application by 1H 2012. The lead candidate in the company's novel drug portfolio is ISU201, a recombinant Fc fusion protein that is indicated for severe asthma (sepsis), asthma refractory to steroids. If successful, ISU201 could compete with the globally successful Xolair.

Aprogen

Aprogen was established in 2000 as a biotechnology company that developed and produced monoclonal antibodies through its advanced antibody, protein and animal cell engineering technologies. The company's core strength lies in the area of biosimilar development and it boasts of four molecules in its pipelines, namely, GS071 (Remicade), AP032 (Aranesp), AP052 (Rituxan) and AP062 (Herceptin). GS071 is the most advanced molecule in the pipeline and is currently in Phase I clinical trials, while the other molecules are in pre-clinical stages.

In October 2010, Japan's Nichi-Iko acquired a 33.4% stake in Aprogen for JPY1bn, thereby gaining access to its Remicade biosimilar and others. Through the deal, Nichi-iko received exclusive development and marketing rights for products made using Aprogen's technologies for the Japanese market. Apart from biosimilars, Aprogen is more focused on developing novel biotherapeutic molecules and has three leading candidates in its pipeline – AP102 (COMP-Ang1), AP202 (DAAP) and AP302 (DIVB). AP102 is an angiogenesis protein that helps damaged tissues regenerate faster without having any negative effects on VEGF. AP202 is a double anti-angiogenic protein (DAAP) that simultaneously binds VEGF-A and angiopoietins, and blocks their actions.

Green Cross

Green Cross was founded as a biopharmaceutical company in 1967 and went onto become Korea's first manufacturer of blood plasma fractions. It is now the single largest player in the plasma and vaccine business in Korea, with an above 80% market share in the domestic blood derivatives market. Green Cross, and its privately held US partner company Jennerex, are developing a drug (JX-594) for liver cancer and have recently reported positive clinical data from a Phase 2 trial which was conducted in South Korea. JX-594 is a proprietary, engineered oncolytic virus that is designed to selectively target and destroy cancer cells.

Another key partnership signed by the company was with the NASDAQ-listed Abraxis BioScience for the exclusive sales of anti-cancer medicine Abraxane in Korea and for the exclusive sales of five biomedicines (under development by Green Cross) in North America. In December 2010, the company signed an USD480mn pharmaceuticals supply contract with Amerisource Bergen, one of the largest pharmaceutical wholesale companies in North America. In April 2011, Green Cross received the WHO's pre-qualification for the flu vaccine. This makes Green Cross eligible to bid for flu vaccine contracts globally and compete with the likes of GSK, Novartis and Sanofi Aventis. The company is already supplying seasonal flu vaccines to the Pan American Health Organization, a regional office of the WHO.

Green Cross's proprietary drug called GreenGene is the world`s fourth drug for the treatment of haemophilia and it was developed using genetic recombination technology. GreenGene could compete with Baxter's products in the international market for haemophilia treatment. On 15 March 2011, Green Cross received approval for trials of

its EPO biobetter GC1113 in Korea. In the non-clinical trials for GC 1113 that were funded by the Ministry of Health, the drug has shown a longer half-life than existing drugs. The robust R&D pipeline of the company also includes drugs and vaccines such as GCSB-5 (osteoarthritis), GC1111 (hunter's syndrome), GC1102 (hepatitis B virus) and GC2101 (Parkinson's disease).

Binex

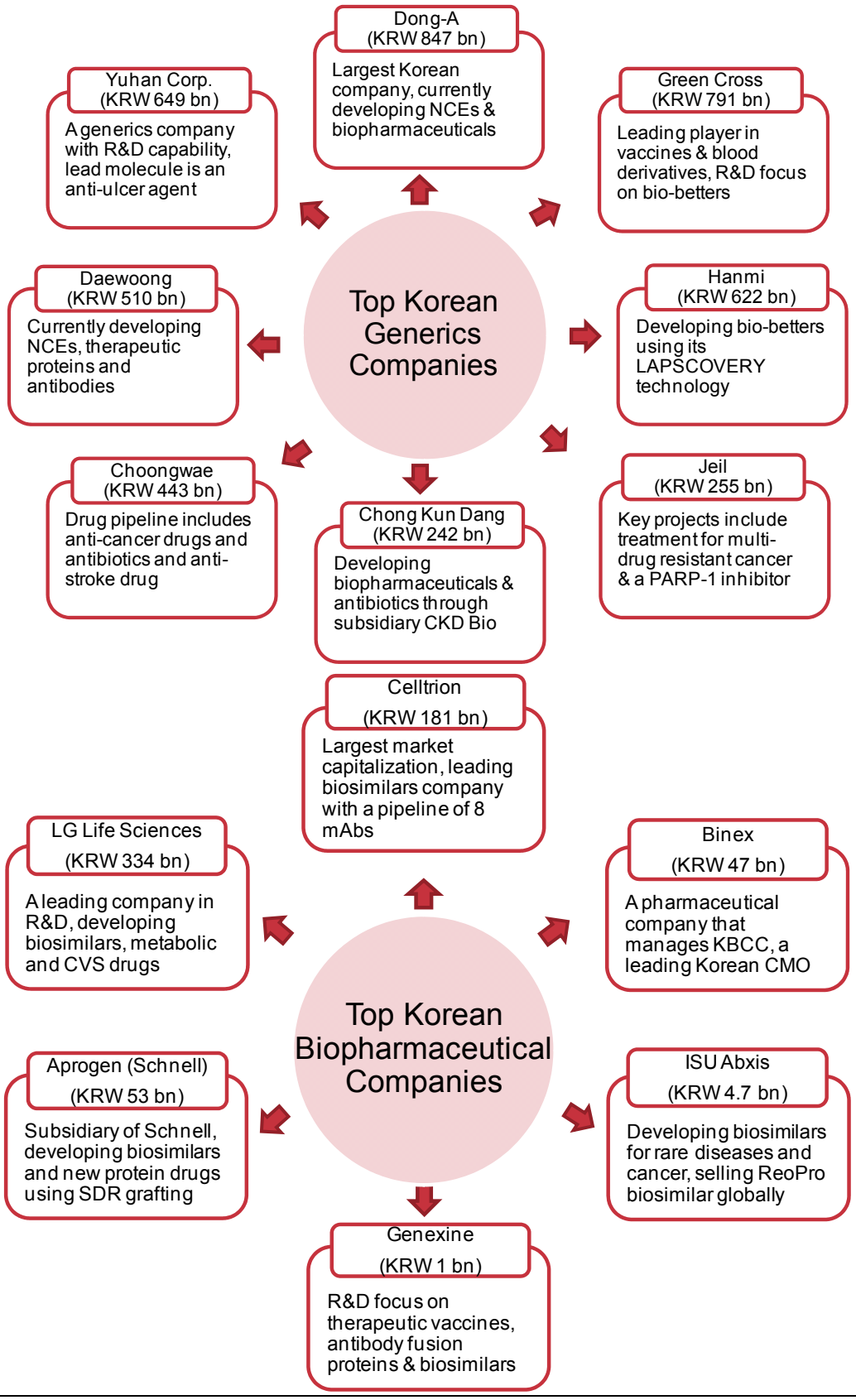
Binex was established in 1957 as a company focused on generic drugs. In 1994, the company received KGMP approval for its manufacturing facility and it established a cell therapy manufacturing facility in 2003. In 2009, Binex signed an agreement with KITECH (Korea Institute of Industrial Technology) for the contract management of KBCC (Korea Biotechnology Commercialization Center), in order to sharpen its expertise in contract manufacturing and development services. Its production capacity consists of a 500L (SUS) and a 1,000L (SUB) mammalian cell culture capacity and the company expects to add an additional 2,000L (SUS) capacity by 2012. The company also has a 500L microbial facility along with a liquid vial, freeze-dried and a pre-filled syringe facility that is currently in operations.

Fig. 7: Financial analysis of Korean companies

Celltrion	**FY08**	**FY09**	**FY10**	**Green Cross**	**FY08**	**FY09**	**FY10**	**LGLS**	**FY08**	**FY09**	**FY10**	**Hanall**	**FY08**	**FY09**	**FY10**
Sales (KRW Bn)	83.7	145.6	181.0	Sales (KRW Bn)	516.1	643.2	791.0	Sales (KRW Bn)	281.9	327.3	334.3	Sales (KRW Bn)	91.9	98.7	106.9
OP (KRW Bn)	30.8	71.8	106.6	OP (KRW Bn)	67.9	119.4	145.6	OP (KRW Bn)	25.1	40.2	11.0	OP (KRW Bn)	1.1	4.0	6.8
OP Margin	36.8%	49.3%	58.9%	OP Margin	13.2%	18.6%	18.4%	OP Margin	8.9%	12.3%	3.3%	OP Margin	1.3%	4.1%	6.4%
Avg OPM	48.3%			Avg OPM	16.7%			Avg OPM	8.2%			Avg OPM	3.9%		
P/EPS Adj.			32.4	P/EPS Adj.			11.0	P/EPS Adj.			39.5	P/EPS Adj.			1,100
ROE			12.8	ROE			27.9	ROE			6.0	ROE			-
P/B			4.7	P/B			2.4	P/B			2.7	P/B			-
EV/EBITDA			33.2	EV/EBITDA			7.5	EV/EBITDA			17.3	EV/EBITDA			-
Binex	**FY08**	**FY09**	**FY10**	**Schnell**	**FY08**	**FY09**	**FY10**	**ISU Abxis**	**FY08**	**FY09**	**FY10**	**Genexine**	**FY08**	**FY09**	**FY10**
Sales (KRW Bn)	29.7	32.3	47.2	Sales (KRW Bn)	17.0	40.6	52.7	Sales (KRW Bn)	3.9	3.5	4.7	Sales (KRW Bn)	1.3	1.1	1.1
OP (KRW Bn)	3.3	0.4	-1.8	OP (KRW Bn)	-2.1	3.7	3.0	OP (KRW Bn)	-4.6	-6.7	-7.4	OP (KRW Bn)	-0.3	-0.5	-1.8
OP Margin	10.9%	1.3%	-3.9%	OP Margin	-12.6%	9.0%	5.7%	OP Margin	-117%	-193%	-157%	OP Margin	-23%	-46%	-162%
Avg OPM	2.8%			Avg OPM	0.7%			Avg OPM	-156%			Avg OPM	-77%		
P/EPS Adj.			-	P/EPS Adj.			-	P/EPS Adj.			-	P/EPS Adj.			-
ROE			-	ROE			-	ROE			-	ROE			-
P/B			-	P/B			-	P/B			-	P/B			-
EV/EBITDA			-	EV/EBITDA			-	EV/EBITDA			-	EV/EBITDA			-

Source: Bloomberg, Nomura research

Fig. 8: Leading Korean pharmaceutical companies



Source: Company data, Bloomberg, Nomura research

What is a biosimilar?

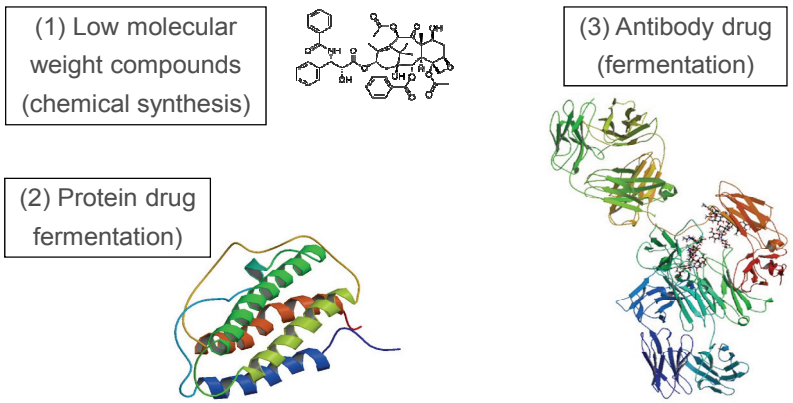
So what is a biosimilar?

Biosimilars is the term for generic versions of biologics (bioengineered drugs). Typically, the generic drugs sold, to date, have been generic versions of low molecular weight compounds. Many new generic drugs are easily administered in oral form and are based on off-patent drugs. Low molecular weight compounds are typically made up of combinations of 2–30 atoms of carbon, hydrogen, oxygen and other elements, and because chemical synthesis is relatively simple, generic versions of low molecular weight compounds can be developed comparatively easily. Discounting differences in purity and other factors related to manufacturing, even high level chemical analysis reveals very little difference between generic versions of low molecular weight compounds and new drugs.

Different types of biologics

Biologics have rapidly gained ground in recent years. Examples of biologics are protein drugs and antibody therapeutics. As with other biological products such as beer and yoghurt, biologics are produced using a fermentation process. Compared with the small number of atoms in low molecular weight compounds, anti-body therapeutics are much larger with upwards of 10,000 Daltons and they have extremely complex structures. Since living cells are used in their production, even drug companies that have originated the biologics cannot consistently produce them with exactly the same composition. Generic versions of biologics are called biosimilars, because they are not exactly the same as the innovator drug. For more details on the biologic manufacturing process, please refer to our report on the pharmaceuticals sector (10-236), “Inexpensive drugs from India to transform the global pharmaceutical industry: trend toward biosimilars”, issued 21 June 2010.

Fig. 9: Comparison of different drugs: small molecules, protein drugs, antibody drugs



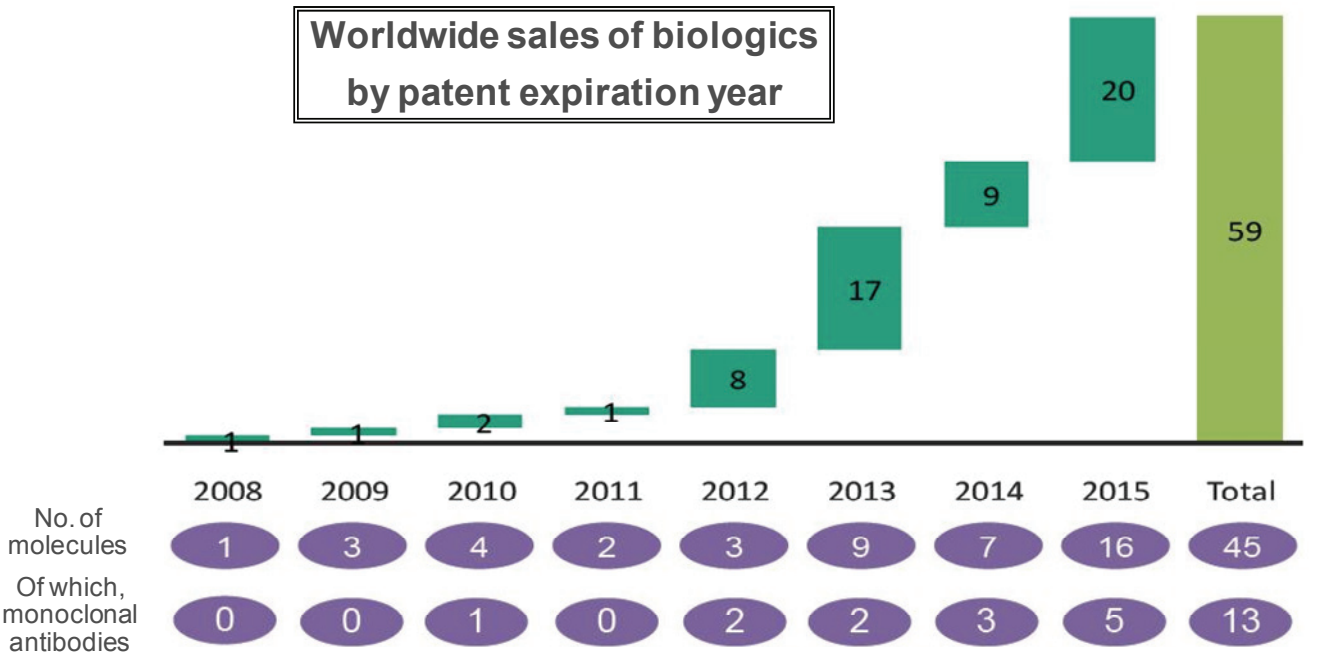
Note: (1) Cheetham, J.C.; Smith, D.M. et al. NMR structure of human erythropoietin and a comparison with its receptor bound conformation Nat. Struct. Biol. 1998 5, 861-866. (Diagram courtesy of RCSP Protein Data Bank, structure ID: 1BUY). (2) Furtado, P.B.; Whitty, P.W.; et al. Solution structure determination of monomeric human IgA2 by X-ray and neuron scattering, analytical ultracentrifugation and constrained modellins: a comparison with monomeric human IgA1 J. Mol. Biol. 2004, 338: 921-941 (Diagram courtesy of RCSB Protein Data Bank, structure ID: 1IGT).

Source: Nomura research

Biologics cost significantly more than ordinary tablets because they are harder to develop and manufacture. Well-known low molecular weight compounds (tablets) hyperlipidemia treatment Lipitor, diabetes treatment Actos, and antihypertensive Norvasc cost USD0.30, USD0.35, and USD0.76 per mg, respectively, with daily costs not exceeding more than several dollars for a normal dosage. In contrast, the per mg costs of biologics Herceptin, a breast cancer drug, and Avastin, a colon cancer drug, are high at around USD8.00 per mg, and it is not unusual for one treatment to cost upward of USD1,000. One treatment for Gaucher’s disease with Cerezyme, the highest-priced biologic, costs USD10,000, with annual treatment costs running at almost USD1 million. Sales in FY09 reached USD58bn for the major biologics alone.

Sales of biologics are on a long-term upward trend. Major global drug companies' pipelines contain a large number of biologics. Antibody therapeutics is also on the rise. Antibody therapeutics are derived from the human immune system, and thus tend to be safer than low molecular weight compounds. They also offer a much higher degree of selectivity than low molecular weight compounds because they attach to certain targeted proteins.

Fig. 10: Lonza estimates of potential global market for biosimilars and number of biologics scheduled to go off-patent



Source: Lonza

With biologics worth around USD80bn worldwide projected to go off patent by 2020, biosimilars are seen as a promising growth market. According to the Lonza Group, the world's leading custom manufacturer of biologics, combined global sales for the biologics losing patent protection in 2008–15 add up to around USD59bn. Rheumatoid arthritis treatment Enbrel is due to go off-patent in 2012, and patent expirations are also due for some other blockbuster drugs, including Remicade (also a rheumatoid arthritis treatment) in 2013 and Rituxan (malignant lymphoma treatment) and Herceptin (primarily a breast cancer treatment) in 2015. Presentations by Teva Pharmaceutical Industries [TEVA] also suggest that the market for biologics going off patent in 2016–20 amounts to USD23bn, with the result that biosimilar makers could have a business opportunity worth more than USD80bn in the years through 2020. We also see scope for further expansion later on when the many biologics currently under development lose their patents as well.

Celltrion Inc 068270.KQ 068270 KS

HEALTH CARE & PHARMACEUTICALS

NOMURA
EQUITY RESEARCH

BUY Celltrion – Korea's "generic Genentech"

Emerging market demand to drive growth of biosimilars

May 30, 2011

Rating Starts at	**Buy**
Target price Starts at50,000	KRW 50,000
Closing price May 26, 2011	KRW 34,200
Potential upside	+46.2%

Action: BUY on the strength of biosimilar global penetration

We forecast a 35% EPS CAGR in FY11-15F, with sales exceeding W900bn in FY15F on global penetration of biosimilars. We think biosimilars will remain the topic *du jour* of global pharmaceuticals. As the 2013/14 expiry of biologics patents nears, we expect interest from global investors to increase, implying sustained share price momentum.

Catalyst: Emerging market demand to drive revenue growth

Biosimilar expansion is a story of access, not cost; if prices are halved in emerging markets, we see a tripling in patient volume and an even more pronounced effect when greater patient affordability meets Celltrion's world-class quality products. Clinical trial results and regulatory approval in Korea in 1H FY12 may be near-term triggers.

We expect higher penetration in Japan than in Europe; US unclear

In Europe, we forecast 10% peak volume penetration for Celltrion's biosimilars; slow acceptance of biosimilars should continue unless governments actively intervene. We forecast a bullish 30% penetration in Japan; in our view, the 30% copayment with biologics in Japan is unaffordable. We assume just 10% US penetration on lack of clarity.

Valuation: Ahead of consensus on emerging market outlook

Our KRW50,000 TP is based on DCF. Availability of biosimilar guidelines from the US FDA may present upside, while downside would come if clinical data do not meet the regulatory threshold; an ORR of ~50% for CT-P06 and ACR20 of >50% for CT-P13 is necessary for EMEA approval.

31 Dec	FY10		FY11F		FY12F		FY13F
Currency (KRW)	Actual	Old	New	Old	New	Old	New
Revenue (mn)	180,948		300,000		377,000		523,000
Reported net profit (mn)	108,372		146,100		177,800		250,450
Normalised net profit (mn)	108,372		146,100		177,800		250,450
Normalised EPS	979.3		1,259.6		1,532.9		2,159.3
Norm. EPS growth (%)	71.0		28.6		21.7		40.9
Norm. P/E (x)	33.9	N/A	26.3	N/A	21.6	N/A	15.3
EV/EBITDA	32.2	N/A	19.5	N/A	16.5	N/A	11.6
Price/book (x)	4.6	N/A	4.0	N/A	3.3	N/A	2.7
Dividend yield (%)	na	N/A	0.2	N/A	0.2	N/A	0.2
ROE (%)	20.3		17.3		18.0		21.0
Net debt/equity (%)	21.2		9.6		24.4		17.3

Source: Nomura estimates

Key company data: *See page 2 for company data, and detailed price/index chart.*
Rating: *See report end for details of Nomura's rating system.*

Anchor themes

We believe the entry of biosimilars will be a game-changing theme in pharmaceuticals over the next five years, and we think Celltrion is uniquely positioned to be the global leader.

Nomura vs consensus

Our target price is 7.5% above street estimates due to our expectation of greater revenues from emerging markets. Our developed market forecasts are below consensus.

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Key data on Celltrion Inc

Income statement (KRWmn)

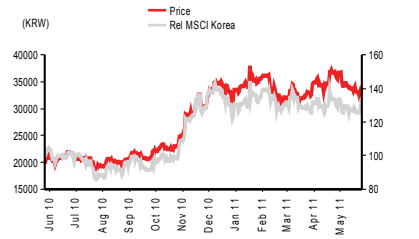
Year-end 31 Dec	FY09	FY10	FY11F	FY12F	FY13F
Revenue	**145,551**	**180,948**	**300,000**	**377,000**	**523,000**
Cost of goods sold	-51,592	-39,431	-56,000	-78,000	-100,000
Gross profit	**93,960**	**141,517**	**244,000**	**299,000**	**423,000**
SG&A	-22,207	-34,898	-71,300	-90,000	-121,000
Employee share expense	0	0	0	0	0
Operating profit	**71,752**	**106,619**	**172,700**	**209,000**	**302,000**
EBITDA	**84,857**	**125,246**	**201,900**	**250,300**	**352,000**
Depreciation	-10,375	-14,100	-18,300	-24,500	-26,300
Amortisation	-2,730	-4,527	-10,900	-16,800	-23,700
EBIT	71,752	106,619	172,700	209,000	302,000
Net interest expense	-1,940	4,911	-5,200	-5,500	-5,850
Associates & JCEs	-518	-297	-200	-200	-200
Other income	-2,889	-1,375	-1,300	-1,300	-1,300
Earnings before tax	**66,405**	**109,859**	**166,000**	**202,000**	**294,650**
Income tax	-7,917	-1,487	-19,900	-24,200	-44,200
Net profit after tax	**58,488**	**108,372**	**146,100**	**177,800**	**250,450**
Minority interests	0	0	0	0	0
Other items	0	0	0	0	0
Preferred dividends	0	0	0	0	0
Normalised NPAT	**58,488**	**108,372**	**146,100**	**177,800**	**250,450**
Extraordinary items	56	0	0	0	0
Reported NPAT	**58,544**	**108,372**	**146,100**	**177,800**	**250,450**
Dividends	0	0	-8,699	-8,700	-8,700
Transfer to reserves	**58,544**	**108,372**	**137,401**	**169,100**	**241,750**
Valuation and ratio analysis					
FD normalised P/E (x)	61.0	33.9	26.3	21.6	15.3
FD normalised P/E at price target (x)	91.9	51.1	39.6	32.5	23.1
Reported P/E (x)	57.9	33.9	26.4	21.7	15.4
Dividend yield (%)	na	na	0.2	0.2	0.2
Price/cashflow (x)	79.4	109.4	24.7	24.6	17.9
Price/book (x)	11.9	4.6	4.0	3.3	2.7
EV/EBITDA (x)	48.1	32.2	19.5	16.5	11.6
EV/EBIT (x)	56.9	37.8	22.9	19.7	13.5
Gross margin (%)	64.6	78.2	81.3	79.3	80.9
EBITDA margin (%)	58.3	69.2	67.3	66.4	67.3
EBIT margin (%)	49.3	58.9	57.6	55.4	57.7
Net margin (%)	40.2	59.9	48.7	47.2	47.9
Effective tax rate (%)	11.9	1.4	12.0	12.0	15.0
Dividend payout (%)	0.0	0.0	6.0	4.9	3.5
Capex to sales (%)	18.5	42.9	23.3	26.5	9.6
Capex to depreciation (x)	2.6	5.5	3.8	4.1	1.9
ROE (%)	23.2	20.3	17.3	18.0	21.0
ROA (pretax %)	13.7	12.8	14.7	15.6	19.5
Growth (%)					
Revenue	73.9	24.3	65.8	25.7	38.7
EBITDA	175.8	47.6	61.2	24.0	40.6
EBIT	133.2	48.6	62.0	21.0	44.5
Normalised EPS	6,933.3	71.0	28.6	21.7	40.9
Normalised FDEPS	-	80.1	29.0	21.7	40.9
Per share					
Reported EPS (KRW)	573.40	979.33	1,259.61	1,532.92	2,159.28
Norm EPS (KRW)	572.85	979.33	1,259.61	1,532.92	2,159.28
Fully diluted norm EPS (KRW)	543.83	979.33	1,262.88	1,536.89	2,164.87
Book value per share (KRW)	2,786.72	7,223.85	8,361.93	9,923.91	12,156.97
DPS (KRW)	0.00	0.00	80.35	80.36	80.36

Source: Nomura estimates

Notes

We believe volume increase will drive better margins as material costs for antibody production are small

Price and price relative chart (one year)



(%)	1M	3M	12M
Absolute (KRW)	-9.8	2.3	50.6
Absolute (USD)	-9.5	4.9	63.2
Relative to index	-8.4	-1.4	21.1
Market cap (USDmn)	3,550.5		
Estimated free float (%)	76.3		
52-week range (KRW)	39200/18500		
3-mth avg daily turnover (USDmn)	26.26		
Major shareholders (%)			
Ion Investments BV	0.1		
Celltrion Holding Co. Ltd.	0.1		

Cashflow (KRWmn)

Year-end 31 Dec	FY09	FY10	FY11F	FY12F	FY13F
EBITDA	84,857	125,246	201,900	250,300	352,000
Change in working capital	-151,406	-15,968	43,820	-169,066	-74,200
Other operating cashflow	111,502	-75,682	-90,329	74,600	-63,350
Cashflow from operations	**44,954**	**33,596**	**155,390**	**155,834**	**214,450**
Capital expenditure	-26,927	-77,613	-70,000	-100,000	-50,000
Free cashflow	**18,027**	**-44,017**	**85,390**	**55,834**	**164,450**
Reduction in investments	-3,712	-96,124	68,415	0	0
Net acquisitions					
Reduction in other LT assets	-1,115	-40,281	-14,424	-11,000	-11,000
Addition in other LT liabilities	-6,380	38,312	310	0	0
Adjustments	-19,331	-90,628	-95,701	-90,000	-110,000
Cashflow after investing acts	**-12,512**	**-232,739**	**43,990**	**-45,166**	**43,450**
Cash dividends	0	0	-8,699	-8,700	-8,700
Equity issue	3,186	210,413	0	0	
Debt issue	27,497	23,954			
Convertible debt issue					
Others	540	8,533	8,979	8,000	10,000
Cashflow from financial acts	**31,223**	**242,900**	**280**	**-700**	**1,300**
Net cashflow	**18,711**	**10,162**	**44,270**	**-45,866**	**44,750**
Beginning cash	302	19,013	29,175	73,446	27,580
Ending cash	19,014	29,175	73,446	27,580	72,330
Ending net debt	200,274	165,032	86,554	262,420	227,670

Source: Nomura estimates

Notes

Large capital expenditure expected in FY12F for a third facility to meet increasing demand

Balance sheet (KRWmn)

As at 31 Dec	FY09	FY10	FY11F	FY12F	FY13F
Cash & equivalents	19,013	29,175	73,446	27,580	72,330
Marketable securities	5,000	69,000	0	0	0
Accounts receivable	19,973	81,688	100,000	134,643	193,704
Inventories	17,361	21,748	18,700	26,000	33,300
Other current assets	25,599	64,276	54,616	60,739	68,578
Total current assets	**86,947**	**265,888**	**246,762**	**248,962**	**367,912**
LT investments	24,290	56,415	57,000	57,000	57,000
Fixed assets	367,863	640,799	696,700	778,400	803,900
Goodwill	0	0	0	0	1
Other intangible assets	69,308	141,283	230,400	313,600	409,900
Other LT assets	10,795	51,076	65,500	76,500	87,500
Total assets	**559,204**	**1,155,461**	**1,296,362**	**1,474,462**	**1,726,213**
Short-term debt	96,987	42,181	40,000	80,000	100,000
Accounts payable	1,480	1,577	2,000	3,000	3,000
Other current liabilities	41,285	129,999	179,000	57,000	57,000
Total current liabilities	**139,752**	**173,757**	**221,000**	**140,000**	**160,000**
Long-term debt	122,301	152,027	120,000	210,000	200,000
Convertible debt	0	0	0	0	0
Other LT liabilities	11,478	49,790	50,100	50,100	50,100
Total liabilities	**273,532**	**375,574**	**391,100**	**400,100**	**410,100**
Minority interest	0	0	0	0	0
Preferred stock	0	0	0	0	0
Common stock	53,980	57,994	58,000	58,000	58,000
Retained earnings	64,757	173,130	301,600	470,700	712,450
Proposed dividends	0	0	0	0	1
Other equity and reserves	166,935	548,764	545,662	545,662	545,662
Total shareholders' equity	**285,672**	**779,887**	**905,262**	**1,074,362**	**1,316,113**
Total equity & liabilities	**559,204**	**1,155,461**	**1,296,362**	**1,474,462**	**1,726,213**
Liquidity (x)					
Current ratio	0.62	1.53	1.12	1.78	2.30
Interest cover	37.0	na	33.2	38.0	51.6
Leverage					
Net debt/EBITDA (x)	2.36	1.32	0.43	1.05	0.65
Net debt/equity (%)	70.1	21.2	9.6	24.4	17.3
Activity (days)					
Days receivable	49.2	102.5	110.5	113.9	114.6
Days inventory	149.3	181.0	131.8	104.9	108.2
Days payable	15.6	14.1	11.7	11.7	11.0
Cash cycle	182.9	269.4	230.7	207.0	211.8

Source: Nomura estimates

Notes

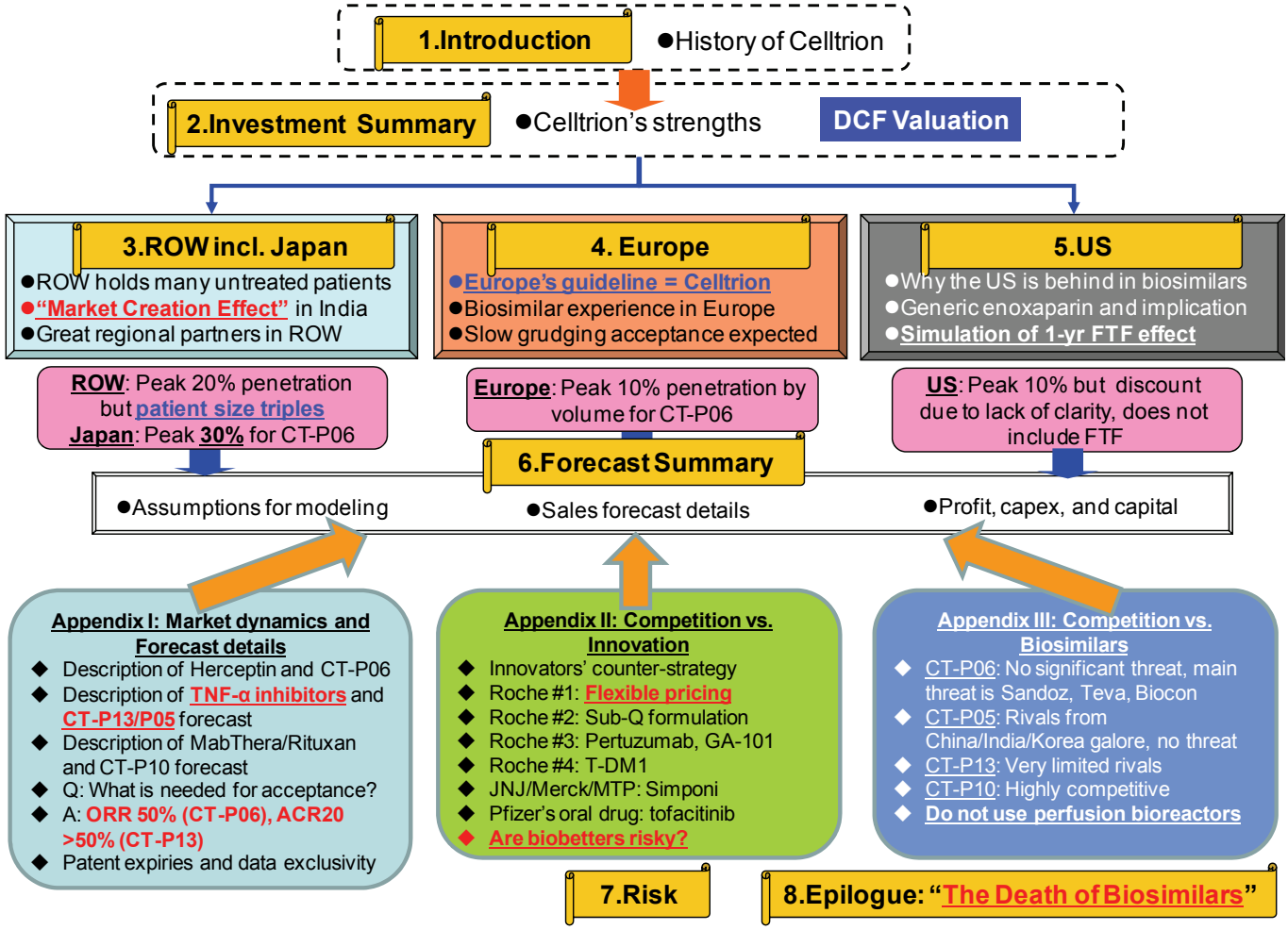
Long lead times at present due to validation batches that require 1+ years for cash generation; commercial batches have a much shorter lead time (<1 year)

Introduction

Logical Flow Diagram

The figure below is meant as a guide to the structure of this report. We introduce Celltrion in the Introduction section, and a brief synopsis of strengths, forecasts and valuation follows in the Investment Summary section. This is followed by detailed discussion of sales divided into three regions: ROW including Japan, Europe and US. Forecast summary gives a more detailed discussion of sales, profit and capital. Appendix I is a detailed look at patent expiries, data exclusivities, launch timings, and forecasts by region. Appendix II is a discussion of counter-strategies by innovative companies. Appendix III is a discussion of other biosimilar companies.

Fig. 11: Logical Flow Diagram



Source: Nomura

History

Celltrion was founded as a joint venture with an ex-subsidiary of Genentech

Celltrion was founded in February 2002 as a joint venture comprising four companies: VaxGen (which has subsequently merged with DiaDexus), Korea Tobacco & Ginseng, and venture capital companies Nexol and J. Stephen & Co. Ventures. VaxGen is a bioventure that listed in July 1999, and was formerly GenenVax, a company spun off by Genentech. Total investment in Celltrion was reported to be more than USD120mn, with VaxGen agreeing to provide Celltrion with mammalian cell culture-based manufacturing technologies. At the time of Celltrion's founding, VaxGen held a 48% share, Nexol 13% and KT&G 13%.

Fig. 12: Celltrion History

Date	History
Feb-02	Celltrion established as joint venture between Korean investors an VaxGen, as a manufacturing facility for AIDSVAX
Jun-05	Signing of contract manufacturing agreement with Bristol-Myers Squibb for Abatacept (Orencia)
Jul-06	Commissioning of first production facility, with 50,000L of cell culture production capacity
Dec-07	Signing of contract manufacturing agreement with Australia's CSL for an antibody therapy for leukemia in clinical trials
Sep-08	Signing of contract with Sanofi-Aventis for process development and commercial production of biologics under development by Sanofi
Aug-09	Completion of sales network in emerging markets
Sep-09	IND approval on CT-P06 by KFDA
Oct-09	Signing of co-exclusive sales agreement with Hospira, covering the US, Canada, Europe, Australia, and New Zealand
Dec-09	First CTA approval in Europe (in Latvia) on CT-P06
Mar-10	First Asian IND approval on CT-P13 (Philippines)
Jul-10	IND approval complete for CT-P06 (Asia ex-Japan & Europe)

Source: Celltrion presentation

Celltrion trained by Genentech

Celltrion was originally established as a contract manufacturer for VaxGen's AIDS vaccine, AIDSVAX, for which positive Phase 3 trial results were anticipated. Celltrion employees received training at VaxGen's US facilities, and the technology used by Celltrion was originally developed by Genentech.

The AIDSVAX failure and its aftermath

Results on Phase 3 clinical trials for AIDSVAX were announced on 24 February 2003. VaxGen fell into a prolonged slump when it was revealed that AIDSVAX did not show a statistically significant reduction of HIV infection. In 2006, it became evident that VaxGen had also failed in development of the only remaining product in its pipeline: anthrax vaccine. At this point, VaxGen sold its stake in Celltrion to Nexol.

Targeting innovation from the beginning: three phases of growth

Although originally established as a vaccine production facility for VaxGen, Celltrion, in our view, has from the outset had new drug development in its sights. The company's business plan calls for establishing a financial foundation in Phase 1 through work as a CMO for protein drugs, and expanding to include biosimilar development in Phase 2, with the goal of funding development of new biologics from 2015 onwards. It is important to keep in mind that the ultimate goal of Celltrion is not biosimilars, but innovation. From very early on, Celltrion was committed to the future of biosimiars – a remarkable view when we consider that this was formulated in the early 2000s.

Early focus on biosimilars

Celltrion began developing an erythropoietin biosimilar very early in 2003. This was successfully developed in 2005. The drug was not commercialized, however, because of the extent of the competition already in Europe. Celltrion then switched instead to developing biosimilars for antibody therapeutics.

Listing through merger with Orchem

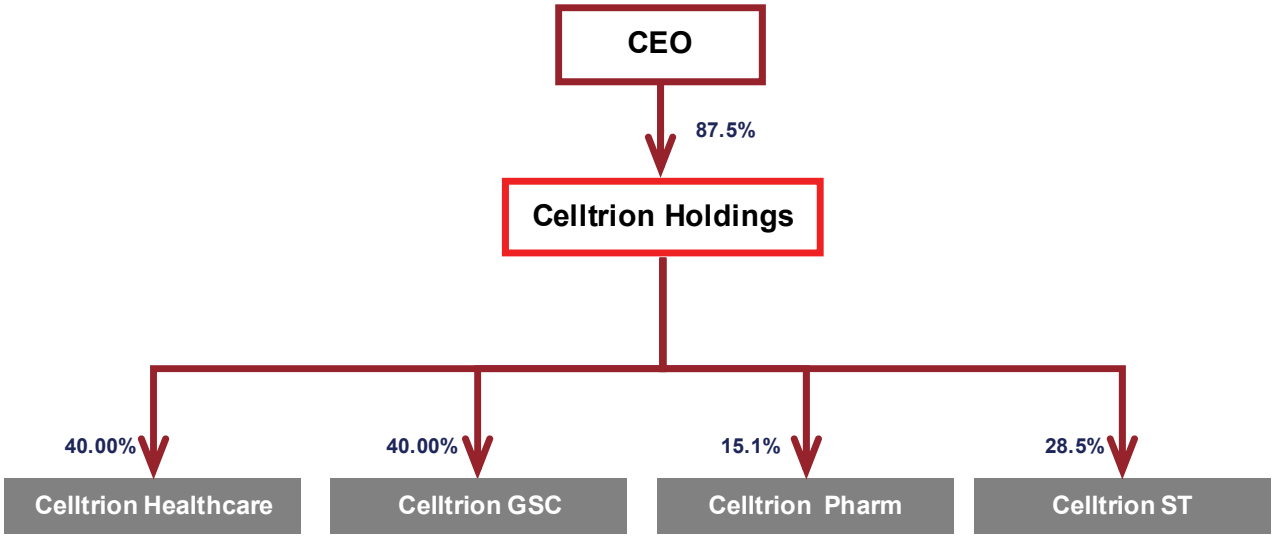
In May 2008, Celltrion was listed on the Kosdaq through a merger with Orchem, a chemicals company. Celltrion had initially planned for public listing in late 2007 but the plan had to be put on hold in light of the sub-prime financial crisis. Around the same time, the Korean stock exchange revised IPO regulations. According to the revised listing guidelines, companies were required to have three years of consecutive revenues of KRW 20bn or more in order to get listed. Celltrion was unable to meet the revised criteria and therefore had to take the alternate route of a "backdoor listing". Orchem was later spun-off from Celltrion in December 2009.

Current shareholder structure

Celltrion group transferred to a holding company model in November 2010. Celltrion Holdings now holds 28.5% of Celltrion, 40% of Celltrion Healthcare, 15.1% of Celltrion Pharmaceutical, among others. Celltrion Healthcare handles Celltrion's sales to various marketing partners around the world. Celltrion Pharmaceutical is responsible for sales

within Korea. Both of these companies are affiliate companies of Celltrion and are not subsidiaries.

Fig. 13: Current Ownership Structure of the Celltrion Group



Source: DART Filings

Investment Summary

Global leader in biosimilars: FY11-15F CAGR EPS growth of 35%
We believe that Celltrion is on its way to becoming the global leader in biosimilars. Sales growth will begin in FY12F, we forecast, upon launch of CT-P06 (biosimilar Herceptin) and CT-P13 (biosimilar Remicade) in ROW countries where the sales potential is the greatest, in our view. Unlike the developed markets, reducing prices in the ROW region tends to increase the number of users, sometimes very significantly as seen in India with the case of Reditux and Grafeel [source: Dr. Reddy's]. In our view, this "market creation effect" will be the most significant driver of Celltrion's biosimilar growth, rather than the slow, small stream of revenues forecast for Europe/Japan. FY11 sales are already determined by the master service agreement released in January to be near KRW300bn. We forecast 26% y-y growth in FY12F, amid the launch of biosimilars in ROW and validation batch sales of CT-P10 (Rituxan) and CT-P05 (Enbrel). Even though FY13F is scheduled to see the launch of CT-P06 and CT-P10 in Eastern Europe, and FY14F is scheduled to see approvals in Europe/Japan, we believe that the principal driver over those years as well will be ROW sales. Our forecast suggests more than KRW900bn in FY15F on the back of strong biosimilar sales.

Quality: Early consultations with EMEA has led to world-class quality
Celltrion's foremost strength, in our view, is its world-class quality. The single-most important distinguishing feature of Celltrion is that they have consulted the European Medicines Agency (EMEA) for the development of biosimilars as far back as 2006. By working with the world's pioneering biosimilar regulatory authority, Celltrion learned from the Chemistry, Manufacturing and Controls (CMC) level standards that are required for European acceptance. Celltrion is distinct from all other Korean biopharmaceutical companies, we believe, because it is the only Korean company to have an Investigational New Drug (IND) approval from the EMEA for conducting clinical trials of biosimilars.

Speed: Strategic focus to market biosimilars in ROW first, first-mover
In our view, the go-to-market strategy of Celltrion also distinguishes the company not just from the Korean competitors, but also from global rivals such as Sandoz and Teva. Although other companies have been fixated on the prospects of the EU/US market, Celltrion recognized the tremendous potential of biosimilars in ROW. This fuelled Celltrion's development of CT-P06, biosimilar Herceptin (trastuzumab) and CT-P13, biosimilar Remicade (infliximab), both of which are patent-protected in the US until 2018-19, while all other companies have focused on rituximab, which expires in the US in 2015. Thus, we believe that Celltrion has a three to five year advantage in these two drugs over other global competitors. Additionally, when biosimilars are launched in emerging markets, Celltrion should also have a significant advantage over its competitors, we believe, due to its world-class quality – a significant factor even in ROW. While most competitors largely rely on clinical data collected domestically, Celltrion's global clinical data and European approval provide a competitive advantage.

Focus: Relying on regional giants is better, in our view
We also believe that the Celltrion's global marketing network, built on the partnerships it has formed, will actually prove advantageous over rivals relying on their own networks (eg, Sandoz, Teva). Antibodies are injectables in very specialized therapeutic areas such as rheumatology and oncology. In developed countries, specialized companies that cater to this specific segment can often be just as strong – or even stronger than – large multinationals (eg, Nippon Kayaku in Japan). In emerging market countries, regional giants (eg, Hikma in the Middle East, EGIS in Eastern Europe) have home ground advantage and brand recognition.

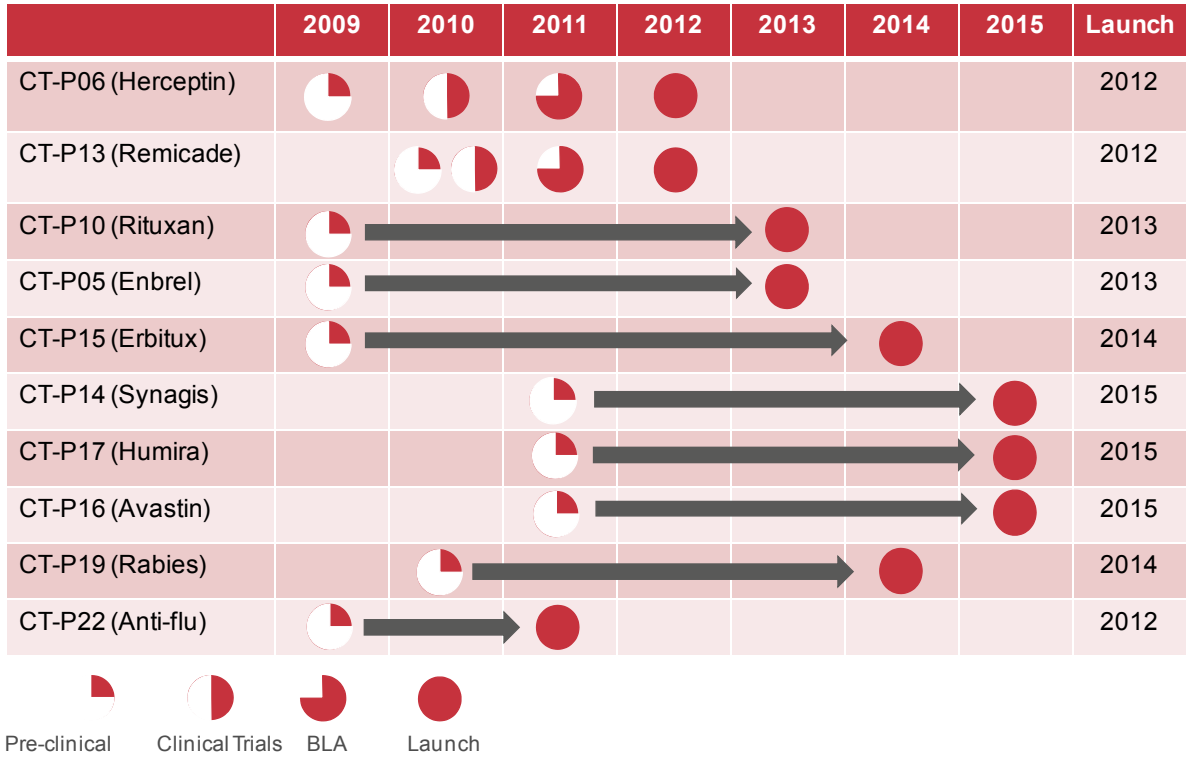
Experience: Solid track record in making antibodies
Celltrion's track record of producing antibody therapeutics is another advantage. As a CMO, Celltrion has experience supplying biopharmaceuticals for innovators such as Bristol-Myers Squibb, Sanofi Aventis and CSL. Celltrion started supplying Abatacept (Orencia) to Bristol-Myers Squibb in 2005 and received the FDA's supplemental Biologics License Application (sBLA) approval in 2007. In October 2010, Celltrion signed another contract with Sanofi Aventis worth KRW18bn for developing and supplying

biopharmaceuticals. All these achievements, in our view, highlight Celltrion's ability of producing global quality pharmaceuticals as core strength.

Capacity: US/Europe/Japan will not allow clinical trials without capacity

Lastly, we see Celltrion's large capacity as an important advantage. Celltrion's first facility was fully operational from mid-2006, and in December 2007, it was recognized as cGMP-compliant by the FDA. At present, its production capacity is 50,000L. Validation of an additional 90,000L of production capacity will be completed by 2H12. The advantage of having a large capacity is that process validation for commercial production is possible from the IND/NDA stage. This is a crucial distinction, given that EMEA/FDA/PMDA are extremely reluctant to allow clinical trials of biosimilars on a small-scale production level. For typical innovative biopharmaceuticals at the IND/NDA stage, products are commonly prepared on production lines of a few hundred litres capacity, then subsequently ramping up to commercial-level production capacity when the drug is approved. This involves substantial changes to production processes, which could result in varying quality. Therefore, most developed world regulators will not permit clinical trials for small-scale capacity due to quality concerns. However, as Celltrion already has sufficient capacity for commercial production when filing for regulatory approval, it has no need for scale-up.

Fig. 14: Celltrion's Biosimilar pipeline



Source: Celltrion presentation

Pipeline: Among the strongest biosimilar pipelines worldwide

Celltrion's biosimilar pipeline includes Herceptin (trastuzumab), Remicade (infliximab), Erbitux (cetuximab), and Synagis (palivizumab) − four products for which no patent is registered in Korea or indeed in many emerging markets. Outside Japan, New Zealand, Western Europe, the US and Canada, these drugs have no patent protection. Being based in Korea, Celltrion has been able to develop Herceptin and Remicade biosimilars with no fear of patent infringement. As such, we note its advantage over biosimilar manufacturers based in Europe and the US.

Celltrion's pipeline of antibody biosimilars is the richest of any biosimilar developer in the world. At this stage, the products furthest along in development are CT-P06 (Herceptin) and CT-P13 Remicade). CT-P06 is now the subject of global clinical trials, following IND approval from authorities in Europe and several emerging markets. Celltrion aims to

conclude clinical studies on CT-P06 by 1H11, with a view to launching in emerging markets by year-end, according to management. The company is now seeking IND approval for CT-P13, and as with CT-P06, is aiming for an emerging market launch by end-FY11.

Peer comparison

In our opinion, Celltrion is the only biosimilar manufacturing company with the necessary quality, production capacity and pipeline to supply biosimilars products globally and, hence, it does not have a proper peer in Korea or in the world – only Green Cross and LG Life Sciences have either signed a sizeable supply contract with US/European companies or had biosimilars accepted by the EMEA, on our understanding. We believe that Celltrion should command a premium above these companies because LG Life Sciences' main product is a human growth hormone biosimilar which has limited market potential, and Green Cross sells vaccines/plasma derivatives which are not usually classified as biosimilars. We also note that Celltrion has not yet generated sales of commercial batches of biosimilars; its FY10 sales shown in the table below is due entirely to validation batches supplied to the emerging world. We believe the company's high valuation is warranted due to: 1) its distinct positioning in the biosimilar market and 2) extremely high EPS growth of a 35% CAGR over FY11-FY15.

Fig. 15: Peer Comparison

Company	Ticker	Price (Local)	Market Cap (USD)	Nomura Rating	FY10 Sales (USD)	Price / EPS Adjusted			EV / EBITDA			Return on Equity		EPS CAGR Growth %
						FY10	FY11E	FY12E	FY10	FY11E	FY12E	FY10	FY11E	FY11-15E
Celltrion	068270 KS	33,950	3,621	BUY	157	32.4	25.3	20.8	33.2	20.5	16.2	12.8	12.2	35.0
Biosimilars														
Teva	TEVA US	49.4	46,396	Not-Rated	16,121	10.8	9.7	8.7	9.1	8.5	7.5	18.9	17.8	5.6
Dr. Reddy's	DRRD IN	1,544	5,754	BUY	1,640	23.8	19.1	16.8	16.7	13.0	11.2	13.6	15.9	7.7
Biocon	BIOS IN	332	1,463	Not-Rated	608	19.7	17.5	14.5	12.2	10.8	9.2	12.0	11.9	7.0
Innovators														
Abbott	ABT US	53.0	82,330	Not-Rated	35,166	13.0	11.7	10.9	9.1	8.7	7.9	26.7	30.4	8.5
Amgen	AMGN US	59.8	55,635	Not-Rated	15,053	11.7	11.6	10.7	7.2	7.8	7.6	19.0	18.3	8.9
Biogen Idec	BIIB US	93.7	22,634	Not-Rated	4,716	19.4	16.3	15.5	17.1	9.9	9.7	16.7	20.8	10.5
JNJ	JNJ US	66.3	181,710	Not-Rated	61,587	14.0	13.4	12.6	8.8	8.4	8.0	23.8	21.9	7.7
Merck	MRK US	36.7	113,247	Not-Rated	45,987	11.1	10.0	9.7	6.6	6.5	6.7	17.7	20.4	4.1
Novartis	NOVN VX	53.9	128,792	BUY	50,624	10.8	9.7	9.2	6.8	6.3	6.2	18.5	19.1	3.0
Roche	ROG VX	147.7	112,085	NEUTRAL	45,672	10.5	10.0	9.9	8.3	7.5	7.5	103.0	91.0	2.9
Korean Biopharmaceuticals														
Green Cross	006280 KS	136,500	1,235	Not-Rated	684	11.0	16.3	13.2	7.5	10.5	8.8	27.9	15.4	19.6
LG Life Sciences	068870 KS	44,000	670	Not-Rated	289	39.5	34.5	27.0	17.3	16.9	14.6	6.0	6.8	19.4

Note: FY11, FY12E and FY13E figures for Dr. Reddy's and Biocon. Consensus estimates used for 'Not Rated' companies
Source: Nomura, Bloomberg, Prices as of 25 May 2011

Valuation

Our DCF valuation suggests a target price of KRW50,000

Our target price of KRW50,000 is calculated using a DCF valuation that extends to FY20F. We assume a market risk premium of 8%, a risk-free rate of 3.5% and a beta of 0.9. The beta is considerably higher than that of peers in the Korean pharmaceutical sector (0.4-0.7) to reflect greater uncertainties concerning regulatory approval of biosimilars. We have calculated a WACC of 8.7% and a terminal growth rate of 1.8%. We discount cashflows back to 2011.

Fig. 16: DCF Valuation

Fiscal Year	Sales	OP	EBT	Depreciation	Capex	Working Capital	Other Adjust.	FCF	Discount Rate	Present Value	Per Share Value
FY	(mn KRW)	(mn KRW)	(mn KRW)	(mn KRW)	(mn KRW)	(mn KRW)	(mn KRW)	(mn KRW)		(mn KRW)	(KRW)
2011	300,000	172,700	166,000	14,100	70,000	71,041		61,500	1.09	56,571	511
2012	377,000	209,000	202,000	18,300	100,000	50,943		-39,350	1.18	-33,295	-301
2013	523,000	302,000	294,650	24,500	50,000	76,361		50,200	1.28	39,071	353
2014	654,000	379,300	371,600	26,300	50,000	87,596		107,700	1.40	77,104	697
2015	927,800	598,400	579,500	28,000	75,000	127,820		217,800	1.52	143,429	1,296
2016	1,208,100	781,700	762,800	31,400	80,000	145,820		347,800	1.65	210,681	1,904
2017	936,600	503,500	491,600	34,900	80,000	-101,900		373,900	1.79	208,337	1,883
2018	1,064,000	584,500	572,600	38,100	100,000	69,960		241,800	1.95	123,932	1,120
2019	1,159,900	638,800	633,900	42,600	100,000	54,960		309,400	2.12	145,869	1,318
2020	1,279,900	732,900	728,000	46,700	100,000	62,700		389,100	2.31	168,741	1,525
Terminal Value	1,279,900	732,900	728,000	46,700	80,000	62,700		10,529,913	2.31	4,566,511	41,267
FCF Present Value										5,706,953	51,572
(Adjustments)											
+Short term investments (easily turned into cash										89,661	810
+Cash										29,175	264
+Other										0	0
=Enterprise Value										5,825,789	52,646
-Interest bearing debt										274,997	2,646
=Enterprise Value-Debt										**5,550,792**	**50,000**

(Assumptions)			
Diluted Shares	110,659.0 Million	Risk Free Rate	3.50 %
Tax rate	12-20 %	Risk Premium	8.00 %
Terminal Growth Rate	1.8 %	Beta	0.90
		Cost of Equity	10.70 %
		WACC	8.71 %

Source: Nomura estimates

Fig. 17: Celltrion's Income Statement and Balance Sheet in KRW mn

Income Statement	FY 08	FY 09	FY10	FY11E	FY12E	FY13E	FY14E	FY15E
Sales Revenue	83,690	145,551	180,948	300,000	377,000	523,000	654,000	927,800
Costs of Goods and Services Sold	36,138	51,592	39,431	56,000	78,000	100,000	135,000	160,000
Gross Profit or Loss	47,552	93,960	141,517	244,000	299,000	423,000	519,000	767,800
Selling and Administrative Expenses	16,780	22,207	34,898	71,300	90,000	121,000	139,700	169,400
Salary	3,479	4,137	8,650	11,500	16,100	22,700	26,800	32,100
Retirement Costs	0	138	530	1,000	1,300	1,500	1,700	1,900
Benefits	0	1,018	787	1,000	1,300	1,500	1,700	1,900
Depreciation	0	286	249	300	300	300	300	300
R&D Costs	3,308	5,762	16,141	30,000	40,000	50,000	50,000	60,000
Amortization	2,486	2,483	2,472	6,000	9,200	12,900	16,800	20,800
Advertisement Cost	251	1,170	390	21,500	21,800	32,100	42,400	52,400
Others	7,256	7,213	5,679	0	0	0	0	0
Operating Income or Loss	30,772	71,752	106,619	172,700	209,000	302,000	379,300	598,400
Non-Operating Revenues	27,666	5,074	7,638	5,300	5,300	5,300	5,300	5,300
Interest Income	346	525	5,981	5,000	5,000	5,000	5,000	5,000
Other	27,320	4,549	1,658	300	300	300	300	300
Non-Operating Expenses	40,821	10,421	4,399	12,000	12,300	12,650	13,000	24,200
Interest Expenses	6,622	2,464	1,070	10,200	10,500	10,850	11,200	22,400
Other Non-Operating Expenses	34,199	7,957	3,330	1,800	1,800	1,800	1,800	1,800
Earnings Before Income Tax	17,616	66,405	109,858	166,000	202,000	294,650	371,600	579,500
Income Tax	2,576	7,917	1,487	19,900	24,200	44,200	55,700	98,500
Ongoing Business Income	15,040	58,488	108,372	146,100	177,800	250,450	315,900	481,000
Discontinued Operations Income or Loss	-469	56	0	0	0	0	0	0
Net Income or Loss	14,571	58,544	108,372	146,100	177,800	250,450	315,900	481,000
Capital Expenditure	0	0	60,000	70,000	100,000	50,000	50,000	75,000
R&D	0	0	80,141	130,000	140,000	170,000	180,000	200,000
EBITDA	30,772	84,840	121,521	197,700	244,100	350,200	436,400	664,500
EBITDA+R&D	30,772	84,840	201,662	327,700	384,100	520,200	616,400	864,500
Cash income	14,571	68,902	118,747	160,200	196,100	274,950	342,200	509,000
No. of shares (mn)	-5	-5	0	0	0	0	0	0
Shares out (mn)	107	103	116	116	116	116	116	116
EPS (KRW)	148	573	979	1,260	1,533	2,159	2,724	4,147
Cash EPS (KRW)	0	1	1	1	2	2	3	4
BPS (KRW)	0	0	0	0	0	0	0	0
Dividends (KRW)	0	0	75	75	75	75	75	75
Aggregate dividend value	0	0	0	8,699	17,399	26,099	34,799	43,499
Payout ratio (%)	0	0	8	6	5	3	3	2
% y-y								
Sales	24	43	20	40	20	28	20	30
COGS	12	43	-24	42	39	28	35	19
Gross profits	53	98	51	72	23	41	23	48
SG&A expenses	-2	32	57	104	26	34	15	21
R&D expenses	-28	74	180	86	33	25	0	20
Personnel expenses	47	52	88	35	39	37	18	19
Advertisingexpenses	53	4	-1	54	0	0	0	0
Other SG&A expenses	0	0	0	0	0	0	0	0
Goodwill amortizationexpenses	-1	0	0	143	53	40	30	24
Operating profits	121	133	49	62	21	44	26	58
Recurring profits	-36	277	65	51	22	46	26	56
Pretax profits	-36	277	65	51	22	46	26	56
Net profits	-65	302	85	35	22	41	26	52
EBITA	-36	292	65	55	24	45	26	53
As % of sales								
Gross profits	57	65	78	81	79	81	79	83
SG&A expenses	20	15	19	24	24	23	21	18
R&D expenses	4	4	9	10	11	10	8	6
Personnel expenses	4	3	5	4	4	4	4	3
Advertisingexpenses	0	1	0	7	6	6	6	6
Other SG&A expenses	0	1	1	1	1	1	1	0
Goodwill amortizationexpenses	3	2	1	2	2	2	3	2
Operating profits	37	49	59	58	55	58	58	64
Recurring profits	21	46	61	55	54	56	57	62
Pretax profits	21	46	61	55	54	56	57	62
Net profits	17	40	60	49	47	48	48	52
Effective tax rate (%)	17	12	1	12	12	15	15	17

Balance Sheet	FY 08	FY 09	FY 10	FY 11E	FY 12E	FY 13E	FY 14E	FY 15E
Total Assets	499,264	559,204	1,155,461	1,296,362	1,474,462	1,726,212	2,045,412	2,517,712
Current Assets	77,565	86,947	265,888	246,762	248,962	367,912	553,212	865,612
Quick Assets	52,732	69,585	244,139	228,062	222,962	334,612	508,212	812,312
Cash and CashEquivalents	302	19,013	29,175	73,470	27,600	72,400	173,500	373,100
Marketable Securities	3,890	5,000	89,661	21,000	21,000	21,000	21,000	21,000
Trade Receivable	19,268	19,973	81,688	100,000	134,643	193,704	261,600	371,120
Advance Payments	695	2,206	8,217	10,200	12,200	14,200	16,200	18,200
Others	28,576	23,393	35,398	23,392	27,519	33,309	35,912	28,892
Inventories	24,834	17,361	21,748	18,700	26,000	33,300	45,000	53,300
Fixed Assets	421,699	472,257	889,573	1,049,600	1,225,500	1,358,300	1,492,200	1,652,100
Investment Assets	21,781	24,290	56,415	57,000	57,000	57,000	57,000	57,000
Long-term Loans	0	1,464	23,119	23,000	23,000	23,000	23,000	23,000
Long-term Investment in Securities	20,651	20,726	27,763	28,000	28,000	28,000	28,000	28,000
Other	1,129	2,101	5,532	6,000	6,000	6,000	6,000	6,000
Property, Plant and Equipment	350,990	367,863	640,799	696,700	778,400	803,900	827,600	874,600
Intangible Assets	39,248	69,308	141,283	230,400	313,600	409,900	509,100	611,000
Other Fixed Assets	9,680	10,795	51,076	65,500	76,500	87,500	98,500	109,500
Total Liabilities	279,547	273,531	375,574	391,100	400,100	410,100	422,100	422,100
Current Liabilities	220,344	139,752	173,756	221,000	140,000	160,000	172,000	172,000
Trade Payable	2,933	1,480	1,577	2,000	3,000	3,000	5,000	5,000
Short-term Borrowings	15,641	96,987	42,181	40,000	80,000	100,000	120,000	120,000
Current Portion of Long Term Debt	174,948	28,538	80,789	132,000	10,000	10,000	0	0
Other Payables	26,822	12,826	49,210	47,000	47,000	47,000	47,000	47,000
Fixed Liabilities	59,203	133,779	201,817	170,100	260,100	250,100	250,100	250,100
Long-term Borrowings	20,000	122,301	152,027	120,000	210,000	200,000	200,000	200,000
Other	39,258	9,597	1,059	1,100	1,100	1,100	1,100	1,100
Total Stockholders Equity	219,717	285,672	779,887	905,262	1,074,362	1,316,112	1,623,312	2,095,612
Capital Stock	53,325	53,980	57,994	58,000	58,000	58,000	58,000	58,000
Capital Surplus	185,313	190,142	390,189	390,000	390,000	390,000	390,000	390,000
Retained Earnings or Accumulated Deficit	6,213	64,757	173,130	301,600	470,700	712,450	1,019,650	1,491,950
Capital Adjustments	-24,089	-24,117	-2,759	-4,738	-4,738	-4,738	-4,738	-4,738
Accumulated Other Comprehensive Income	-1,046	910	161,333	160,400	160,400	160,400	160,400	160,400
Total Liabilities and Stockholders Equity	499,264	559,204	1,155,461	1,296,362	1,474,462	1,726,212	2,045,412	2,517,712

Accounts receivable turnover	4	7	2	3	3	3	3	3
Inventory turnover ratio Cost of sales	1	3	2	3	3	3	3	3
Cost of sales turnover payable	12	35	25	30	30	30	30	30
Change in Working Capital	6,391	-5,315	66,005	71,041	50,943	76,361	87,596	127,820
Interest bearing debt	231,989	247,826	274,997	292,000	300,000	310,000	320,000	320,000
ROA	3	10	9	11	12	15	15	19
ROIC	9	11	9	13	12	15	15	19
ROE	7	20	14	16	17	19	19	23
D / E Ratio	1	1	0	0	0	0	0	0
Fixed asset ratio	7	4	4	6	5	5	6	7
Current ratio	0	1	2	1	2	2	3	5

Source: Company data, Nomura estimates

Fig. 18: Celltrion's Cash Flow Statement in KRW mn

Cash Flow Statement	FY 08	FY 09	FY 10	FY 11E	FY 12E	FY 13E	FY 14E	FY 15E
Cash Flows from Operating Activities	47,238	44,954	33,596	155,390	155,834	214,450	280,763	424,269
Net Income	14,571	58,544	108,372	146,100	177,800	250,450	315,900	481,000
Depreciation	9,171	9,387	9,437	14,100	18,300	24,500	26,300	28,000
Amortization of Intangible Assets	2,680	2,654	4,432	10,900	16,800	23,700	30,800	38,100
Interest Expenses	41	80	25	10,200	10,500	10,850	11,200	22,400
Interest Revenues	0	0	-1,620	-5,000	-5,000	-5,000	-5,000	-5,000
Decrease or Increase in Trade Receivables	7,054	-704	-55,115	-18,300	-34,600	-59,100	-67,900	-109,500
Decrease or Increase in Inventories	-4,066	-6,773	-21,017	3,000	-7,300	-7,300	-11,700	-8,300
Taxes	3,440	3,909	-3,665	14,100	-5,000	-5,000	-1,000	-1,000
Other	14,348	-21,974	-7,252	-19,710	-15,666	-18,650	-17,837	-21,431
Cash Flows from Investing Activities	-76,916	-57,466	-266,334	-101,400	-201,000	-171,000	-181,000	-216,000
Purchase of Property, Plant and Equipment	-57,397	-26,659	-77,613	-70,000	-100,000	-50,000	-50,000	-75,000
Purchase of Intangible Assets	-3,782	-20,438	-63,776	-100,000	-100,000	-120,000	-130,000	-140,000
Other	-15,738	-12,369	-124,945	68,600	-1,000	-1,000	-1,000	-1,000
Cashflows from Financing Activities	19,083	31,223	242,900	-9,720	-700	1,300	1,300	-8,700
Change in Borrowings	-10,288	27,497	23,954	17,000	8,000	10,000	10,000	0
Issuance of Common Stock	35,649	3,186	210,413	0	0	0	0	0
New Stock Issuance Cost	-354	-10	-1,928	0	0	0	0	0
Purchase of Treasury Stock	29,368	0	-29,368	10,000	0	0	0	0
Other	-2,052	551	10,460	0	0	0	0	0
Increase in Cash and Cash Equivalents	-10,595	18,711	10,162	44,270	-45,866	44,750	101,063	199,569
Cash and Cash Equivalent at Beginning	10,898	302	19,013	29,200	73,470	27,600	72,400	173,500
Cash and Cash Equivalent at End	302	19,013	29,200	73,470	27,600	72,400	173,500	373,100

Source: Company data, Nomura estimates

Forecast: ROW including Japan

ROW: The most important region for biosimilar sales

Biosimilars: Access to medicine far more important than lowering costs

In our view, biosimilar expansion is not a story of cost but one of access. Despite industry discussion mainly being focused on rising fiscal costs in the developed world, we believe that ultimately the ROW region is the largest and most important market for biosimilars. Whereas biosimilar penetration in Europe and the US is a zero-sum game − ie, what the generics company gains, the innovator loses − we see the ROW region having an entirely different dynamic. Because price sensitivity in these regions is much higher than in the developed world, as evidenced by Dr. Reddy's Reditux, price cuts are accompanied by a large volume increase. Coupled with high rates of economic growth, we think this "market creation effect" could well drive Celltrion's sales in the future. In this section, we first describe insurance systems and health care expenditure in the emerging world, followed by an analysis of the "market creation effect" as seen by Biocon/Dr. Reddy's in India as well as some other companies. From our conclusions, we apply similar variables to our forecast for Celltrion's ROW sales.

Fig. 19: Health Insurance Systems of Emerging Market Countries

Russia	Mandatory Health Insurance (OMS): Covers entire population, premiums for active population paid by companies and institutions, non-active population paid by govts, pays for services at government hospitals but usually not private clinics
	Voluntary Health Insurance (DMS): additional insurance, mostly funded by companies and purchased for employees, mostly for services at private clinics
	Outpatient drugs are not reimbursed, some very expensive drugs (i.e. Herceptin/Rituxan) are reimbursed by govt
Turkey	SSK: Main insurance for private sector and blue-collar public sector, co-payments around 10-20%, largest insurance system
	Bag-Kur: Social insurance for self-employed, co-payment of 10-20%
	GERF: Pension system that also provides health insurance for retired civil servants
Brazil	Sistema Único de Saúde (SUS): Provides coverage for 75% of the population, remaining 25% covered by the Supplementary System, access to essential medicine guaranteed but out of pocket spending on drugs remains very high
Argentina	Public Sector: Main insurance system, government funded health care, outpatients pay for medicine
	Obras Sociales: Administered by trade unions and organized by professions, highly fragmented
	Private Sector: Voluntary insurance plans
India	ESIS (Employees' State Insurance): Covers employees earning under 6,500 Rupees per month, limited enrollment
	CGHS (Central Government Health Scheme): all employees of central government are covered, Rituxan/Herceptin/Remicade is on the CGHS Life Saving Drug List
	Private Health Insurance: For urban private sector employees
Indonesia	There are three main components of social insurance in Indonesia: Civil Servant Social Health Insurance Scheme (Askes), Private Employee Social Health Insurance Scheme (Jamsostek) and Commercial Health Insurance (JPKM). Large portions of the population of the country are not covered by any form of insurance.
Saudi Arabia	The Ministry of Health is the biggest provider of health care, (providing more than 60% of health services, the rest provided by other governmental and non-governmental sectors). Saudi Arabia is a welfare state and health care financing is provided mainly from government revenues.

Source: WHO

Quality comes first … especially in ROW

Patient safety and drug efficacy are among the most important factors for doctors in the ROW, as they are in the developed world. In our view, Celltrion's major advantage over biosimilar competitors from unregulated countries is the mark of approval from global regulators such as the EMEA, PMDA or the US FDA. We believe this is a significant mark of distinction, especially in the ROW where counterfeits and low-quality products abound. According to our interviews with oncologists in India with whom we spoke, the

cost benefits of using biosimilars are evaluated in light of the risks that they may pose to patients; therefore extensive clinical data is necessary. Many oncologists we spoke with also predict patient population using biologics would expand by at least 2x if prices were halved.

Emerging markets currently do not reimburse for high-priced biologics

Our first assumption is that the majority of patients in the ROW are not given access to antibodies. Price sensitivity is accordingly much higher compared with developed countries. Health insurance systems in the emerging world are shown in Figure 20. Generally, health insurance in most emerging countries offers very little biologics coverage; the poorest countries (eg, India, Indonesia) offer little or no such coverage to the majority of its citizens. More developed countries, such as Brazil, Argentina, Turkey and Russia, offer essential medicine at either free of charge or a relatively low cost. We assume that monoclonal antibodies are not fully reimbursed, though some (eg, India CGHS, Russia, Saudi Arabia) appear to reimburse them to a degree.

Biologics prices in emerging countries are similar to those in Japan

Our research suggests that the price of biologics such as Herceptin is not substantially different in any part of the world. According to MIMS.com, 440mg Herceptin prices in China (RMB93,600) and India (INR25,800) are almost equivalent to Japanese prices (JPY165,000), which is usually the lowest among the developed countries. Our interviews with companies from the emerging regions also suggest that originator prices of biologics are not substantially different from prices in the developed world. Thus, we estimate that the annual cost of Herceptin in the ROW is the similar to prices in Japan – ie, USD20,000 a year. The same parity assumption applies to all other biologics.

Fig. 20: Healthcare Expenditure Data and Nomura Assumption for Out-of-Pocket Payment on Biologics

Country	Health expenditure per capita, PPP (constant 2005 international $)	General government expenditure on health as % of Total expenditure on health	Out of Pocket Expenses as % of Total expenditure on health	Nomura Assumption Out-of-Pocket Payment for Biologics	Price Sensitivity	% of Population aged 65+
(MENA)						
Egypt	310	41%	58%	80-100%	High	4.4%
Saudi Arabia	768	67%	17%	10-20%	Medium	2.9%
Algeria	338	86%	13%	10-20%	Medium	5.1%
(Asia)						
India	109	33%	50%	80-100%	High	5.3%
China	233	50%	41%	80-100%	High	8.6%
Indonesia	81	52%	35%	80-100%	High	6.1%
Japan	2,696	80%	15%	20-30%	Medium	22.6%
South Korea	1,688	54%	35%	50-80%	High	11.1%
(Eastern Europe and CIS)						
Czech Republic	1,626	80%	15%	10-20%	Medium	15.9%
Hungary	1,388	70%	23%	50-80%	Medium	16.7%
Russia	797	64%	29%	50-80%	High	13.3%
Poland	1,035	68%	22%	50-80%	Medium	13.5%
Turkey	677	75%	16%	10-20%	Medium	6.2%
(South America)						
Brazil	799	46%	31%	50-80%	High	6.6%
Argentina	1,332	66%	20%	50-80%	High	10.9%
Mexico	877	48%	48%	80-100%	High	6.4%
(EU)						
Germany	3,737	76%	11%	0-10%	Low	20.6%
(US)						
US	7,290	49%	12%	10-20%	Medium	13.0%

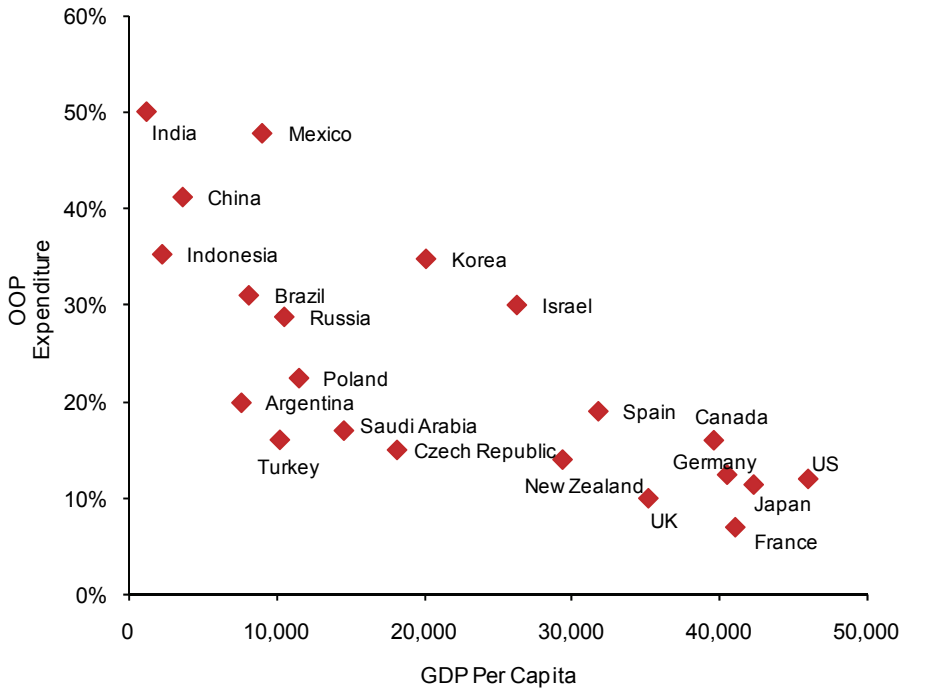
Note: Price sensitivity defined as: Low (0-10%); Medium (10-30%); High (>30%)

Source: World Bank, Nomura estimates

The poorer they are, the more they pay

As shown in the chart below, poorer countries shift more costs onto patients. Regions where governments pay less than 60% of healthcare expenditures coincide with regions that have little national health coverage (the only outlier is the US, where healthcare is funded not through national insurance, but through a tax concession for employers). In these regions, we estimate that out-of-pocket payment for biologics would be 50-100% of the drug price. Generally, countries where the government is paying for more than 70% of total health expenditure coincide with countries where biologics are comparatively affordable (eg, Germany). If, as we assumed in the paragraph above, that the price of biologics is about equal everywhere in the world, it seems that the poorer you are, the more you will pay for the same exact drug.

Fig. 21: Out-of-Pocket Expenditure as % of Health Spending vs. GDP per Capita (USD)



Source: World Bank

Significant pool of potential patients in ROW

The table overleaf is a rough calculation of the financial burden borne by breast cancer patients in each country. The average annual cost of Herceptin was calculated by multiplying USD20,000 (the estimated annual cost of Herceptin in Japan and ROW) against the estimated out-of-pocket biologics expenditure percentage from the table above. In many countries, even biosimilars would be beyond the reach of ordinary citizens since the cost of the drug is far beyond annual disposable income. Note our view that even poorer nations can afford biosimilars if the social safety net is well-developed (eg, Algeria whose insurance system is styled after that of France, according to Hikma Pharmaceuticals). In regions where the annual cost of biosimilar treatment is about equal to annual disposable income, we would expect rapid patient volume expansion (eg, Eastern Europe, Turkey, Korea) upon the introduction of biosimilars.

Current number of Herceptin users in ROW is small; potential for large volume expansion

A rough calculation of the number of Herceptin users is also given in the table overleaf. The number was calculated by taking the incidence of HER2+ breast cancer patients in each country based on WHO statistics (GLOBOCAN 2008) and multiplying by the number of patients who belong to the most affluent sector. As shown in the figure, the number of patients who can currently afford Herceptin treatment is extremely small in ROW. But if biosimilars become available, we believe that penetration into the middle class (defined by the ADB as those with daily consumption of USD4-10 a day) is

possible. We estimate that the number of potential patients is much larger. We have found that the same would apply to Remicade and all other biologics.

Proof in point: Penetration of Herceptin in China and Russia is low

In its 2 February 2011 investor presentation, Roche claimed that the penetration of Herceptin was only 7% in China and 25% in Russia. In contrast, Herceptin penetration in US/EU is near saturation. We believe that penetration in ROW is likewise limited for all other biologics.

Fig. 22: Calculation of Biosimilar Cost Per Patient and Number of Potential Patients (USD)

Data	Saudi Arabia	Egypt	Algeria	Russia	Poland	Czech	China	Turkey
GDP in $bn	435	220	160	1,500	440	200	5,745	730
Population	26,000,000	83,000,000	35,000,000	142,000,000	38,100,000	10,500,000	1,331,000,000	75,000,000
GDP per capita $	16,600	2,800	4,500	10,500	11,500	19,000	3,620	10,200
Average annual wages $	4,000	2,000	2,000	7,000	15,200	17,500	2,000	10,000
Food	800	600	600	2,100	4,256	3,150	800	2,700
Housing and Utilities	800	400	400	1,470	3,192	2,800	300	2,800
Transport	80	40	40	132	287	1,575	80	1,000
Est. Disposable Income	2,320	960	960	3,298	7,465	9,975	820	3,500
Est. Out of Pocket Expenditure	10-20%	80-100%	10-20%	50-80%	50-80%	10-20%	80-100%	10-20%
Annual Cost of Herceptin	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000
Annual Cost for Biosimilar	10,000	10,000	10,000	10,000	10,000	14,000	10,000	10,000
Est. Cost per Patient	1,000-2,000	8,000-10,000	1,000-2,000	5,000-8,000	5,000-8,000	1,400-2,800	8,000-10,000	1,000-2,000
Cost Burden on Patient	MEDIUM	VERY HIGH	MEDIUM	VERY HIGH	MEDIUM	LOW	VERY HIGH	MEDIUM
Size of middle class	6,500,000	8,300,000	1,050,000	56,800,000	22,860,000	6,300,000	391,180,900	45,000,000
Size of upper class	260,000	415,000	175,000	7,100,000	1,905,000	525,000	56,168,200	13,500,000
Calc. # of Current Patients	30	130	40	5,250	1,560	650	7,170	1,800
Calc. # of Potential Patients	900	2,700	300	47,200	20,200	8,400	57,100	7,800
Breast Cancer Incidence Per Year	1,681	12,621	4,271	52,469	15,571	6,486	170,000	10,000
Incidence %	0.01%	0.03%	0.02%	0.07%	0.08%	0.12%	0.01%	0.01%
Est. HER2+ Incidence Per Year	420	3,155	1,068	13,117	3,893	1,622	42,500	2,500

Data	India	Indonesia	Brazil	Argentina	Mexico	Korea	Japan	Germany
GDP in $bn	1,430	690	2,020	350	1,000	985	5,390	3,305
Population	1,200,000,000	230,000,000	193,000,000	40,200,000	108,000,000	49,000,000	127,500,000	81,000,000
GDP per capita $	1,170	2,230	8,100	7,600	9,000	20,100	42,300	40,500
Average annual wages $	600	2,000	6,000	6,000	6,500	18,700	41,625	47,000
Food	240	800	2,400	2,400	1,495	3,740	8,325	2,820
Housing and Utilities	90	300	780	780	1,430	1,309	5,828	7,520
Transport	24	80	600	600	715	2,805	5,411	3,290
Est. Disposable Income	246	820	2,220	2,220	2,860	10,846	22,061	33,370
Est. Out of Pocket Expenditure	80-100%	80-100%	50-80%	50-80%	80-100%	30-50%	20-30%	0-10%
Annual Cost of Herceptin	20,000	20,000	20,000	20,000	20,000	20,000	20,000	20,000
Annual Cost for Biosimilar	10,000	10,000	10,000	10,000	10,000	14,000	14,000	14,000
Est. Cost per Patient	8,000-10,000	8,000-10,000	5,000-8,000	5,000-8,000	8,000-10,000	7,000-11,200	2,800-4,200	0-1,400
Cost Burden on Patient	VERY HIGH	VERY HIGH	HIGH	HIGH	VERY HIGH	MEDIUM	LOW	VERY LOW
Size of middle class	55,200,000	25,024,000	106,150,000	30,552,000	32,400,000	49,000,000	127,500,000	81,000,000
Size of upper class	6,600,000	3,266,000	9,650,000	2,010,000	7,560,000			
Calc. # of Current Patients	630	570	2,100	950	980			
Calc. # of Potential Patients	5,900	4,900	25,200	15,400	5,200	12,500	50,000	64,000
Breast Cancer Incidence Per Year	115,000	40,000	42,000	19,000	14,000	12,450	50,000	64,000
Incidence %	0.01%	0.02%	0.02%	0.05%	0.01%	0.03%	0.04%	0.08%
HER2+ Incidence Per Year	28,750	10,000	10,500	4,750	3,500	3,113	12,500	16,000

Note: Est. Disposable Income = Average annual wages - Food - Housing and Utilities - Transport

Note 2: Average annual cost of Herceptin assumes the standard AC + T treatment with trastuzumab (Herceptin)

Note 3: Out of pocket expenditures estimated from figure 21 above, Calc. # of current patients = upper class x cancer incidence, Calc. # of potential patients = (middle class + upper class) x cancer incidence

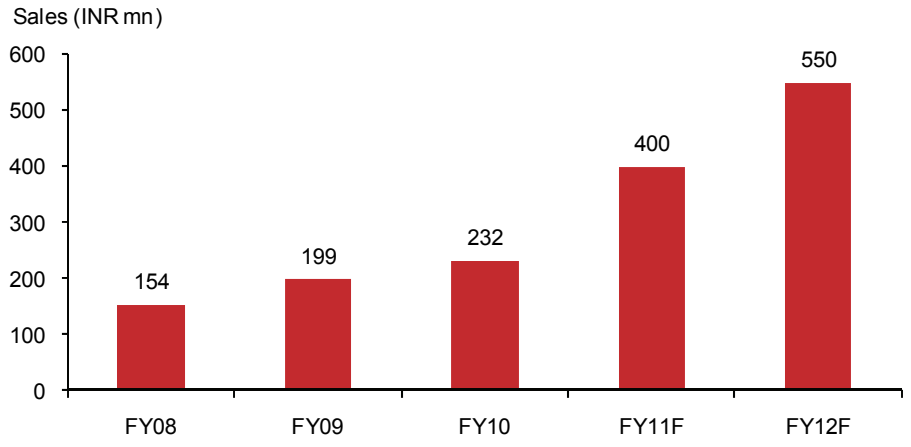
Source: World Bank (GDP, Population), ILO LABORSTA (Average annual wages, food, housing, transport), ADB for Asia (middle class = $4-20 consumption per day, upper class = >$20 consumption per day), WHO GLOBOCAN (breast cancer incidence data), Latam Economy.org for Latin America (middle class = 50-150% of national median income, upper class = >150% of median income), Nomura Estimate

Examples of the market creation effect in India

The “market creation effect” mentioned above can also be seen from the market experience of the few biosimilars that have already been launched in emerging countries. Here, we analyze the market acceptance of Reditux (biosimilar rituximab), Grafeel (biosimilar G-CSF) in India. It must be emphasized that we do *not* view Indian/Chinese biosimilars as equivalent to Celltrion’s product, since they have not been accepted by the top three regulators in the world, FDA/EMEA/PMDA. We believe that Celltrion’s products are competitive precisely because of their quality and also because of their strong local marketing network.

Case #1: Reditux (biosimilar rituximab) sold in India by Dr. Reddy’s Laboratories
In April 2007, Dr. Reddy’s launched Reditux in India. Reditux is the world’s first approved biosimilar monoclonal antibody. Dr. Reddy’s started selling Reditux at approximately a 40% discount to Roche’s brand-name MabThera. Dr. Reddy’s coupled the launch with social promotion schemes such as ‘Sparsh’, through which it distributed Reditux for free to extremely poor patients who could not receive antibody cancer treatment. Sparsh introduced poor patients, in the first place, to the existence of antibody cancer treatments and secondly, to the cost-effectiveness of biosimilars. Roche then responded by offering one free vial with each vial purchased, thereby effectively lowering the price by 50%. Nevertheless, Dr. Reddy’s claims that Reditux has gone on to capture close to 50% of the market by volume for rituximab. What is most interesting is that the size of the market has grown over six times since Reditux’s launch. Reditux sales in India have witnessed a CAGR of 27% since its launch in 2007, and in FY11 the biologic broke into Dr. Reddy’s top-five products sold in India and touched approximately INR400mn (USD2mn) in sales.

Fig. 23: Reditux India Sales



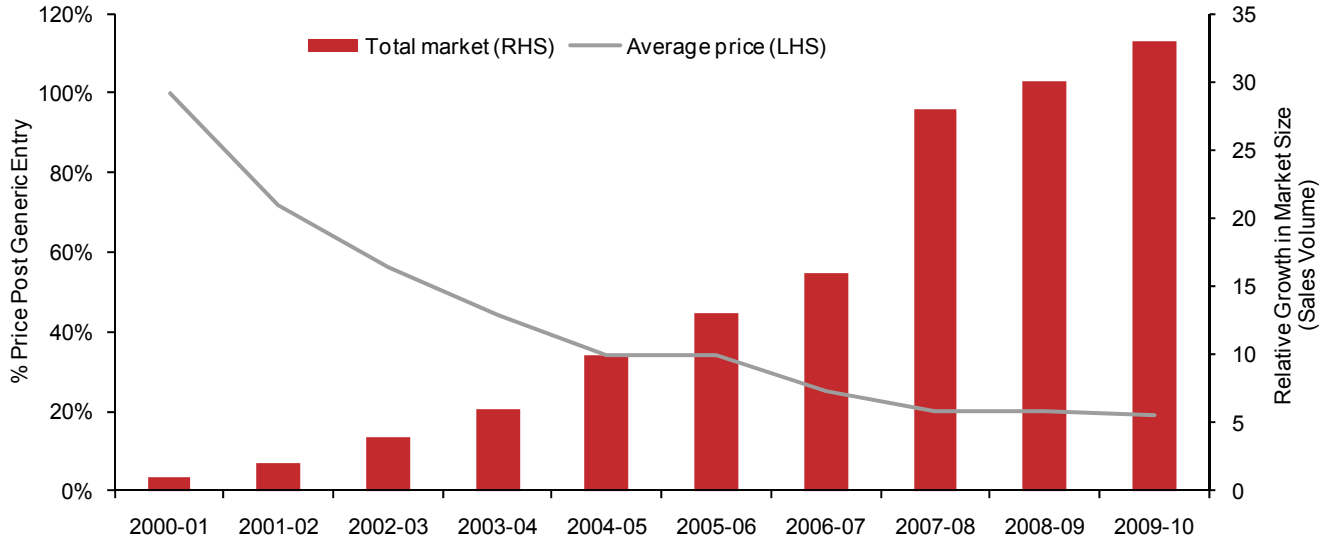
Source: Company data, Nomura estimates

Biosimilars seen from the viewpoint of an Indian Oncologist
Oncologists in India are of the opinion that most patients visiting private hospitals across the country are unable to afford original biologics and that there is an urgent need for biosimilars of drugs such as Herceptin. Since innovator antibody drugs remain out of reach for a very large portion of the patient population, they largely rely on traditional chemotherapy treatment that is provided at some large hospital across cities in India. Asia's oldest cancer registry, the Indian Cancer Society, estimates that over 80% of all cancer patients in India do not have any medical insurance and they do not fall under an employee benefit scheme.

Case #2: Grafeel (biosimilar G-CSF) sold in India by Dr. Reddy’s Laboratories
Dr. Reddy’s first biosimilar was biosimilar G-CSF (filgrastim) sold under the brand-name Grafeel. According to the company, prior to the launch of the biosimilar, the total market for filgrastim was very small due to the high price of the innovator’s product. Grafeel was launched in 2001 at approximately half of the price of the original drug. Since then, the market for filgrastim expanded rapidly immediately. One decade after the launch of the first biosimilar, the market volume size of G-CSF has grown by over 30 times and prices

have fallen by approximately 80%. Currently, there are over 10 brands of biosimilar filgrastim in India, and they are priced at a 20-25% discount to the innovator's product. Grafeel holds almost one-third of the market share and is the value and volume leader in the market. Biocon, another major biosimilar player that sells biosimilar G-CSF under the brand Nufil and has also launched Nufil Safe, a pre-filled syringe with advanced safety features that makes it easier for patients to self-inject.

Fig. 24: Impact of Grafeel on Accessibility of Filgrastim in India



Source: Dr. Reddy's

Analysis of Celltrion's ROW Partners

Tying up with regional giants – a good strategy

At an earlier point, Celltrion had originally planned to license out biosimilars to multinational companies for sales in the ROW. We surmise that Celltrion wanted to leave an option for direct sales in some regions in the future. Celltrion adopted the strategy of tying up with regionally players with extensive access to doctors in hospitals, where most of biologics will have to be prescribed. We believe that this strategy is one of the great strengths of Celltrion. Although multinational companies such as Pfizer or GlaxoSmithKline would have global reach and wide therapeutic portfolio, more often than not they are not the number one player in each region when the portfolio is limited to specialized areas such as oncology. As is shown in Figure 26, we believe that, even though many of their partners are obscure to people outside the region (e.g., Nippon Kayaku, Dexa Medica), close scrutiny shows that they are in fact quite competitive or even dominant.

Having good marketing partners is key

The strength of marketing partners is probably the most important factor for the commercialization of biosimilars. Unlike small-molecule generics, which do not generally require a pharmaceutical marketing and detailing team, biosimilars require persuading oncologists and orthopaedic physicians to prescribe biosimilars instead of the brand-name drugs. While physicians in the ROW are often forced to prescribe biosimilars because of their patients' limited ability to pay, doctors in the ROW are nevertheless as concerned about safety and efficacy as doctors in the developed world.

Fig. 25: Celltrion's marketing partners in the ROW region

Marketing partners classified from Excellent -> Strong -> Competitive

Partner	Strengths	Key Market(s)	Ranking
Abdi Ibrahim	• Largest pharmaceutical company in Turkey • Sales network of 2,000 medical representatives domestically	Turkey	Excellent
Shenzhen Main Luck	• Seventh largest oncology brand in China • Marketing network of 600 sales force and 300 AAA grade hospitals	China	Strong
CCPC	• One of the largest domestic companies • Marketing network of 200 sales force and 500 hospitals	Taiwan	Excellent
Hospira	• Established global network • Extensive experience of selling biosimilars in 19 countries in Europe	Germany, UK, US	Excellent
Bharat Serums & Vaccines	• Specializes in selling vaccines • Marketing network consists of about 200 medical representatives and 30 distributors	India	Strong
Hikma	• Top 5 player in MENA market • Strong marketing force consisting of over 1,600 medical representatives	Saudi Arabia, Algeria, Jordan	Excellent
Oli Med	• Established network in Latin America • Experience of selling oncology drugs including biosimilar G-CSF	Argentina, Chile, Peru	Competitive
Nippon Kayaku	• A specialist oncology player with 40% market share in products such as paclitaxel • Strong marketing force of 400 medical	Japan	Excellent
EGIS	• Strong player in the Eastern European market • Total sales and marketing force of almost 1,400 employees	Russia, Poland, Hungary, Czech Republic, Ukraine	Strong
Dexa Medica	• A top 3 pharmaceutical company in Indonesia • Generics player with extensive experience of in-licensing branded products	Indonesia, Malaysia	Strong
Perrigo	• Established network in Israel • Experience of selling branded drugs to HMOs, drug chains and the government	Israel	Competitive

Source: Company webpages, Hikma Pharmaceuticals, EGIS, Nippon Kayaku, Hospira, Nomura

Hikma Pharmaceuticals: regional giant

First and foremost is Hikma Pharmaceuticals, based in Jordan, and listed in London and the US, is the fifth-largest player in the MENA markets. Hikma's core strength lies in markets such as Jordan, Algeria and Saudi Arabia, as well as in Egypt, where it grew by 17% in 2009. Hikma's marketing network consists of 1,625 sales representatives who market generics, injectables and branded products across the Middle East and North Africa. Hikma's global revenues grew 15% in 2010 to USD730mn, with the MENA region accounting of over 60% of its revenues and the US contributing 28%. The CEO of Hikma, Mr. Said Darwazah, served as the Jordanian Minister of Health from 2003 to 2006. Possible competitors in this region include Sandoz.

MENA biologics opportunity: USD600mn market

According to our interviews with Hikma, the largest markets in the MENA regions are Egypt, Saudi Arabia, and Algeria, the last of which is expected to be one of the fastest-growing pharmaceutical markets due to its generous healthcare safety net, which was styled after the French system. The market size for just six of the nine biosimilars that the company will be selling is estimated to be around USD600mn. Oral generic prices in the MENA region are set by the government. The first entrant receives a 30% discount to the brand-name drug and subsequent entrants receive lower prices. Hikma has been actively taking authorities from each region to the Korean FDA to introduce them to biosimilars. Although Hikma was not willing to comment on future expected sales, company management believes strongly in the potential for biosimilars to become a future driver for growth.

Abdi Ibrahim: very strong partner for the Turkish market

According to the company's website, Abdi Ibrahim was founded in 1912 and is currently the largest pharmaceuticals company in Turkey by sales, commanding a 7.2% market

share. Backed by a sales force of over 2,000 representatives, Abdi Ibrahim's revenues for 2010 were in excess of USD800mn. According to IMS, in 2008, the Turkish oncology market was estimated to be USD700mn, while the monoclonal antibody market was estimated to be USD250mn. The privately held generics company exports products to 15 international markets in the CIS and MENA regions and is the only Turkish company in the top 100 pharmaceutical companies globally. The largest possible competitor in Turkey is Sandoz.

EGIS: Strong player in Eastern Europe and Russia

Budapest-based EGIS was established in 1913 as a subsidiary of a Swiss company. During the communist era, Hungary was positioned as the pharmaceutical center of the COMECON (Council for Mutual Economic Assistance). Thus, Hungarian companies such as EGIS and Gedeon Richter have broad brand recognition and quality image in the CIS/Eastern Europe regions. EGIS derives over 80% of approximately USD600mn revenue from the region, while the remainder coming from Hungary. Recently, the Hungarian government has been actively cutting prices of pharmaceuticals, prompting EGIS's drive to expand into other countries. Possible competitors in the region include Gedeon Richter, Teva, Sandoz, Dr. Reddy's and Biocad in Russia.

Fig. 26: EGIS's sales network

Region	Marketing Network
Hungary	208
Russia and CIS	623
Central and Eastern Europe	566
Total	1,397

Source: EGIS Gyogyszergyar Nyrt Annual Report

Disparity between Eastern Europe and CIS

According to EGIS, most of the Eastern European countries have an obligatory reimbursement system, where the governments pay about 50-60% of medical costs, though there are differences in each country. CIS regions have little to no direct state reimbursement. Some CIS countries have state tenders, but this only accounts for 20-30% of reimbursement. Therefore, the two markets are very different. Also, biosimilars have not yet been approved/marketed in the region, but because of the financial benefit, EGIS believes that they will be welcomed.

No price difference between Eastern Europe and Western Europe

Because many countries from Eastern Europe are in the EU, there are no material differences in prices among countries. During the Greek financial crisis, when the government drastically cut drug prices, many concerns were raised of intra-EU exports of cheap generics to other countries within the EU. Therefore, biosimilar prices will be equivalent across Europe, also.

EGIS forecast: EUR30mn in 2012/2013

EGIS expects to launch biosimilar products in CIS/Eastern Europe from 2012 in some countries, and 2013 in others. Although the target penetration rate has not been disclosed, EGIS expects EUR30mn in revenue in the first year. The potential market size of CIS/Eastern Europe according to EGIS is EUR600mn. The company estimates that the biggest markets for biosimilars amongst its network of 18 countries are expected to be Russia, Poland, Hungary, Czech Republic, Romania and Ukraine. EGIS believes that major risks associated with biosimilars are lack of transparency in CIS/Eastern Europe over approval and financing of biosimilars, acceptance of biosimilars by doctors, innovators protective action, and logistics – since a box of vials of biosimilars could be as much as two years' worth of salary for a worker at a wholesale warehouse.

China Chemical and Pharmaceutical Company

CCPC is one the largest domestic pharmaceutical companies in Taiwan and has the experience of partnering with global companies such as Pfizer, Roche, Takeda, Astellas, Daiichi Sankyo and GSK. CCPC leverages the extensive Taiwanese sales network of its fully owned subsidiary, Chunghwa Yuming Healthcare, which consists of approximately

200 sales representatives that cover over 500 hospitals. CYH currently markets products of companies such as Baxter, Abbott, Ajinomoto and Ono Pharmaceuticals.

Dexa Medica
Dexa Medica is amongst the top three pharmaceutical companies in Indonesia. The company is largely a generics player that partners with global companies and in-licenses their products for the Indonesian market. It has a history of partnering with innovators such as Pfizer, Bayer, Meiji, Novartis, GSK and generics companies such as Dr. Reddy's and Sun Pharmaceuticals.

Shenzhen Main Luck Pharmaceuticals
The Chinese company was founded in 1990 as a joint venture between Shenzhen Accordance Pharmaceutical (China), Mercian Business Corporation (Japan) and Main Life (Hong Kong) with the aim of developing and marketing cancer drugs in China. With a market force of over 600, Shenzhen Main Luck's marketing network consists of over 300 AAA hospitals across 29 provinces and municipalities in China. In 2010, Main Luck's oncology brand was recognized and awarded as the seventh-best oncology brand in China. Over the years, the company has exported its products to markets in the Middle East, South America, South Asia and Eastern Europe.

Perrigo
The Israel-based company derived over 60% of its USD2.2bn revenues in 2010 from the US market and under 5% from its home market. Perrigo's strength in Israel lies in selling branded pharmaceuticals to domestic HMOs, drug chains and the government. The company also sells consumer healthcare products in the domestic market. Its main competitor in the home market is the global giant, Teva. We believe that Perrigo would be at a significant disadvantage against Teva, as Teva is a larger player than Perrigo, and the Israeli market for biosimilars is probably small.

Oli Med Peru
Oli Med is a privately held pharmaceutical company that is based out of Caracas, Venezuela. The network of the company spans across Latin American countries such as Peru, Chile, Argentina, Panama, etc. Oli Med currently markets oncology products including biosimilar G-CSF under the name Filgrastima along with carboplatin, epirubicin and calcium folinate.Possible competitors in the region is CFR Pharmaceuticals (who is marketing Dr. Reddy's Reditux), and Sollievo Ltd (who has in-licensed Mycenax Biotechnologies' biosimilar etanercept).

Bharat Serums and Vaccines
Arguably the most unknown of marketing partners is India's BSV. BSV is a privately held company promoted by the Daftary Group and is based out of Mumbai, India. The company largely sells acute therapy products in the domestic market and its top selling products include RhoClone (anti Rho-D Immunoglobulin vaccine), Hucog (human chronic gonadotropin), U Frag (urokinase agent) and Tetglob (Tetanus vaccine). The total revenues of BSV are estimated to be in excess of INR2bn with the top four products contributing nearly 50% of total revenues. BSV has appointed 30 super distributors across India and the estimated sales force size is 500. In April 2010, OrbiMed advisors invested an undisclosed amount in acquiring an equity stake in BSV.

Celltrion's global CRO partner: Pharmaceutical Product Development Inc.
On 9 May 2011, Celltrion signed a memorandum of understanding with global CRO major Pharmaceutical Product Development Inc. (PPD) for running its global clinical trials and providing support for regulatory approval. Celltrion's strategic alliance covers clinical planning, operations and regulatory support for the company's 10 products that are currently under development. As a result of this partnership, we expect Celltrion's burden of recruiting patients and conducting clinical trials to reduce as PPD brings to the table extensive experience of conducting over 5,000 clinical trials across the world. The partnership also provides Celltrion with access to already established and efficient clinical infrastructure. PPD is already conducting CT-P13 clinical trials in patients with ankylosing spondylitis as well as rheumatoid arthritis in Peru and Portugal for Celltrion. NASDAQ-listed PPD has a network of 44 countries with over 11,000 professionals and clocked revenues of over USD1.4bn in FY10.

Celltrion's ROW sales forecast

Assumption for Celltrion: ROW market creation effect of 2x the number of patients
Similar to Reditux or Grafeel, Celltrion expects to launch monoclonal antibody biosimilars at a 50% discount in emerging countries. As we have shown in the previous section, most emerging world patients are currently priced out of the market. Although a 50% cut is still insufficient to cover most of the population, experience in India would suggest that over time, with increasing affluence and incremental insurance coverage, the drug will become accessible to a much larger group of patients. Note that average rituximab prices (including Reditux and MabThera) have gone down by another 50% since launch, and the price of G-CSF, due to biosimilar competition, has fallen by 80%. Thus, we believe Celltrion should contemplate even lower prices in ROW areas. But the important thing to note is that volume for rituximab has simultaneously increased 6x, and for G-CSF 30x. This would mean that the market overall has grown 3x and 24x since biosimilar launch – a pronounced "market creation effect".

It is very difficult to accurately predict the market creation effect in each region. But based on the Indian experience, we think that a twofold increase over time in the number of patients as a "market creation effect" is a conservative but appropriate estimate for Celltrion's ROW sales. Since the emerging market economy is expected to grow rapidly, this may be a conservative estimate. But taking into account the fact that ROW sales usually contains Canada, Australia, and some relatively affluent countries of Eastern Europe, we think that the market creation effect should be tempered compared to the very rapid growth seen in India.

Patient number forecast: Two-fold increase by 2020
Our baseline forecast is based on Roche forecasts made by Nomura Europe team. Note that the sales forecast for all monoclonal antibodies does *not* assume significant sales erosion from biosimilar launches. The baseline is thus the sales expected where innovators sell biologics with minimal price cuts. We have approximated the number of patients using Herceptin in the ROW as 70,100 (for more information on the details of the calculation, please refer to Appendix I on pg. 64). Applying a twofold increase to the 2020 baseline population, we estimate the number of HER2-positive metastatic breast cancer/breast cancer patients undergoing adjuvant therapy to be about 330,000. The same calculation has been applied to CT-P13 and CT-P05 (summarized as TNF-alpha inhibitors) and CT-P10 (Rituxan/MabThera).

Peak market share of 25%
Celltrion is targeting market share in the ROW end market of 50% or higher by volume. While this may be possible in some regions where the marketing partner is especially strong (e.g. Nippon Kayaku in Japan, Hikma Pharmaceuticals in the Middle East), other market partners may be more limited in its commercial reach. Additionally, extremely cheap low-quality biosimilars from other emerging countries are likely to flood the market within five years' time, possibly eroding Celltrion's patient base. In our view, fierce competition with the likes of Pfizer, Merck, and Sandoz is likely after 2016. Therefore, we believe that a 25% peak market share by patient population in ROW is a reasonable estimate for all of Celltrion's biosimilars in FY2016-2017. Note that a 15% market share in 2020 with a market creation effect is equivalent to about a 50% market share that Celltrion claims, since we are assuming that the patient volume triples with the introduction of biosimilars. We refer the reader to Appendix I for more detailed consideration of patient volume calculation and the competitive landscape.

Fig. 27: Celltrion – ROW patient population assumptions and end-market sales (marketing partner's sales) estimate 2010-20

Herceptin and CT-P06: ROW assumptions	2010	2011F	2012F	2013E	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast ($ mn)	1,403	1,502	1,655	1,800	1,850	1,900	1,938	1,977	2,016	2,057	2,098
Baseline Calc. Patient Pop.	70,100	78,200	86,200	93,800	96,400	99,000	100,900	103,000	105,000	107,100	109,300
Biosimilar Market Creation Effect	0	0	5,000	15,000	30,000	50,000	67,200	90,300	121,300	162,900	218,600
Total Patient Pop. After Biosimilar Launch	70,100	78,200	91,200	108,800	126,400	149,000	168,100	193,300	226,300	270,000	327,900
CT-P06 Penetration by Patient Pop. (%)	0	0	5	10	15	20	25	25	15	13	10
Estimated End Market Sales ($ mn)	0	0	46	109	190	298	420	483	339	351	328
CT-P13 and CT-P05: ROW assumptions	2010	2011F	2012F	2013E	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast ($ mn)	2,600	3,082	3,520	3,737	3,895	3,931	4,008	4,079	4,151	4,223	4,297
Baseline Calc. Patient Pop.	131,000	156,000	178,000	189,000	197,000	199,000	202,400	206,000	209,700	213,400	217,200
Biosimilar Market Creation Effect	0	0	20,000	40,000	60,000	83,500	116,100	161,500	224,600	312,400	434,400
Total Patient Pop. After Biosimilar Launch	131,000	156,000	198,000	229,000	257,000	282,500	318,500	367,500	434,300	525,800	651,600
CT-P13/05 Penetration TNF-alpha User Pop. (%	0	0	5	9	10	15	16	18	13	9	6
Estimated End Market Sales ($ mn)	0	0	109	227	283	466	561	728	621	521	430
CT-P10: ROW assumptions	2010	2011F	2012F	2013E	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast ($ mn)	1,418	1,451	1,496	1,541	1,587	1,635	1,684	1,735	1,787	1,840	1,860
Baseline Calc. Patient Pop.	68,000	75,600	77,900	80,300	82,700	85,200	87,700	90,300	93,100	95,800	98,600
Biosimilar Market Creation Effect	0	0	0	0	4,000	10,000	18,100	32,700	59,200	107,100	193,800
Total Patient Pop. After Biosimilar Launch	68,000	75,600	77,900	80,300	86,700	95,200	105,800	123,000	152,300	202,900	292,400
CT-P10 Penetration by Patient Pop. (%)	0	0	0	0	10	15	20	19	13	13	10
Estimated End Market Sales ($ mn)	0	0	0	0	69	114	169	187	158	211	234

Source: Nomura, adapted from Nomura Europe forecasts

Still insufficient to supply most of the world

In forecasting ROW sales, we believe our estimate may be conservative. This may be surprising to the global investor, who could well be shocked by our estimate of end-market sales of CT-P13/05 approaching USD1bn in 2020 (the estimate assumes that CT-P13/05 will steal market share not just from Remicade and Enbrel, but also from global leader Humira in the ROW). In terms of global prevalence of HER2-positive breast cancer (CT-P06), rheumatoid arthritis and other autoimmune diseases (CT-P05 and CT-P13), and Non-Hodgkin's Lymphoma (CT-P10), a doubling in the patient population is not at all sufficient. For example, the percentages of the female total population using Herceptin in the US and Europe are estimated to be 0.028% and 0.034%, respectively. Even after doubling via market creation in 2020, we estimate the ROW equivalent is a mere 0.005%.

Upside: increasing health insurance coverage, Downside: fierce price competition

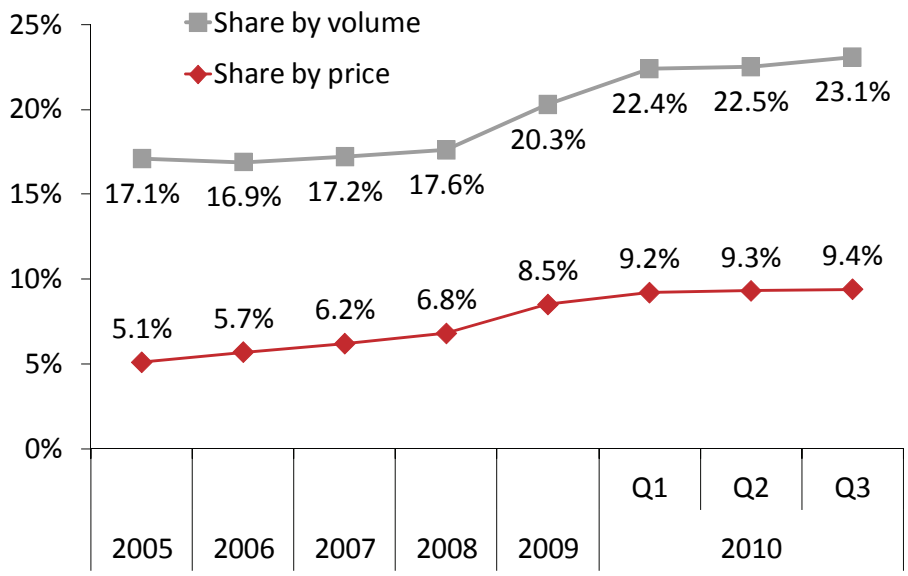
There are upside and downside risks to our forecast. The largest upside risk factor is the increase of insurance coverage in ROW. There are many efforts underway in a number of emerging countries to establish a basic insurance system. A good example is China which is aiming to cover the entire population. As seen in Figure 21 on page 29, any increase in insurance coverage is likely to bring down out-of-pocket spending significantly, further magnifying the market creation effect. The downside risk is steep price decline from increasing competition. While competition for CT-P06 (Herceptin) and CT-P13/05 (Remicade/Enbrel) are mainly manufacturers from non-regulated regions of unproven quality, CT-P10 (Rituxan) will face competition from large multinational generics companies. Beyond 2016, competition is expected to be especially fierce, with large multinational such as Pfizer and Merck joining the fray. We believe that price may fall dramatically in these periods. However, as was the case with Grafeel, we believe that as prices fall, more demand tends to be created.

Japan as a mid-way between US/Europe and ROW

Why Japan is closer to Eastern Europe than US/Western Europe

Insofar as biologics are considered, we see Japan as being closer to the ROW than US/EU. This may be surprising; after all, Japan is a developed nation with universal healthcare, and the government is shouldering 80% of healthcare spending, as shown above. On first sight, it would seem to be closer to Germany than Turkey or Russia. On closer inspection, one aspect of Japan stands out: it is the only developed country where the patient pays fully 30% of any drug price as copayment. For an annual Herceptin treatment, the out-of-pocket expenditure is a whopping USD6,000. This is unaffordable for many, especially since breast cancer afflicts elderly women, who tend to be unemployed and have substantially lower income. In fact, this is not very different from Eastern European countries, where the government is paying 40-60% of medical care. Therefore, we find it expedient to include Japan in the ROW.

Fig. 28: Japanese generic market share: by volume and price



Source: Japanese Generic Association

Market creation effect applies to Japan

We believe that the market creation effect applies to Japan, but only to a limited extent. Chugai Pharmaceuticals claims that the Japanese penetration rate of Herceptin in HER2 positive breast cancer patients is 90%, while Remicade has a comparable penetration rate among rheumatoid arthritis patients. However, we believe that there are a significant number of patients who consciously opt out of Herceptin/Remicade treatment because of the financial burden imposed. Including all of the additional payments for IV infusion, which costs about USD70 per visit, the annual out-of-pocket payment for HER2-positive metastatic breast cancer patients is about JPY700,000-750,000 (about USD8,000-9,000), depending on whether oncology generics are used. As shown in Figure 30, if a patient uses CT-P13 instead of Remicade, our simulation suggests that the patient saves JPY20,000 per visit, with an annual savings of JPY110,000 (around USD1,300). Nippon Kayaku believes that the patient pool would expand if biosimilar prices are lowered to mitigate the financial burden on patients. We believe that the patient volume would expand by 30% from the introduction of more affordable biosimilars in Japan.

Hospira also saw volume growth from cheaper G-CSF and EPO (in Europe)

Hospira, in its 19 August, 2010 Biosimilar Investor Education seminar, commented that the market volume of both G-CSF and erythropoietin (EPO) actually increased after introduction of biosimilars. G-CSF, in particular, has seen 14% overall market growth (including brand-name and biosimilars) since the launch of biosimilars. EPO and G-CSF are two of the most heavily used and highly penetrated protein therapeutics, fully

reimbursed by most developed countries, especially in Europe where coverage is generally more generous. If G-CSF and EPO can create additional volume in Europe, we think that it is reasonable to expect some market growth through the introduction of biosimilars in Japan.

Fig. 29: Brand-name Remicade vs CT-P13: Cost saving in per treatment copayment

(Per visit fee details, JPY)	Govt Reimbursement	Copayment (30%)
Remicade RA treatment (3mg/kg, 60kg)	200,570	60,171
Prednisolone 10mg injection	119	36
Revisit Fee	690	207
Additional Fee for Outpatient Chemotherapy	5,500	1,650
Additional Fee for Sterile Product Use	500	150
IV infusion with 150 yen additional for biologics	450	135
Prescription Fee	420	126
Total per visit	208,249	62,475

(Per visit fee details, JPY)	Govt Reimbursement	Copayment (30%)
CT-P13 RA treatment (3mg/kg, 60kg)	140,399	42,120
Prednisolone 10mg injection	83	25
Revisit Fee	483	145
Additional Fee for Outpatient Chemotherapy	3,850	1,155
Additional Fee for Sterile Product Use	350	105
IV infusion with 150 yen additional for biologics	315	95
Prescription Fee	294	88
Total per visit	145,774	43,732

Source: Nomura, shirobon.net

Fig. 30: Generic market share of select oncology drugs

(Annual Sales: ¥mn)	2006	2007	2008	2009	2010A	2011F
Paclitaxel						
Brand-name Taxol	35,675	31,015	26,052	20,952	14,900	10,700
Generic Paclitaxel (Kayaku)	800	2,500	3,800	5,900	7,000	7,800
Epirubicin						
Brand-Name Farmorubicin	7072	6849	5,812	4,478	3,200	2,500
Epirubicin (Kayaku)	0	0	1,100	1,400	1,700	2,000
Carboplatin						
Brand-name Paraplatin	11790	10268	8,704	6,391	4,200	3,200
Generic Carboplatin (Kayaku)	1000	1400	1,900	2,600	3,000	3,400
Generic Carboplatin (Sandoz)				682	900	1,100

(Market share by vol., %)	2006	2007	2008	2009	2010A	2011E
Paclitaxel						
Brand-name Taxol	97%	89%	89%	78%	67%	56%
Generic Paclitaxel (Kayaku)	3%	11%	14%	25%	36%	47%
Epirubicin						
Brand-Name Farmorubicin	100%	100%	76%	66%	56%	46%
Epirubicin (Kayaku)			21%	31%	41%	51%
Carboplatin						
Brand-name Paraplatin	100%	100%	76%	55%	41%	31%
Generic Carboplatin (Kayaku)			24%	32%	42%	47%
Generic Carboplatin (Sandoz)				12%	18%	21%

Source: Nippon Kayaku, Nomura estimates

Japan does not incentivize generic penetration adequately …

The classic counterargument to biosimilar penetration in Japan is that Japan is the most resistant to generic penetration among all developed countries. Japanese generic penetration as of 31 December, 2010 was 23.1% by volume and 9.4% by price, a paltry number compared to >70% generic penetration in US, >30% in many European countries.

Many innovator companies in Japan mistakenly claim that the Japanese are inherently brand-conscious and generic-resistant. Unlike Europe or US, where generics are either automatically substituted or the US, where private insurance companies have much more clout, Japanese generics promotion is driven ultimately by basically only one factor: price differential. Generics in Japan are sold at a 30% discount to the innovator drug price. For common drugs, cost savings are on the order of couple US dollars. It is not surprising to us, therefore, that generic penetration remains low.

… but when drugs become expensive, generic penetration increases dramatically

But what happens when the drug costs USD1,000 a vial? All of a sudden the generic discount becomes USD300, not a trivial amount. Therefore, expensive drugs such as oncology drugs and imaging agents have seen heavy generic penetration. The table on the previous page shows the sales and market share of select oncology drugs in Japan. Nippon Kayaku, Celltrion's marketing partner, began selling oncology generics from 2004. We estimate that Nippon Kayaku as of the end of 2011 May will hold about 40% market share by volume of paclitaxel, epirubicin, and carboplatin, as shown below. This is estimated to grow to near 50% in 2011. Thus, once doctors are persuaded that biosimilars are both safe and effective, we would expect them to follow much the same trend.

Fig. 31: Japan patient population assumptions and end market sales 2010-2020

Herceptin and CT-P06: JP assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (¥ mn)	25,242	25,765	27,667	30,260	34,583	36,313	36,313	36,313	36,313	36,313	36,313
Baseline Calc. Patient Pop.	16,700	17,000	19,200	21,000	25,300	26,600	28,000	28,000	29,400	29,400	31,000
Biosimilar Market Creation Effect	0	0	0	0	500	1,000	1,600	2,500	3,900	6,100	9,300
Total Patient Pop. After Biosimilar Launch	16,700	17,000	19,200	21,000	25,800	27,600	29,600	30,500	33,300	35,500	40,300
CT-P06 Penetration by Patient Pop. (%)	0	0	0	0	1	5	15	30	30	30	30
Estimated End Market Sales (¥ mn)	0	0	0	0	277	1,455	4,364	8,729	8,707	8,707	8,722
CT-P13 and CT-P05: JP assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (¥ mn)	96,700	120,600	143,600	161,800	165,300	171,300	171,300	171,300	171,300	171,300	171,300
Baseline Calc. Patient Pop.	55,600	68,100	82,800	92,400	96,800	99,800	99,800	99,800	99,800	99,800	99,800
Biosimilar Market Creation Effect	0	0	0	0	1,000	2,000	6,000	12,000	18,000	24,000	30,000
Total Patient Pop. After Biosimilar Launch	55,600	68,100	82,800	92,400	97,800	101,800	105,800	111,800	117,800	123,800	129,800
CT-P13/05 Penetration TNF-alpha User Pop. (%)	0	0	0	0	0.1	5	10	14	16	15	14
Estimated End Market Sales (¥ mn)	0	0	0	0	121	6,370	13,241	18,610	22,410	19,871	19,446
Rituxan and CT-P10: JP assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (¥ mn)	22,971	24,480	24,376	24,684	24,579	24,893	25,216	25,549	25,893	26,246	26,246
Baseline Calc. Patient Pop.	13,407	14,288	14,977	15,166	15,896	16,099	17,166	17,393	18,555	19,798	20,840
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	13,407	14,288	14,977	15,166	15,896	16,099	17,166	17,393	18,555	19,798	20,840
CT-P10Penetration rituximab User Pop. (%)	0	0	0	0	0	5	10	25	25	25	25
Estimated End Market Sales (¥ mn)	0	0	0	0	0	871	1,769	4,473	4,542	4,594	4,584

Source: Nomura estimates

Nippon Kayaku dominates the Japanese oncology generic market

It is important to note that the generic market share shown in Figure 31 is for *all* drugs from *all* companies, while Nippon Kayaku, by itself, is claiming about 40-50% of the Japanese oncology generic market share. Nippon Kayaku has been dedicated to oncology since the 1970s, and oncology generics since 2004. With a large, dedicated marketing force of 400 MRs, as well as one of the largest portfolios of branded/generic oncology drugs in the world, the company far outpaces all other oncology generics makers in terms of product offering and market share. Since oncology drugs are often used in complicated regimens and accompanied by serious or, sometimes, fatal adverse events, we think doctors may favor Nippon Kayaku over other generic players due to its established expertise in the field. Thus, we believe that Nippon Kayaku is probably the best biosimilar marketing partner possible in Japan.

Japan market forecast: peak market share of 30% for CT-P06, 15% for CT-P13

We forecast peak market share of 30% for CT-P06 and 15% for CT-P13 in Japan. Nippon Kayaku sells generic epirubicin, paclitaxel, doxorubicin, as well as other older brand-name drugs. Nippon Kayaku also has a co-marketing agreement with GSK for the oral drug Tykerb. Thus, sales synergy with their breast cancer oncology drugs is strong. Along with their expertise in oncology generics, we believe that the company can reach peak market share of 30% in FY17F, according to Nomura Japan's MedTech and Generic Pharmaceuticals Analyst Motoya Kohtani.

An even more ambitious target for the Japanese market is a 15% market share in all TNF-alpha drugs for CT-P13. Our scenario suggests that biosimilar infliximab CT-P13 will be competitive not only with brand-name Remicade but with self-injectable TNF-alpha inhibitors such as Enbrel and Humira. Despite the well-known incidences of infusion reactions with Remicade, we believe that the Japanese are fundamentally averse to self-injection, and prefer IV injection in a clinical setting. Moreover, cost-saving from biosimilar infliximab at JPY110,000 is large enough to prompt many users to switch. Although it will require time to convince doctors and medical personnel that biosimilars are a viable option, patients with strained purses will inevitably embrace biosimilars. For more details of the Japanese market dynamics, please see Appendix I.

Who is going to sell biosimilar rituximab in Japan?

Unlike other existing partnerships that comprise eight biosimilars, Nippon Kayaku has signed marketing agreements for only two biosimilars, CT-P06 and CT-P13. Therefore, CT-P10 does not currently have a marketing partner. We have, however, included CT-P10 sales in our forecast for the Japanese market, since willing partners are plenty. We believe the best case for a partnership in Japan would be Nippon Kayaku, but other candidates exist.

Biosimilar Opportunities in Australia

Biosimilar expansion expected in Australia

Nomura Australia healthcare analyst Dave Stanton believes that biosimilar expansion in Australia is also possible. Given the ongoing pressure to decrease the cost of drugs paid for by the government as a part of the Pharmaceutical Benefits Scheme (PBS), described below, we believe that should biosimilars be approved, they are likely to gain market share in Australia.

The View from Down-Under: The Australian Pharmaceutical Benefit Scheme (PBS)

Australian Medicare provides subsidized access to prescription medicines for the people of Australia under the Pharmaceutical Benefits Scheme. This scheme aims to provide necessary and life saving medications at affordable costs. The funding to run this scheme comes from the public by means of taxes; it is about AUD2bn annually. It covers around 93% of Australian prescriptions. In Australia, the Therapeutic Goods and Administration (TGA) provides market approval for the pharmaceutical products. If the new product is found to be safe and effective, the TGA approves it for marketing.

PBAC evaluates cost-effectiveness

The manufacturer (sponsor) then applies to the Pharmaceutical Benefits Advisory Committee (PBAC) for listing in the PBS Scheme. This committee includes medical practitioners and pharmacists and it advises the Ministry of Health on which drugs to include in the scheme. The company must identify a comparator drug already listed in PBS, and the new entrant should prove that their products are more cost- effective than the comparator drugs. On the basis of the reports submitted, the PBAC evaluates the effectiveness and cost effectiveness of these products and recommends to the Ministry of Health whether to include them or not. For those products whose treatment costs exceed AUD10mn, their inclusion must be approved by the government.

PBPB determines drug prices

After approval, prices of the included products are determined by the Pharmaceutical Benefits Pricing Authority (PBPB). It is an independent body with representatives from the pharmaceutical industry, consumers and representatives from the government to negotiate the prices. The prices are fixed based on several methods such as reference pricing, price volume agreements and generic substitution incentives. The dispensing fee for dispensing PBS medicines is determined by the Pharmaceutical Benefits Remuneration Tribunal (PBRT).

The patients are required to pay a fixed co-payment for the subsidized items. The co-payments are less for concession card holders i.e. those who are in the low-income bracket, disabled, senior citizens, etc. Products that are not included in the PBS are not subsidized by the government. The list of these products includes non- prescription drugs and other complementary medicines. The PBS was amended in 2007, after which the products were classified into two formularies. Formulary 1, or F1, includes patented medicines and Formulary 2, or F2, covers generic medicines.

Approval pathway same as in EU

Australia has adopted EU guidelines for the regulatory approval of biosimilars. No separate pathway will be established. Hence, all statements made regarding the EU are relevant for Australia. As is required in Europe, biosimilars must take the “similar biological medicinal products” approach with comparability exercises for approval.

Biosimilar approach may not be suitable for plasma derivatives

The ‘similar biological medicinal product’ approach is more difficult to apply to other types of biological medicinal products, which by their nature are more difficult to characterise, such as biological substances arising from extraction from biological sources and/or those for which little clinical and regulatory experience has been gained. EMEA has stated in the 2005 guideline that plasma proteins should not be allowed to take the abbreviated biosimilar application, requiring a full review of safety and efficacy. Biosimilars for recombinant Factor VIII can be developed, however we believe that expansion is difficult due to the high rate of inhibitor generation (30% of patients) when switching from one Factor VIII to the other. This market is also highly specialized with many entrenched players such as CSL in Australia.

Europe: Government action required to open the floodgates

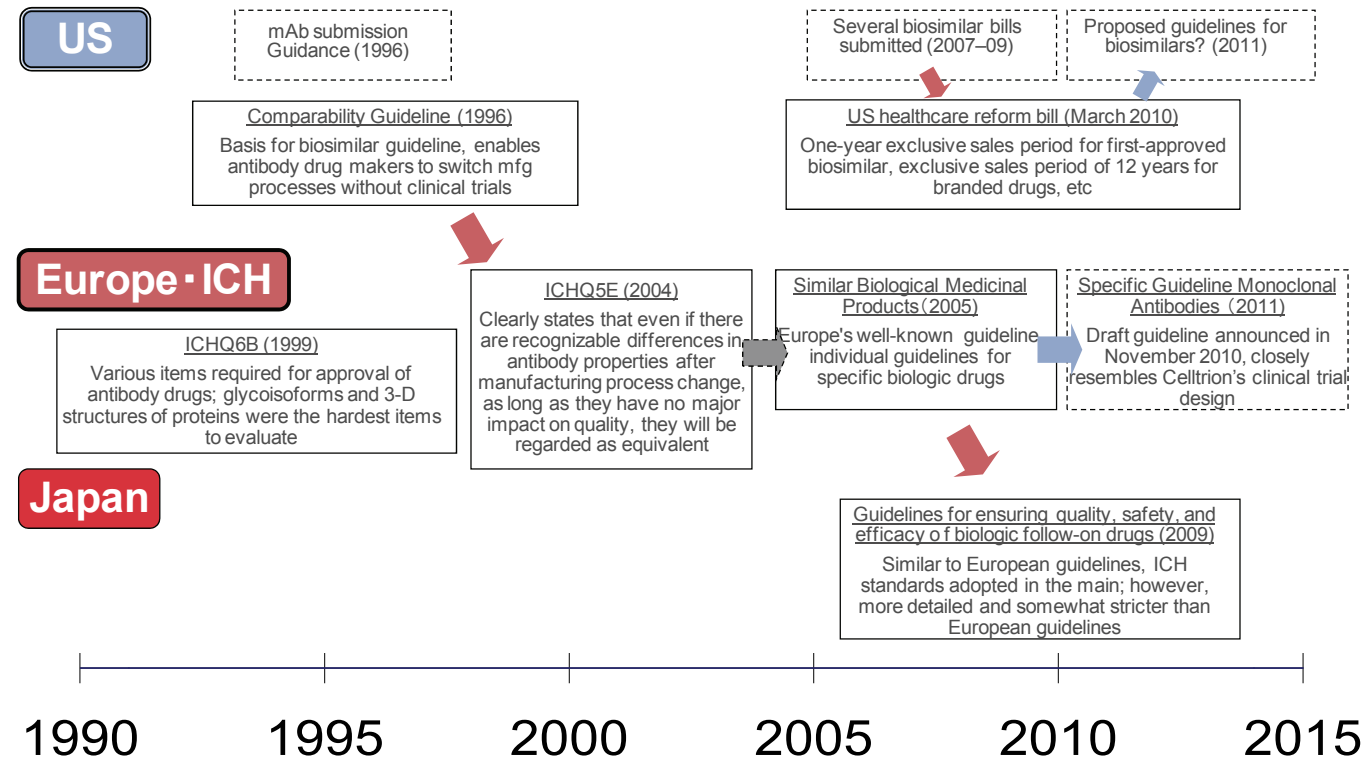
You win by making the guideline, not waiting for it

In the biosimilar market, the winner is often the company that makes the industry guidelines along with the regulator. This was the case with Biocon's biosimilar insulin in India (2003), Dr. Reddy's Reditux in India (2007), Sandoz's Binocrit in Europe (2008), JCR's Epoetin kappa in Japan (2009), and now with Celltrion's CT-P06 and CT-P13. Although subsequent commercial success is dependent on other factors, what all of these companies have in common is that they proactively engaged the regulators from early on in development. By engaging the regulators from the beginning, whatever the company does, from analytical studies for bioequivalence to Phase III clinical trial design, were used as a base case for the guidelines later issued by the authorities.

The evolution of US/European guidelines

We believe the present biosimilar guidelines could have been anticipated. US/European guidelines are based on guidelines concerning changes in production methods of branded biologics. Manufacturers of branded biologics needed to scale-up production when proceeding from clinical trial to commercial launch. In some cases, there were changes in master cell lines, culture mediums, culture conditions, and manufacturing methods. At the time, additional clinical trials were necessary, as changes in biologic manufacturing conditions could result in major changes in glycoisoform distribution (distribution of proteins with specific oligosaccharide chains, changes may cause immunogenicity) and production yield.

Fig. 32: The evolution of biosimilar guidelines



Source: MHLW, Nomura research

Biosimilar regulations are based on innovator's rules

The origin of biosimilar regulation dates back to April 1996, when the FDA released its "Guidance Concerning Demonstration of Comparability of Human Biological Products," a set of guidelines regarding the equivalence of biologic drugs. These guidelines stated that new clinical trials would not be needed so long as equivalence could be shown via a combination of analytical testing, biological testing, pharmacokinetics, pharmaco-dynamics studies, and toxicity trials. *ICH5QE*, published in 2004, advanced this another step by clearly stating that even if some changes in antibody properties are detectable after changes in manufacturing, if safety and efficacy are unchanged, the drug would be regarded as being equivalent. We believe this is the core regulation of biosimilars and that US/Japan biosimilar regulations would also incorporate this core concept.

Applying the same regulations to biosimilars resulted in Europe's guideline

The application of this principle is evident in the world's first guideline on biosimilars: "The Guideline on Similar Biological Medicinal Products," established by European authorities in October 2005. Although the guidelines state that verification based on comparability protocols is required in biosimilars, approval was possible even if there were slight differences in the distribution of impurities and in glycoisoform distribution, so long as there was no impact on safety and efficacy.

Fig. 33: Comparison of Clinical Trial Design : CT-P06

	H0648g Trial (2001)	CT-P06
Inclusion Criteria	Women with HER2 overexpressing cancers who had not received prior chemotherapy	Women with HER2 overexpressing cancers who had no prior Herceptin/chemotherapy treatment or **as adjuvant/neoadjuvant discontinued >12 months** before trial
	-	Have at least 4 weeks since last surgery or radiation therapy
	-	AST and ALT < 2.5x ULN
Exclusion Criteria	Received prior chemotherapy	Received prior chemotherapy (for metastatic breast cancer)
	Brain metastases	Brain metastases
	-	Receiving concurrent hormonal therapy or immunotherapy
	-	**CHF patients in any NYHA class, LVEF < 50%**
	Have received treatment with any other investigational drug in the last 30 days	Have received treatment with any other investigational drug in the last 30 days
Dosage	Loading dose 4mg/kg, maintenance dose 2mg/kg once a week	Loading dose 4mg/kg, maintenance dose 2mg/kg once a week
Primary Endpoint	Time to Disease Progression	ORR at 6 months by Response Evaluation Criteria in Solid Tumours RECIST 1.1
Secondary Endpoint	ORR, Duration of response, time to treatment failure, OS	Comparable safety, pharmacokinetic bioequivalence in CtroughSS
Sample Size	469	84 (Europe) 536 (global)
Primary Endpoint Results	Median Time To Progression: 7.2 (Herceptin) 4.5 (Chemotherapy)	-
Secondary Endpoint Results	**ORR 50% (Herceptin) 38% (Chemotherapy)**	-
PK	t1/2 = 6days, **CtroughSS = 79mcg/mL**, CpeakSS = 123mcg/mL	-
Adverse Events	Infection 47% (Herceptin + Chemo) 29% (Chemo alone) **18 patients in the trastuzumab subgroup discontinued due to cardiac dysfunction**	-
Immunogenicity	Among 903 women with metastatic breast cancer, only 1 tested positive to HAHA (human anti-human antibody)	-

Source: Clinicaltrials.gov

Draft guideline of the monoclonal antibody biosimilar
In November 2010, the European Medicines Agency (EMEA) released a draft "guideline on similar biological medicinal products containing monoclonal antibodies." The guideline states that the focus of the biosimilarity exercise is to demonstrate similar efficacy and safety compared with the reference product, not patient benefit per se, which has already been established by the reference product. For anti-cancer drugs in particular, the guideline states that there is no need to determine either progression-free survival (PFS) or overall survival (OS) – a mainstay of oncology new drug clinical trials. Rather, it is suggested that a clinical endpoint that measures activity as primary endpoint may be considered, examples being overall response rate (ORR, the proportion of patients in whom a complete response [CR] or partial response[PR] was observed), or percentage change in tumor mass from baseline. Of interest also is the suggestion that selection of "the most sensitive patient population" is preferred as a means of reducing the sample size needed to prove equivalence.

Draft guideline developed using Celltrion's clinical trial design as a template
We believe that the body of the European monoclonal antibody guideline was formed using Celltrion's clinical trial design as a base case. Celltrion's CT-P06 and CT-P13 are the first antibodies to obtain IND for clinical trials from the European authority. The table on the previous page is Celltrion's clinical trial design for CT-P06. Note that it closely mirrors many aspects of the original pivotal trial for Herceptin conducted in 1999. There are some minor differences in the inclusion and exclusion criteria, which are explored in Appendix I. The most important difference is the primary endpoint. While the older pivotal trial used Time to Disease Progression, Celltrion uses overall response rate (ORR). ORR is no longer used as a primary endpoint in phase III novel drug clinical trials, because it does not measure the durability of the clinical effect. Thus, for Celltrion to use ORR as a primary endpoint, it would have required specific guidance from the EMEA. The second important difference is that the patient group uses chemotherapy-naïve patients – or as close to naïve as possible in this age when chemotherapy is readily available. Naïve patients are "the most sensitive patient population," as referred to in the draft guideline.

Celltrion's chance of success should be reasonably good
We believe that the EMEA has a vested interest in assuring accessibility to biosimilars. For the very first clinical trial of a high-publicity biosimilar to fail would have repercussions on other biosimilars in the pipeline. One would rationally think that every aspect of CT-P06 and CT-P13 had been hammered out with the European authorities, starting from the CMC and safety data for manufacturing, down to the phase III clinical trial design. We believe that these products should have reasonably good chance of being approved. Therefore, we are assuming an 80% discount to the sales projected from patient volume market share.

Lukewarm acceptance to continue

Three types of first-generation biosimilars: hGH, G-CSF, EPO
Currently there are no approved biosimilar monoclonal antibodies in Europe. Approved European biosimilars are protein formulations, sometimes referred to as first-generation biosimilars. The current list of approved biosimilars in Europe is listed in the table overleaf. Human growth hormone (hGH) and G-CSF, unlike antibody drugs, are not glycosylated (do not have sugar chains attached), therefore they can be manufactured using E. coli and S. cerevisiae and present fewer manufacturing challenges compared to mammalian cells. At present, EPO (erythropoietin), which is glycosylated, is the closest product in complexity to monoclonal antibodies.

Hospira: Celltrion's partner already sells first-generation biosimilars in Europe
Hospira, Celltrion's marketing partner in Europe, currently sells two biosimilars in Europe, Retacrit, a short-acting erythropoietin and Nivestim, biosimilar filgrastim. Retacrit has been successfully growing in Europe with the help of its strong sales force and has managed to capture over 50% of the market share of biogeneric short-acting EPO.

Fig. 34: Approved Biosimilars in Europe

Generic Name	Brand Name	Approval Date	Marketing Company	Manufacturer	Cell Type
Somatropin	Omnitrope	4/18/2006	Sandoz GmbH	Sandoz GmbH	E. Coli
	Valtropin	5/4/2006	BioPartners GmbH	BioPartners GmbH	S. Cerevisiae
Epoetin alfa	Binocrit	8/31/2007	Sandoz GmbH	Rentschler Biotechnologie GmbH	CHO
	Epoetin alfa HEXAL	8/31/2007	Hexal Biotech GmbH		
	Abseamed	8/31/2007	Hexal Medice GmbH		
Epoetin theta	Biopoin	10/23/2009	CT Arzneimittel GmbH	Merckle Biotec GmbH	CHO
	Eporatio	10/23/2009	Ratiopharm GmbH		
Epoetin zeta	Retacrit	12/18/2007	Hospira	Norbitec GmbH	CHO
	Silapo	12/18/2007	Stada Arzneimittel GmbH		
Filgrastim (G-CSF)	Biograstim	9/15/2008	CT Arzneimittel GmbH	SICOR Biotech UAB	E. Coli
	Filgrastim Ratiopharm	9/15/2008	Ratiopharm GmbH		
	Ratiograstim	9/15/2008	Ratiopharm GmbH		
	Tevagrastim	9/15/2008	Teva		
	Nivestim	6/8/2010	Hospira	Hospira Zagerb d.o.o.	E. Coli
	Filgrastim Hexal	2/17/2009	Hexal AG	Sandoz GmbH	E. Coli
	Zarzio	2/6/2009	Sandoz GmbH		

Source: EMEA EPAR information

hGH: The difficulty of prescribing biosimilars to children

There are two growth hormones marketed in Europe: Omnitrope, developed by Sandoz GmbH under Novartis, and Valtropin, marketed by BioPartners GmbH and developed by LG Life Sciences of Korea. Neither product has had any commercial success. The market share of human growth hormone biosimilars in Germany – the only country in Europe with any meaningful market for biosimilars – is under 1% for Omnitrope. We estimate that Valtropin has even less market share. (Omnitrope has also been approved in Japan since 2009, but with very similar commercial results.) We believe that hGH is a poor target for biosimilars for a number of reasons: 1) the number of doctors prescribing growth hormones is very limited, and a very specialized sales force is necessary; 2) there are at least three established players (Eli Lilly, Pfizer, Novo Nordisk) with over 20 years experience each in catering to this niche market; and 3) parents are extremely reluctant to prescribe biosimilar human growth hormones to their children.

G-CSF: The most successful biosimilar in Europe

According to Roche's presentation, G-CSF, a granulocyte colony stimulating factor for neutropenia patients undergoing chemotherapy, reached 13% market share by volume as of 3Q10. Since patients only use G-CSF for up to 20 weeks, most patients who are introduced to G-CSF are new patients. Unlike erythropoietin, where many patients have been using it for years, new patients are less averse to switching, which could explain the rapid uptake of G-CSF biosimilars.

Nivestim shows Hospira's tactic for differentiation

Hospira was a late-comer to G-CSF biosimilars, launching Nivestim in 2010. In order to differentiate Nivestim from the other six G-CSF biosimilars already approved in Europe, Hospira developed a syringe with an integrated needle safety device. This prevents accidental needle stick injury for patients self-injecting at home. Hospira also added a 48 hour out-of-fridge stability to its product information. Neither of these features is available from the brand-name Neupogen or from competing biosimilars. Although the features are small, we believe that companies need a proactive differentiation strategy in order to retain competitiveness. In this sense, we believe that Hospira has the right strategy.

EPO: German quotas driving European market growth

According to Hospira, by the end of 2010 biosimilar erythropoietin in Europe was able to capture 12% of the short-acting erythropoietin market by volume. Retacrit, Hospira's biosimilar, had slightly greater than 50% of the biosimilar market. The growth is clearly driven by Germany, where the market share of EPO biosimilars has approached 60%. Biosimilar uptake in Germany has been very rapid because: 1) all EPO biosimilars are

manufactured in Germany; and 2) German sickness funds are able to set independent quotas for use of generics in certain therapeutic areas.

Pricing trend of biosimilar EPO: stable at around 12% discount for biosimilars
Hospira, during its 29 August 2010 conference call, showed that the price differential between biosimilars and original EPOs have stabilized after 30 months of launch 12% discount to brand-name drugs. Biosimilar EPOs launched with a 15-20% price differential compared to brand name Eprex. Market share has been growing consistently over the last 30 months, even though the price differential is only 12%. Most European countries do not enforce price discounts for biosimilars. Thus, the price differential is expected to remain small.

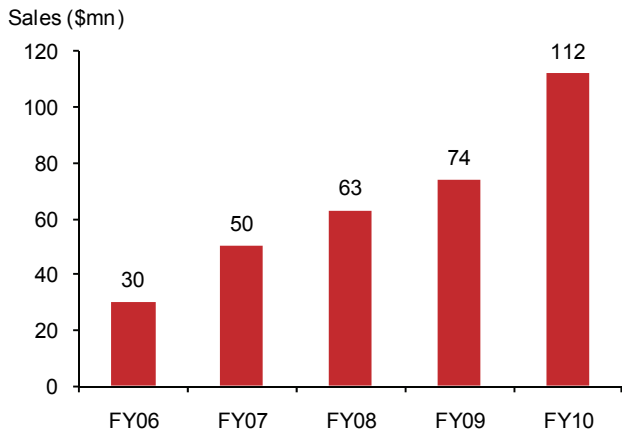
Marketing in Europe: lack of automatic substitution and what this means
EMEA explicitly stated that biosimilars are not identical to its original, and that biosimilars should only be taken following the opinion of a doctor. In addition, five major European countries (UK, France, Germany, Italy, Spain) have banned automatic substitution (substituted automatically by the pharmacist) of biosimilars. This implies that European biosimilar sales would require good access to hospital formularies, as well as an active detailing sales force to convince doctors.

Hospira as an able partner in Europe …
We believe that Hospira, though not of European origin, will be a strong partner for Celltrion. Hospira, as a US company, has lower name recognition than Sandoz or Ratiopharm (now part of Teva). But Hospira has succeeded in acquiring a 50% German market share by volume for EPO, which is one of the largest markets for first-generation biosimilars. Hospira has only an estimated 100 MRs in the all of Europe. According to Hospira, the key to its success was the “hybrid approach” to its sales strategy that it adopted. Hospira’s biosimilar specialty sales force uses a hybrid of the proprietary product approach, where manpower is needed, and a generic approach. Hospira believes that over time as biosimilar acceptance spreads, the model will come closer to the generic approach. Hospira has also focused on specialized fields such as oncology (G-CSF and EPO) and nephrology (EPO). The oncology sales network could prove valuable when CT-P06 (trastuzumab) is approved.

… but tough competition in Europe is expected: Sandoz and Teva
We expect competition in Europe will be fierce and that Hospira may not be able to gain as much market share going forward. Teva and Sandoz have been active in marketing biosimilars, as shown in Figures 36 and 37. Neither of these two companies has disclosed the geographic distribution of their sales, but we assume that a majority of sales comes from Europe (EPO and G-CSF) and from the US (growth hormone). We expect that both Sandoz and Teva will launch biosimilar rituximab before Hospira, since they are already conducting clinical trials for both drugs (see Appendix III for more details). Thus, Hospira’s edge is likely limited to CT-P06 (Herceptin biosimilar) and CT-P13 (Remicade biosimilar).

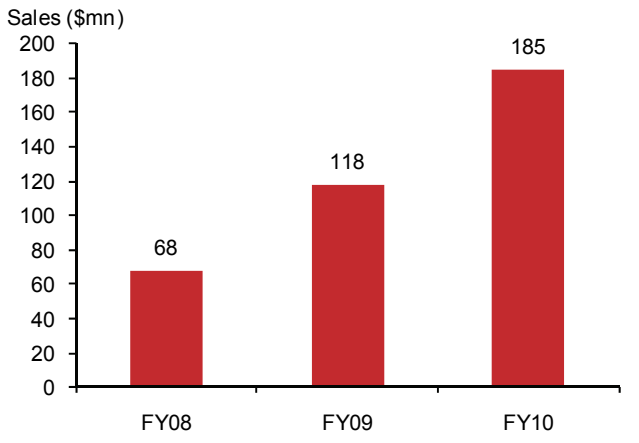
Expect slow but steady uptake for Celltrion’s biosimilars in Europe
All indications suggest that the uptake of Celltrion’s biosimilars will follow a slow and gradual uptake, much like G-CSF biosimilars, in the European market. Although the German EPO penetration is an appealing example of success in biosimilars, we believe that it is a special case. It is not representative of Europe; according to the European Generic Agency, small-molecule generic penetration in France, Spain, and Italy is limited compared to Germany and the UK. We have assumed a peak market share by volume of 10% for CT-P06 (to be reached in 2017) and 7% for CT-P13 (among all TNF-alphas, to be reached in 2017).

Fig. 35: Teva Biosimilar Sales



Source: Company data, Nomura research

Fig. 36: Sandoz Biosimilar Sales



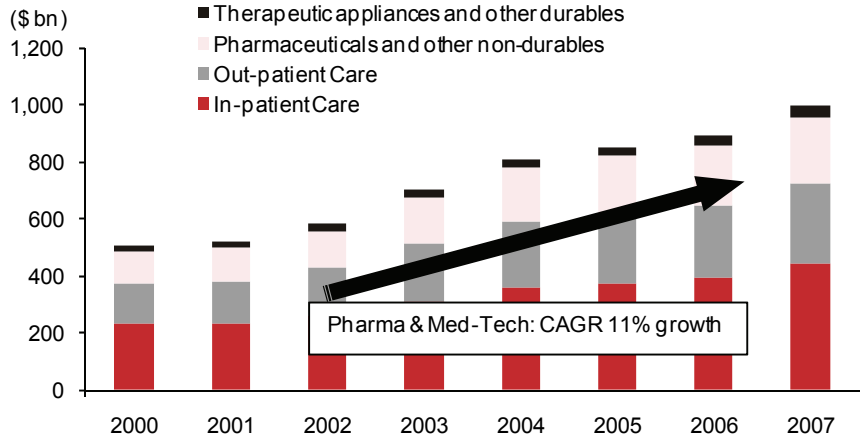
Source: Company data, Nomura research

Fig. 37: European patient population assumptions and end market sales forecast 2010-2020

Herceptin and CT-P06: Europe assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (€ mn)	2,075	2,133	2,154	2,176	2,173	2,195	2,195	2,195	2,195	2,195	2,195
Baseline Calc. Patient Pop.	56,800	55,400	55,900	56,500	56,400	57,000	57,000	57,000	57,000	57,000	57,000
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	56,800	55,400	55,900	56,500	56,400	57,000	57,000	57,000	57,000	57,000	57,000
CT-P06 Penetration by Patient Pop. (%)	0	0	0	0	1	3	7	10	9	8	7
Estimated End Market Sales (€ mn)	0	0	0	0	12	36	84	120	108	96	84
CT-P13 and CT-P05: Europe assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (€ mn)	5,327	4,939	5,040	4,988	4,841	4,627	4,627	4,627	4,627	4,627	4,627
Baseline Calc. Patient Pop.	238,300	220,600	224,200	221,100	213,800	203,800	203,800	203,800	203,800	203,800	203,800
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	238,300	220,600	224,200	221,100	213,800	203,800	203,800	203,800	203,800	203,800	203,800
CT-P13/05 Penetration by Patient Pop. (%)	0	0	0	0	1	3	5	7	7	6	6
Estimated End Market Sales (€ mn)	0	0	0	0	15	88	146	205	205	175	175
Rituxan and CT-P10: Europe assumptions	2010	2011F	2012F	2013F	2014F	2015F	2016F	2017F	2018F	2019F	2020F
Baseline Forecast (€ mn)	1,185	1,133	1,181	1,224	1,261	1,299	1,338	1,378	1,419	1,462	1,508
Baseline Calc. Patient Pop.	70,528	67,420	71,743	75,886	79,758	83,827	88,104	92,599	97,324	102,289	105,485
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	70,528	67,420	71,743	75,886	79,758	83,827	88,104	92,599	97,324	102,289	105,485
CT-P105 Penetration by rituximab Patient Pop. (%)	0	0	0	0	0	3	5	7	5	3	3
Estimated End Market Sales (€ mn)	0	0	0	0	0	18	31	45	33	20	21

Source: Nomura estimates

Fig. 38: Health Expenditures in the EU-17 (Western Europe): 2000-2007



Source: OECD Health 2010 data, Nomura research

Requires government action for higher penetration

We believe that any change in government regulation would be necessary for further acceptance of biosimilars in Europe. Currently, most nations in Western Europe (UK, France, Germany, Italy, Spain, Greece, Scandinavian countries) have banned automatic substitution of biosimilars at the pharmacy, due to safety and efficacy concerns. Some countries in Eastern and Central Europe (Austria, Slovenia, Slovakia, Hungary and Czech Republic) have either banned or restricted substitution at the pharmacy. As medical practitioners gain more experience with biosimilars, and as governments become more comfortable with the safety profiles of biosimilars, we believe that there will be gradual changes to accommodate substitution of biosimilars. We believe that it will require at least three years of clinical experience with monoclonal antibody biosimilars before this is considered.

Rising pharmaceutical costs = inevitable promotion of biosimilars

The final factor that will compel European governments to move faster, in our view, will be the budget. Facing ever-strained budgets during the financial crisis and the Greek sovereign bond crisis, many European countries were quick to slash the cost of pharmaceuticals. As shown in Figure 39, the CAGR of pharmaceutical and medical non-durables (e.g. catheters, syringes, and other disposable medical devices) was 11% in the EU-17 (Western Europe). Since it is difficult to expect that the European government budget would improve significantly in the near future, we believe governments will be ever more tempted to find effective cost-cutting measures.

US: Possibility of 1-year FTF exclusivity

Why the US is behind, and why letting patents expire is also good

Just as introduction of product patents were important to awaken the Korean/Indian/Japanese pharmaceutical sectors, expiry of patents can also be an incentive for industry – in this case, the generic pharmaceutical industry. US patents that were filed before 8 June, 1995 received either 20 years from the filing date or 17 years from grant, whichever is longer. Since most of the early monoclonal antibody therapeutics were filed before 1995, what resulted was an artificially extended patent term compared to Europe or Japan. For example Remicade expires in 2018 and Herceptin in 2019. Because patent expiry of these blockbuster biologics was delayed, US companies were the slowest to awaken to the biosimilar opportunity.

Although Merck, Pfizer, Amgen, and Biogen-Idec have commented publicly on the attractiveness of the biosimilar market, there has been relatively little progress. Only global generic players from the US such as Hospira or Mylan have been successful so far, though limited to first-generation biosimilars. Since many of the US companies are behind, we believe that many of these companies will seek partners overseas to in-license products that have already been developed. Examples include Hospira-Celltrion, Pfizer-Biocon (insulin), and Mylan-Biocon (monoclonal antibodies).

Fig. 39: List of US Biosimilars marketed or under development

Generic Name	Brand name/ Development Code	Approval date	Manufacturer
Glucagon	GlucaGen	1998	Novo Nordisk
rhGH	Tev-tropin	2005	Teva/Ferring Pharma
	Omnitrope	2005	Sandoz GmbH
Hyaluronidase	Amphadase	2004	Amphastar
	Hylenex	2005	Baxter
Calcitonin	Fortical Nasal Spray	2005	Upsher-Smith/UNIGENE
Filgrastim(G-CSF)	Neutroval	2010 BLA	Teva
	MK-4214	2009 Phase I	Merck (Insmed)
Pegylated Filgrastim	MK-6302	2009 Phase I	Merck (Insmed)
Erythropoietin	-	2010 Phase I	Hospira
Pegylated Erythropoietin	MK-2578	2010 Dropped	Merck
rFSH	-	Preclinical	Watson Pharma/Itero Biopharmaceuticals
taliglucerase alfa	UPLYSO	PDUFA 2011-Feb	Pfizer/Protalix Biotherapeutics
galactosidase	PRX-102	Preclinical	Protalix Biotherapeutics

Source: Nomura

US definition of biosimilars very different from other countries

The US definition of biosimilars differs from that in other countries. There are two categories of biosimilars for purposes of approval. Biosimilars of reference biologics developed in the US during the 1970s-80s − ie, hormones (follicle-stimulating hormone, luteotropic hormone, calcitonin, insulin, growth hormone), specific enzymes (brand name: Cerezyme), and anticoagulants (PEG-Hirudin) − that were approved under the Food, Drugs, and Cosmetics Law follow the same approval pathway as generic low molecular weight compounds. However, antibody therapeutics and most protein therapeutics fall under the Public Health Services Law, which currently does not include a legal regulatory pathway for approval of biosimilars. Consequently, biosimilar developers are required to submit biologics license applications (BLA) − the same process for new biologics. This requires costly large-scale studies.

“Obamacare” and the one-year market exclusivity of biosimilars

The healthcare reform bill signed into law on 23 March 2010 contained a subtitle called “The Biologics Price Competition and Innovation Act of 2009 (BPCI),” which allowed for

approval of biosimilars after makers of the original biologic have had 12 years of patent exclusivity. The law also mentions a one-year market exclusivity for biosimilars that are filed first in the United States, similar to first-to-file small-molecule generics.

Update on the US Guideline Situation: November 2010 discussion
In November 2010, the FDA hosted a public hearing to debate the issues involved in creating an approval pathway for biosimilars. Opinions on the biosimilar approval process were offered by a number of industry participants, including major branded drug makers, leading generic drug makers, universities and state-run research institutions, and consulting firms.

The bulk of comments concerned the respective definitions of “biosimilarity” (highly similar to the reference product notwithstanding minor differences in clinically inactive components) and "interchangeability" (can be expected to produce the same clinical result as the reference product in any given patient), and clinical trial requirements. Branded drug makers demanded head-to-head comparisons between branded drugs and biosimilars, and stressed that even if a biosimilar had been approved for one indication, it must undergo separate trials to obtain approval for another. Generic drug makers, on the other hand, pointed out that even branded drugs can undergo changes in chemical composition. They said that if scientific evidence proves biosimilarity, then additional indications should be automatically approved, as should interchangeability between the biosimilar and branded drug. In addition, some drug makers said there were ethical issues with calling for unnecessary clinical trials.

As a follow up to the November public hearing, on 9 May 2011, the FDA issued a notice requesting stakeholders for inputs on the development of the user fee programme for biosimilars and interchangeable biological products. According to the notice, the proposed fee for interchangeable biosimilars using the abbreviated biologics pathway will be the same as that of the biologics license application (BLA). The FDA estimates that the cost of reviewing biosimilar applications would be comparable to that of original biologics. The proposed fee structure also takes into account that biosimilar application reviews would be complex, technically demanding and resource intensive. The FDA has stated that the annual fee during the IND phase of each application would be approximately USD150,000. We believe that this cost structure presents a high entry barrier and highlights the fact that entry into the US market will neither be easy nor inexpensive. The FDA is also expected to issue a first wave of biosimilar regulatory guidelines by the end of 2011.

Scientific evidence is the key term for US biosimilar approval
In our view, the key phrase to emerge out of the public hearing is “scientific evidence.” The issues arising at the tail end of the development process— such as the need for clinical trials and interchangeability or lack thereof with the branded drug—in our view all boil down to proving, with a high degree of scientific evidence, that a biosimilar is equivalent to the reference drug. In that sense, we think FDA documents concerning generic enoxaparin sodium, approved on 23 July, provide a blueprint for the biosimilar approval process.

Enoxaparin: a template for biosimilar approval
Enoxaparin sodium is a type of low molecular weight heparin, and is a highly complex polysaccharide polymer. Momenta Pharmaceuticals (MNTA) had conducted a sophisticated analysis of the drug’s chemical composition prior to submission of generic approval (ANDA). The FDA granted approval on the premise that equivalence had been determined. Protein preparations and antibody therapies are even more complex in composition than polysaccharide polymers, but we think the requirements for scientific evidence and subsequent approval should be limited to proving, via sophisticated testing, that any change in the biosimilar’s chemical composition is within the scope found in the original branded drug.

Clarity needed for progress
At present, there are two approval pathways for biosimilars in the US – the traditional Biologics License Application (BLA) route and the in-progress Abbreviated BLA route. Companies such as Teva and Hospira have chosen to take the tried and tested BLA route for their G-CSF biosimilars citing the uncertainties that surrounds the ABLA route.

Hospira is conducting Phase I clinical trial for biosimilar erythropoietin in renal patients with the objective of testing the safety and pharmacokinetics in comparison to the original product. Pending the successful completion of the Phase I trial, Hospira aims to launch an expanded Phase III trial in 2011. Pharmaceutical companies believe that taking the ABLA route for biosimilar approval will expose them to extensive patent litigations and delays in launching biosimilars. According to Medco, a leading pharmacy benefit managers, companies will develop biosimilars for the US market with or without the ABLA as they would be able to make use of the traditional BLA route. Through its discussions with manufacturers, Medco has learnt that biosimilars in the US could be priced at a 30-60% discount to the original biologics. The company expects biosimilar penetration in the US to be driven by oncology and rheumatoid arthritis.

Celltrion's sales in US discounted by 50% to account for lack of clarity

While we believe that Hospira will develop biosimilars in the US, the timing and the competitive situation is currently very unclear. Conservatively, we have estimated launch of both CT-P05 and CT-P10 in 2016 – well past the US patent expiry of 2012 for Enbrel and 2015 for Rituxan – to reflect the lack of clarity in guidelines and approval process. We estimate that Hospira will gain 10% of the market share by volume in the first year, resulting in USD360mn for CT-P05 and USD160mn for CT-P10. We have, however, applied a 50% discount for Celltrion's sales to account for the large uncertainty.

Fig. 40: US patient population assumptions and end market sales forecast 2010-2020

CT-P13 and CT-P05: US assumptions	2010	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Baseline Forecast ($ mn)	8,018	8,126	8,332	8,397	8,271	8,184	8,184	8,184	8,184	8,184	8,184
Baseline Calc. Patient Pop.	308,300	305,900	305,600	303,500	294,800	288,000	288,000	288,000	288,000	288,000	288,000
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	308,300	305,900	305,600	303,500	294,800	288,000	288,000	288,000	288,000	288,000	288,000
CT-P13/P05 Penetration by Patient Pop. (%)	0	0	0	0	0	0	10	8	6	6	6
Estimated End Market Sales ($ mn)	0	0	0	0	0	0	359	287	215	215	215
CT-P13/P05 Penetration FTF 1-yr exclusivity (%)	*0*	*0*	*0*	*0*	*0*	*0*	*20*	*8*	*6*	*6*	*6*
Estimated End Market Sales FTF 1-yr ($ mn)							*1,006*				

CT-P10: US assumptions	2010	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Baseline Forecast ($ mn)	2,901	3,057	3,155	3,249	3,347	3,447	3,551	3,657	3,767	3,880	3,958
Baseline Calc. Patient Pop.	103,612	109,169	114,968	120,834	126,999	133,478	140,288	147,446	154,969	162,875	186,515
Biosimilar Market Creation Effect	0	0	0	0	0	0	0	0	0	0	0
Total Patient Pop. After Biosimilar Launch	103,612	109,169	114,968	120,834	126,999	133,478	140,288	147,446	154,969	162,875	186,515
CT-P10 Penetration by Patient Pop. (%)	0	0	0	0	0	0	10	8	5	5	5
Estimated End Market Sales ($ mn)	0	0	0	0	0	0	159	131	85	87	99
CT-P10 Penetration FTF 1-yr exclusivity (%)	*0*	*0*	*0*	*0*	*0*	*0*	*40*	*8*	*5*	*5*	*5*
Estimated End Market Sales FTF 1-yr ($ mn)							*893*				

Source: Nomura estimates

Gaining FTF for biosimilars would be very large, but not included in forecast

Simulation of a scenario in which Hospira gains first-to-file status for both CT-P05 and CT-P10 are shown in the table above. Because the market is large, Hospira could stand to gain considerably from such a scenario. We have not included this scenario in our forecast, due to uncertainties.

Forecast Summary and Valuation

Sales: >W500bn sales in 2013, >W900bn by 2015

Sales contract condition vary by region and company

Sales contract conditions with each marketing partner have been disclosed and are shown in the table below. Sales contract conditions vary by region and company. Marketing partners in emerging nations pay USD5mn per validation batch, and the contracts include no safety stock. EGIS pays 1.5 years' supply spread out over number of years. Hospira pays for 10 batches 18 months prior to approval. Nippon Kayaku pays USD130mn total for validation batch and, presumably, at least a year's worth of safety stock. Payment details for commercial batches have not been disclosed.

Fig. 41: Celltrion's sales contract conditions by company

Country	Company Name	Contract Date	# of Biosimilars	Years	Contract
Venezuela	Oli Med Perú	5/26/2009	9	10	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Peru & nine other countries	Oli Med Perú	5/26/2009	9	10	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Taiwan	China Chemical & Pharmaceutical	6/3/2009	9	12	$5mn per batch in each region per product, 1 batch per validation, prepayment
China	Shenzhen Main Luck Pharmaceuticals	6/4/2009	9	12	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Indonesia and seven other countries	Dexa Medica	6/9/2009	9	12	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Turkey	Abdi Ibrahim	6/22/2009	9	15	$5mn per batch in each region per product, 1 batch per validation, no safety stock
India	Bharat Serums and Vaccines	6/30/2009	9	10	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Argentina	Oli Med Perú	8/12/2009	9	10	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Chile and two other countries	Oli Med Perú	8/12/2009	9	10	$5mn per batch in each region per product, 1 batch per validation, no safety stock
Russia CIS countries (17 in EE)	Egis	2/5/2010	8	-	After market research, 1.5 yrs of stock (for CT-P06 2batches) purchased, 35% 18months prior to approval, 15% after 9months, Approval 20%, Commercialization 30%
Israel	Perrigo	3/23/2009	8	10	Initial Safety Stock at some price
Middle East, Africa	Hikma Pharmaceuticals	4/7/2010	9	10	Initial Safety Stock at some price
US, Canada, Europe, Australia, New Zealand	Hospira	10/9/2009	8	-	18mns prior to approval, $5mn or some other transfer price per batch, 10 batches purchased, 30% on day of receipt, 30% 9 months later, 40% on commercialization
Japan	Nippon Kayaku	11/1/2010	2	5	US $46mn and $84mn for CT-P06 and CT-P13, includes initial safety stock

Source: Company press releases (DART)

Already being paid by EGIS, Hikma, Nippon Kayaku

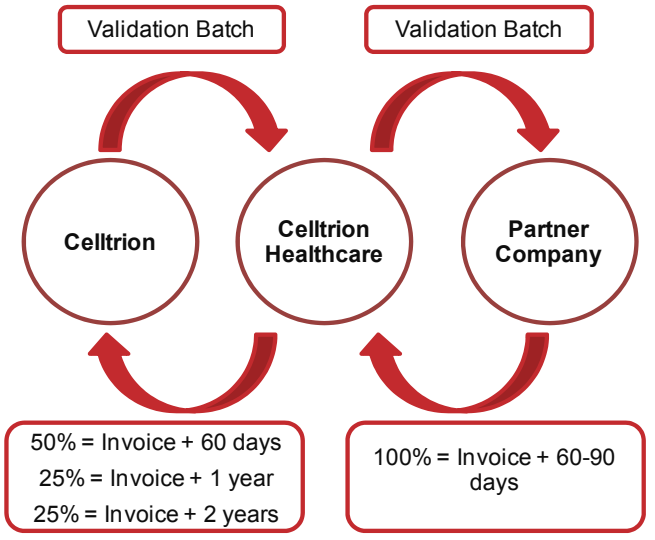
Some companies have publicly commented on payments to Celltrion. EGIS in their quarterly reports, have reported USD17.4mn payment in 2H10. From the contract conditions, this would imply launch in 1H12, presumably in the CIS regions. In its March 16, 2010 conference call for investors, Hikma disclosed an USD10mn upfront payment to Celltrion. Nippon Kayaku has an advance payment of JPY2.6bn in the second quarter (September – November quarter FY11). Although it has not disclosed the nature of the payment, we believe that it is, in fact, payment to Celltrion.

Complicated payment structure between Celltrion and Celltrion Healthcare

All payments from marketing partners go through Celltrion Healthcare. Since Celltrion Healthcare is not a subsidiary but an affiliated company under the Celltrion Holdings

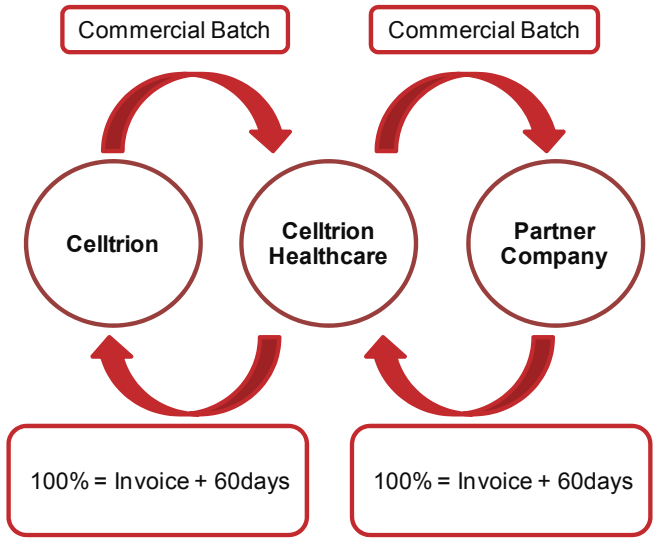
umbrella, there is a delay between the marketing partners' payments and realized cash flow. Although Celltrion realizes sales upon receipt of invoice from Celltrion Healthcare, much of it remains as either trade receivables or long-term trade receivables, for validation batches. This explains the large trade receivables (W82bn) and long-term trade receivables (W46bn) in FY10. However, as shown in the charts below, we believe the cash flow situation will improve dramatically when commercialization batches become prominent starting in FY12.

Fig. 42: Validation batch cash flow diagram



Source: Celltrion, Nomura research

Fig. 43: Commercial batch cash flow diagram



Source: Celltrion, Nomura research

Some assumptions for modelling purposes

For commercial batches, details of profit sharing between Celltrion and various marketing partners have not been disclosed. We have assumed for our forecast that partners will pay Celltrion an estimated 50% of end-market sales in the ROW and 30% for Hospira/Nippon Kayaku. This is based on the assumption that sales of biosimilars would require high overhead in US/Europe/Japan for sales promotion and detailing activity.

According to Celltrion, emerging market validation batches comprised all of FY10 sales. Thus, we have assumed that validation batch sales of CT-P05/P10, planned for FY12, will be about equivalent. Since the products are still being developed, we have applied a 30% discount, resulting in KRW126bn in sales for 2012F.

We have also assumed that Celltrion's sales would be realized a year before end-market sales is recorded, since partners would have to acquire inventory prior to sales. There may be significant discrepancies due to timing, especially on a quarterly basis.

Finally, we have applied a 20% discount to end-market sales when calculating Celltrion's sales, since none of the biosimilars have been approved by EMEA/PMDA. While this assumption is very lenient compared to innovation drugs (usually discounts range from 75-95% in Phase III), the product, after all, is a generic drug. Celltrion has had lengthy discussions with all global authorities prior to IND filing and clinical trials. Celltrion had tested biosimilarity using 40 analytical techniques ranging from basic techniques such as UV-VIS, CD (circular dichroism) to LC-MS/MS peptide mapping and glycosylation analysis. We are relatively confident that the biosimilars will prove equivalent to the original.

FY11F Sales: W300bn

FY11 sales forecast announced by the company on 17 January 2011 disclosed payments of W290bn from Celltrion Healthcare to Celltrion. Since Celltrion recognizes sales upon receipt of invoice, W290bn will be recorded within the year. According to the contract, 75% of sales will be recorded as cash payments from Celltrion Healthcare within a year of receipt. On 16 May 2011, Celltrion issued its January-March quarter

sales report of KRW60bn. The payment is mostly for CT-P06 (Herceptin biosimilar), which is a smaller product compared to CT-P13. We believe that 2H11 sales will be larger than for 1H11.

FY12F Sales: KRW377bn

Celltrion's preliminary estimate for 2012 is KRW400bn. This consists of validation batch payments for CT-P05/P10 from emerging markets, possible additional commercial batches for Hospira/Nippon Kayaku, and commercial batches of CT-P06/P13 in the ROW. We believe that the CT-P06/P13 commercial batches to the ROW will drive sales significantly. As we have stated above, EGIS expects EUR30mn in the first year of launch in 2012/2013F. We assume that Hikma would generate USD10-30mn in Middle East upon launch in 2013. Other regions would also launch in 2013, which would imply significant prior inventory is needed in 2012.

Fig. 44: Celltrion Sales Forecast, 2010-2020FY

Total Sales	2010	2011F	2012F	2013F	2014F	2015F	2020F
CT-P06/P13 Emerging Validation Batch	180,948	0	0	0	0	0	0
CT-P06/P13 Developed Validation Batch	0	290,000	35,000	0	0	0	0
CT-P06/P13/P05 Emerging Commercial Batch	0	10,000	216,000	207,000	336,000	432,000	333,000
CT-P06/P13/P05 Developed Commercial Batch	0	0	0	12,000	74,000	211,900	229,600
CT-P05/P10 Emerging Validation Batch	0	0	126,000	0	0	0	0
CT-P05/P10 Developed Validation Batch	0	0	0	203,000	30,000	0	0
CT-P10 Emerging Commercial Batch	0	0	0	31,000	50,000	74,000	103,000
CT-P10 Developed Commercial Batch	0	0	0	0	17,000	57,900	54,300
Other biosimilars in the pipeline	0	0	0	0	0	126,000	450,000
Others (CT-P19/22/23 + Sanofi-Aventis CMO)	0	0	0	0	0	0	0
Total Sales	180,948	300,000	377,000	523,000	654,000	927,800	1,279,900

Source: Company data, Nomura estimates

Sales to reach KRW500bn in 2013F, KRW900bn in 2015F

Mostly on the strength of emerging market needs, we believe that Celltrion's sales will reach KRW500bn in 2013F and KRW900bn in 2015F. Launch of CT-P06 and CT-P13 in Europe will be delayed until 2014 due to patent/data exclusivity limitations. Although the Japanese Herceptin patent is expected to expire in 2012, Nippon Kayaku believes that bridging clinical studies will take until 2014 to finish. Initial take-up in the developed countries is expected to be slow, for the reasons stated above. For more details on patent expiries, data exclusivity, and launch timings, please refer to Appendix I.

Profit, capex, and capital

Gross profit: rise in labour/depreciation to counter margin expansion from volume

We believe that gross profit margin will be relatively constant at 79-81% of sales until FY15F. According to Celltrion, COGS is composed of 30-40% labour cost, 20-30% materials cost, and about 20% depreciation. Raw materials cost for biosimilars is mostly for reagents for bioreactors, and disposables in the purification process (eg, depth filters in the centrifugation and cell removal process, Protein A chromatographic columns for the purification process). Through interviews with various companies in Japan, India, and Korea, we think that the materials cost for biosimilars is very small. Upon commercial production, the composition of COGS related to materials should decline. Depreciation due to R&D and capital expenditure is also expected to rise, as discussed below.

We believe that labour costs will rise dramatically over the next few years, largely countering the margin expansion from volume. First, rapidly increasing volume will be accompanied by an increase in headcount – Celltrion estimates that headcount should increase by 100 in 2011. Moreover, significant pay raises are expected. Since Samsung

is building its biosimilar manufacturing facility almost adjacent to Celltrion's, it is in the interest of the company to increase salaries for its employees to prevent talent erosion. According to Celltrion, some salaries have already been raised.

Operating profit: Volume expansion to cover increase in labour costs
Celltrion currently does not have any marketing personnel for the Korean market; sales in the Korean market are handled by Celltrion Pharmaceuticals, an affiliated company. Thus, the largest component of Celltrion's SG&A is R&D costs and amortization of capitalized R&D from prior years. Because R&D is capitalized when biosimilarity of the product is established within the company, much of the R&D cost is capitalized and then amortized over 15 years. This may increase dramatically if the company chooses to pursue an aggressive innovation R&D into bio-betters or novel monoclonal antibodies. Currently, the company is not planning to dramatically increase its R&D staff in FY11. Our operating profit forecast is above the Bloomberg consensus of KRW160bn, and represents an operating margin of 54%. Having factored in all of the R&D, headcount increases and salary raises, we think that the volume expansion will handily cover the increase in costs.

Tax rate of 12% for 2011-12FY through tax incentives
Celltrion can take advantage of two tax incentives from the Korean government. First, the biosimilars industry has been designated by the Korean government as a growth priority. Any incremental R&D spending that goes to the development of biosimilars is tax deductible. Because Celltrion spent negligible R&D in 2009 and R&D increased dramatically in 2010, Celltrion's effective tax rate for FY10 was a mere 1%. Second, the Korean government has a Foreign Direct Investment tax incentive. Since 10.5% of the funding for the second facility comes from a foreign investor, 10.5% of CT-P10/05 sales will be subject to tax incentives. With the two effects combined, Celltrion assumes an effective tax rate of near 12% for 2011-12FY, and 15% for 2013F onwards.

Capex and depreciation: Third facility to bring total capacity to 240,000L
Celltrion plans on W190bn in capital expenditures in FY11F. KRW70bn will be used for construction of the second facility, with 90,000L capacity. KRW120bn will be spent as capitalized R&D for biosimilars development. We assume that the company will build a third facility in 2012 to handle increasing volume and the next set of biosimilars. In 2012, the company is planning to spend KRW100bn in R&D. We assume KRW100bn for the third facility, although the number could be much less since land for the third facility has already been purchased.

Capital: Rolling over KRW100bn in 2011, need more for the third plant in 2012F
Celltrion has W132bn worth of long-term debt that matures in FY12F. Celltrion expects to roll over this debt. Additionally, we believe that the company may need additional loans for the third facility. We have assumed another KRW100bn increase in debt in FY12F. Most of the loans can be repaid within three years.

Others: Stable dividends, minimal forex exposure
Celltrion does not have a concrete dividend policy as yet. To appeal to retail investors, Celltrion plans to pay stable dividends for the foreseeable future. Finally, we note that the company has very little forex exposure, since all payments from Celltrion Healthcare are in Korean won.

Risks

1. MAJOR ASSUMPTION: Celltrion's processes more efficient than the innovators

The major assumption behind the forecast is our belief that Celltrion's processes are cost competitive compared to innovators' processes which predate Celltrion by some 20 years. Yet, through numerous interviews with people in the industry, there is some evidence that innovative companies have methodically reduced production costs by streamlining processes in every step of manufacturing/purification. In the worst-case scenario, major innovators may even have a more efficient production process than biosimilar companies. If this is the case, we can anticipate aggressive pricing strategies to fend off biosimilar competition. There is a possibility that innovators' pricing strategies against biosimilars may vary significantly from strategies that have historically been adopted for small molecule drugs going off patent.

2. The result of clinical trials may not be acceptable to the EMEA/PMDA/FDA

It goes without saying that the results of Celltrion's global clinical trials will be the single most critical factor in determining the company's immediate- and long-term success. We believe that the clinical results of CT-P06 must show an ORR of approximately 50% with a 95% confidence interval of 42-58%, equivalent cardiotoxicity, as well as comparably low levels of immunogenicity. Clinical results of CT-P13 must show that approximately 50% of patients have been able to attain ACR20 improvement and that the immunogenicity is under 10%. While we are of the opinion that the quality of Celltrion's biosimilars complies with the highest global standard, the results of the trials must persuade the regulators that the biosimilars are effective and safe to use. As these trials are among the first few global clinical trials for biosimilars, we expect them to face rigorous scrutiny. If the clinical trials show marked disparity between the original and the biosimilar product, Celltrion may have to reinitiate the trial process. This would thus have a very significant negative impact on earnings. Again, we believe that Celltrion's product is most probably the best biosimilar made so far in the world, in terms of bioequivalence, rigorous analytical testing, and experience in manufacturing. We are using a 20% discount rate for CT-P06 and CT-P13 to account for the regulatory risk in Phase III. Note that this is an extremely high discount rate for any innovative drug in Phase III trials and that we are very confident that Celltrion will gain acceptance from global authorities.

3. A "biosimilar cold war"

What began in Korea as a government initiative to boost investment into a growing biosimilar industry could eventually turn out to be a biosimilar cold war of nations, with each nation trying to protect its own biopharmaceutical industry and lower its medical bills. Recent developments in Brazil and Russia indicate the protectionist agenda of governments to promote their domestic biosimilar industries through subsidies and contracts. In February 2011, the Russian government signed a decree to grant a subsidy of USD5mn to Biocad for the production of rituximab, trastuzumab and bevacizumab. In April this year, the Brazilian Ministry of Health (MOH) signed an agreement with PharmaPraxis to manufacture biosimilar adalimumab. PharmaPraxis estimates that the Brazilian government spends BRL2bn (USD1bn) annually on procuring biologics, or 41% of the MOH's medicine budget. We think that the recent developments clearly underscore a growing protectionist attitude of governments, which could overflow to other countries such as China and India amongst others.

4. Opaque payment structure between Celltrion and Celltrion HC does not bolster investor confidence

Celltrion has a complicated cash flow structure wherein it channels all its partner sales via the privately held Celltrion Healthcare. These cash flows further differ for validation batches and commercial batches. When Celltrion sells a validation batch to Celltrion Healthcare, the former is invoiced 50% of payment within 60 days, the next 25% within one year and the remaining amount within two years from the date of invoice. However, when a commercial batch is sold to Celltrion Healthcare, Celltrion receives 100% of the payment within 60 to 90 days from the date of invoice. While this payment structure shields Celltrion from cash flow fluctuations, the payment terms for validation batches significantly increase the accounts receivables and affects cash flows. Until 2015, a

majority of Celltrion's supplies will consist of validation batches, and therefore we expect these to drag the cash flows. We hope that Celltrion Healthcare is merged with Celltrion at the earliest opportunity when cash flow problems are resolved.

5. Innovators spreading fear of biosimilars

Innovator companies have repeatedly claimed in the past that the quality of small-molecule generics is inferior to the original. This can be expected to go up a notch with biosimilars since, by definition, biosimilars are not perfectly equivalent to the original. A good case in point is Reditux in Peru.

Case study in raising doubts about biosimilars: Reditux in Peru

Dr. Reddy's, with its Peruvian partner, registered Reditux with the Dirección General de Medicamentos, Insumos y Drogas (DIGEMID) in 2008, and the product was launched the following year. In 2011, Peruvian newspaper *El Comercio Peru* reported that Roche, in a letter to DIGEMID, had questioned the quality of Reditux and requested for additional clinical studies of the biosimilar. DIGEMID replied to Roche in February 2011 and the correspondence between the government authority and the innovator company was made available to the media. DIGEMID in its reply said that more clinical evidence was required to establish the similarity between the biosimilar and the original product. The news raised some public concern as patients and doctors requested the regulatory authority to establish clear guidelines for the approval of biosimilar products. The local media also attempted to link the deaths of five children suffering from acute lymphocytic leukaemia to the use of Reditux, although no conclusive evidence to support the claim is currently available. It has been reported that the deaths of the children may have been caused by the use of low-quality methotrexate during chemotherapy. Such incidents of leaking confidential information to the media in order to spread panic amongst doctors and patients and gather public opinion may be defence strategies that innovator companies may adopt in the future.

6. Biobetter Competition

The strongest defence strategy of innovator companies in order to stave off biosimilar competition and defend their biologics turf is by developing bio-betters. These enhanced biologics are also being developed by rival innovators as well as several generics and biotech players. If innovators or other companies are successful in developing improved versions of original biologics that can offer greater efficacy and better safety profiles, they could pose a significant threat to the uptake of biosimilars, along with eroding some of the market share of original biologics. Antibody drug conjugates such as T-DM1 have shown significantly higher Progression Free Survival in Phase II clinical trials but the benefits of the biobetter need to be juxtaposed with its adverse effects, such as increased liver toxicity and thrombocytopenia, in order to ascertain the potential of the drug.

7. End-User Acceptance

The safety and efficacy profiles of biosimilars will remain of paramount concern to doctors and patients. For doctors who currently prescribe original biologics, a switch over to prescribing biosimilars to patients will require a shift in mindset. Celltrion and its marketing partners will have to put in a significant amount of effort to convince doctors about the bioequivalence and benefits of these drugs. In case the results of the clinical trials are not as robust as required, Celltrion may face the difficult task of gaining the confidence of the medical and patient community at large. While patients who are currently unable to afford original biologics may be induced to using biosimilars, we believe that patients who are currently able to afford expensive biologics may not switch to biosimilars as easily due to a lack of availability of extensive safety and clinical data.

8. Patent Litigation

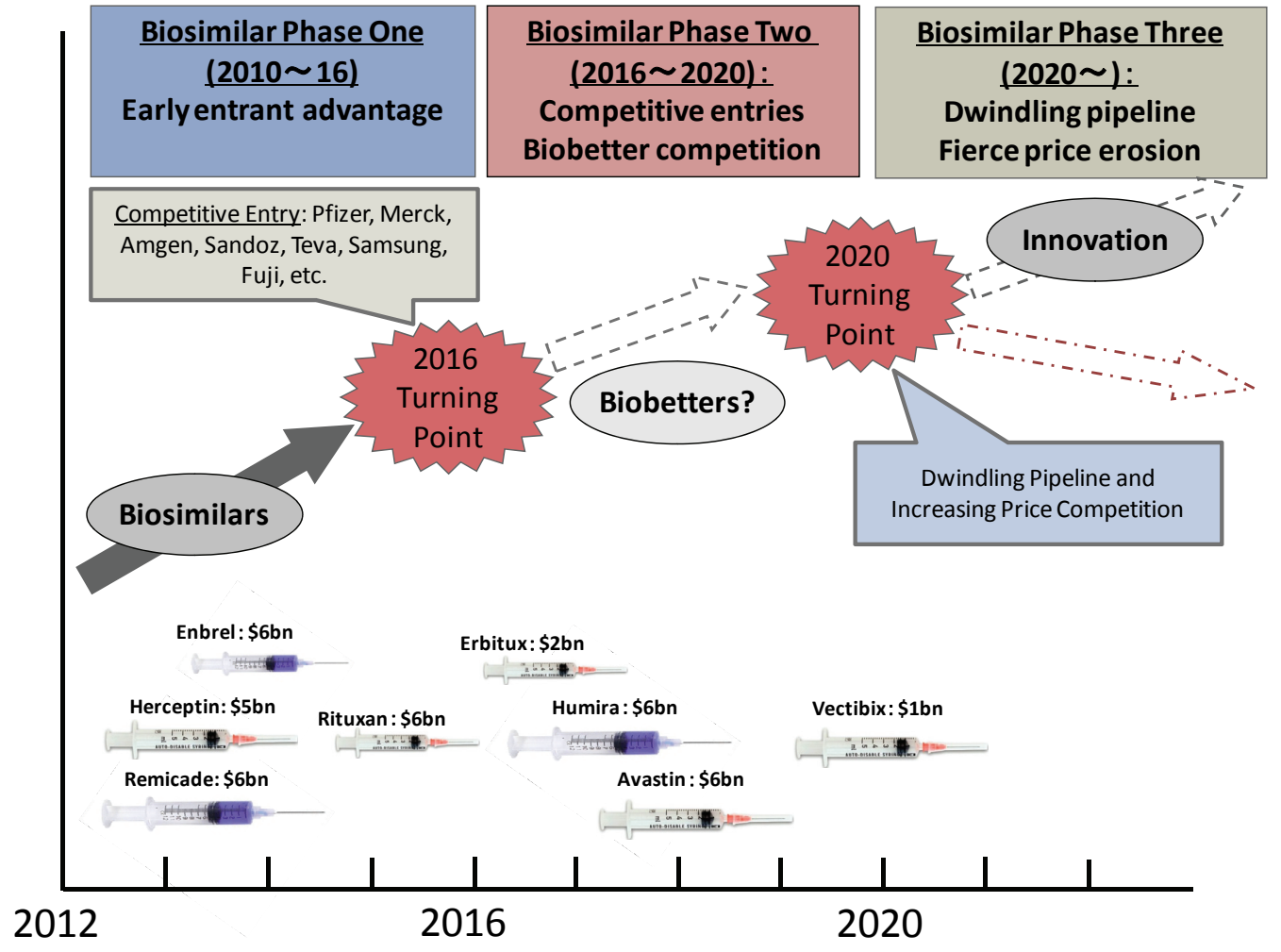
Once biosimilars are approved, biosimilar companies could face patent litigations from innovators who may challenge these companies for infringing patents. While Celltrion and its partners aim to launch biosimilars in regulated and semi-regulated markets after the expiration of the substance patent(s), innovators may challenge biosimilars for infringing non-substance patents such as formulation patents. Lengthy litigation processes can stall the entry of biosimilars in these markets and significantly impact revenues from these regions.

Epilogue: Demise of the biosimilar industry and Celltrion's path forward

The inevitable rise of biosimilars and its equally inexorable demise

Having predicted the inevitable rise of biosimilars worldwide, we end this report by charting the course of what we see as its equally inexorable demise. Growth of the biosimilar industry will end abruptly near 2020, for the very simple reason that beyond Avastin in 2019 (US/EU), patent expiry of blockbuster biologics comes to an end. There are other drugs, such as Vectibix, Lucentis, Actemra, Simponi, but their sales potential is limited. Many competitors will have entered the market, making price erosion increasingly common. The malaise that we see earlier afflicting the oral small molecule generics in 2015-2020 will also come to haunt biosimilars by 2020. A decade is a very short time in the pharmaceutical industry: it is basically the time required between IND and approval of exactly one innovative molecule. It is our opinion that the long-term cash flow, and with it, the actual enterprise value of Celltrion will depend heavily on the actions taken by management within the next five years.

Fig. 45: Three phases of the biosimilar industry: Phase one (2010-16), Phase two (2016-20), Phase three (2020-)



Source: Nomura

In the end, it is always innovation

All industries based on emulation are unsustainable because there will always be new entrants. The only path forward for Celltrion or any other biosimilar player is to find a path toward innovation. We believe that Celltrion already has the right long-term view. The company after all was founded ultimately to develop innovative therapeutics. Biosimilars are merely a source of cash flow that can be reinvested in future R&D.

So what should Celltrion do? Five pointers

To maximize the long-term value, we believe that Celltrion should take the following actions:

- **Learning from big pharma's mistake:** The ever-dwindling returns of in-house R&D over the years is a tired subject in large-cap pharmaceutical companies in US/Europe/Japan. Korean pharmaceutical companies, however, are still fresh to pharmaceutical R&D. They already exhibit all the same warning signals of their ill-fated predecessors: an overreliance on in-house R&D. We believe that Celltrion should learn from the mistakes made by their larger peers and aggressively in-license/acquire technologies rather than attempt to invent everything themselves. In this view, a sure sign of worsening returns is a sustained large increase in R&D personnel without a clear focus of therapeutic area, or direction of R&D. We believe that this is unlikely at the moment, since Celltrion is still preoccupied with biosimilars
- **Be global:** Because of its highly regulated nature, pharmaceutical industries tend to be more domestic in mindset than other industries such as consumer electronics or automobiles. Asian pharmaceutical companies are especially prone to navel-gazing complacency. For example, because Japan had a large pharmaceutical market and saw continuous approvals of small-molecule blockbusters, Japanese companies failed to see the rise of the biopharmaceutical market. Now Japan is far behind US/Europe; Japan currently has just two companies with a successful history of innovative biologics (Kyowa Hakko Kirin and Chugai), and two biologic CMOs of middling size. Although accessing Korean biotechnology is good, Celltrion should look far and wide for investment very early on.
- **Investing and in-licensing novel methods of antibody production:** The biggest long-term threat to bioreactor-based antibody production is the rise of novel antibody production technology. Though antibody production from bio-engineered cattle, mice, chickens and vegetables has long been studied with little success, there is a chance that within the next 10 years a successful alternative to bioreactor-based antibody production might emerge. Investment into transgenic animal/plant production is a plus.
- **Be careful with bio-betters:** As we discuss in Appendix III, most brand-name biologics companies' biosimilar defense strategies involve the development of next-generation antibody therapeutics. Some (Roche's TDM-1 and Biogen-Idec/Roche's GA-101) are bio-betters in the sense that they are slightly modified antibodies. As is also discussed in the same section, none shows significant improvement. If Roche/Genentech with 20+ years of biological experience is not able to create viable bio-betters, biosimilar companies may have even more issues tackling the problem.
- **In the end there is always a big tank:** The most important factor in the long term for Celltrion is that the company has a very large manufacturing capacity, possibly as large as 240,000L in 2013-14F. If biosimilar pipelines dwindle and innovation stalls, the company can always opt for the CMO option and make antibodies for other companies.

Appendix I: Market dynamics and forecast details

Understanding the market dynamics of herceptin

CT-P06: the simplest case

CT-P06 is the biosimilar of brand name Herceptin, common name trastuzumab. We believe that trastuzumab presents the simplest case for biosimilar penetration because: (1) there is basically only one indication, (2) there are no competing antibodies and treatments (though there are bio-betters in development, see Appendix III), (3) it is the gold standard first-line adjuvant/metastatic breast cancer treatment preferably used when possible, and (4) competition with other biosimilars is not anticipated at least until around 2015-16F. We believe that Herceptin will provide a very important revenue stream for Celltrion going forward.

What is Herceptin?

Herceptin is a HER2 inhibitor developed by Genentech, now a part of Roche. HER2 receptors are regulatory proteins that are overexpressed on the surface of cancerous cells in about 25% of breast cancer patients. HER2 acts to regulate cell proliferation. When overexpressed, cells multiply uncontrolled, one of the hallmarks of cancerous cells. HER2 overexpressed breast cancers were known for their aggressiveness and poor prognosis before the advent of Herceptin. Herceptin binds to HER2 receptors, which prevents the activation of the signaling cascade, resulting in cell cycle arrest. Herceptin gained FDA approval in September 1998 for treatment of HER2 positive metastatic breast cancer. Current indications include:

- Adjuvant treatment (chemotherapy after cancer has been surgically to suppress remaining cancer cells) of HER2 overexpressing breast cancer
- HER2 overexpressing metastatic breast cancer
- HER2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma in US/Europe/Japan.

Adjuvant treatment accounts for 75% of Herceptin sales

The bulk of Herceptin sales in any region comes from adjuvant/metastatic breast cancer indications. According to Amit Roy, head of Nomura's European Pharma Team, the sales breakdown by indication for Herceptin is about 75% adjuvant breast cancer and 25% metastatic breast cancer. Since HER2 positive gastric cancer indication was only recently approved in February 2010 in EU, October 2010 in US, March 2011 in Japan, its contribution to sales is limited. We note that gastric cancer is relatively rare in the US/Europe; Roche believes the US market for gastric cancer is about USD50mn. Gastric cancer is extremely common in the Far East; the potential market size expands to USD200-300mn in Japan alone (6 February 6 2010 Roche conference call).

AC+TH treatment standard in US/Europe, Japan uses monotherapy

The recommended regimen in US/Europe for adjuvant patients is AC + TH (anthracyclin followed by trastuzumab concurrent with taxanes, usually paclitaxel or docetaxel). The regimen is shown in the table overleaf. The treatment lasts exactly one year and costs JPY2.63mn in Japan and over USD30,000 in the US. In Japan, Herceptin monotherapy after AC regimen from the HERA clinical trial is generally followed (this is the only regimen that appears on the label). Here, the cost is JPY1.51mn in Japan. Note that Herceptin accounts for some 70% of the cost. Other combinations with chemotherapy are also possible.

Fig. 46: Adjuvant breast cancer treatment in Japan: maximum annual cost with Herceptin monotherapy

Assumes 4x q3w AC treatment, see Figure 48 for AC treatment

Every 3 weeks			
First day	Day 2-21	Day 22	Day 23-42
Herceptin Initial Load 8mg/kg	Rest	Herceptin 6mg/kg	Rest
168,330		112,220	
Total	168,330		112,220
Maximum Annual Cost	**1,514,970**		

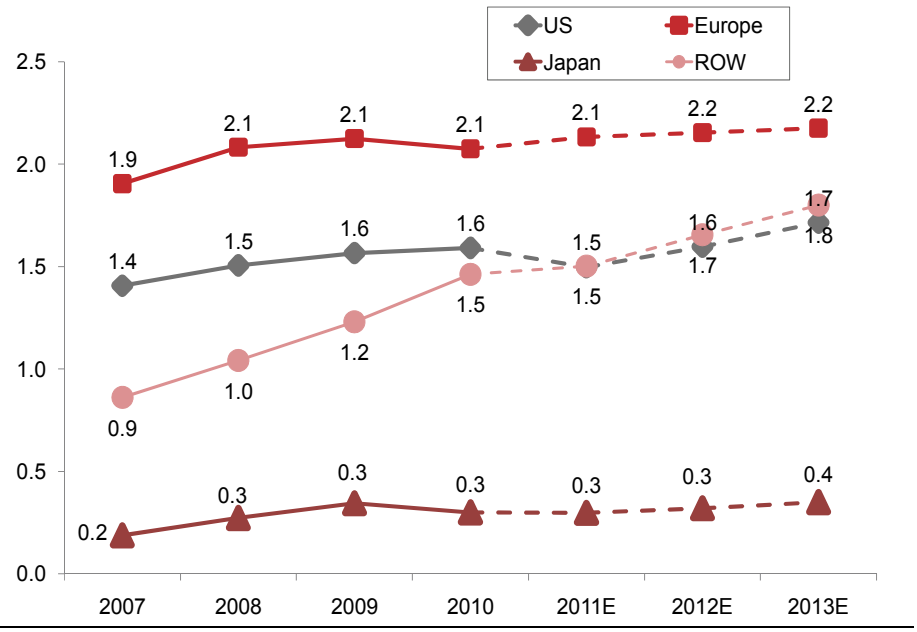
Source: Government drug prices

Fig. 47: Cost of Herceptin adjuvant breast cancer treatment in Japan: Maximum annual cost for AC + T with trastuzumab

Every 3 weeks, repeated 4x			First Week Only		Weekly x11		Weekly x28	
Day 1		Day 2-20	Day 1	Day 2-6	Day 1	Day 2-6	Day 1	Day 2-6
Doxorubicin 60mg/m2	Cyclophosphamide 600mg/m2	Rest	PTX 80mg/m2 IV 1hr		PTX 80mg/m2 IV 1hr			
¥20,934	¥698		¥46,911		¥46,911			
granisetron 40μg/kg	Dexamethasone 8～20mg/day		Herceptin Initial Load 4mg/kg	Rest	Herceptin 2mg/kg	Rest	Herceptin 2mg/kg	Rest
5,494	1,158		80,102		47,984		47,984	
Total JPY		113,138				1,170,858		1,343,552
Maximum Annual Cost - JPY	**2,627,548**							
Herceptin Cost - JPY	**1,951,478**							

Source: Government drug prices

Fig. 48: Herceptin sales forecast



Source: Roche results, adapted from Nomura Europe forecast

Sales forecast: growth in Japan from new gastric cancer indication

Sales trend and Nomura forecast of Herceptin is shown in Figure 49. Roche commented in the conference call on 6 February 2010 that Herceptin is already highly penetrated in the US and Europe and that further growth must come from Japan and ROW. Chugai Pharmaceuticals has also commented that penetration of Herceptin adjuvant/metastatic breast cancer is 90% in Japan. Chugai had also announced in March 2011 that they have received approval for indication in gastric cancer. Since gastric cancer is the most

common cancer in Japan with a yearly patient population of 120,000, we believe that the new indication will contribute significant growth to the brand-name drug.

Roche's Herceptin penetration rates in ROW

Similar to what we have predicted for CT-P06, brand-name drug maker Roche also believes that ROW holds great untapped potential. In its 2 February 2011 investor presentation, Roche claimed that the penetration of Herceptin was only 7% in China and 25% in Russia. By 2012, the ROW market may become 80% of the US market in size. Roche intends to introduce specific pricing programs to widen the user base, called flexible pricing, which we have discussed in the ROW section above.

Patent expiry: US 2019, EU 2014, Japan 2012

Key regional patents of Herceptin are listed in the table below. Our research suggests that the key regional patents for Herceptin have not expired. Roche has claimed that Herceptin expires in the US in 2019, but earlier for Europe and Japan. It appears that Japan may face the earliest expiry in 2012, though biosimilars will not be available until at least 2014. European SPC (supplementary protection certificate for patent extension) for EP0590058 has been granted in multiple countries. According to the European Patent Office, the SPC expires (GB04/015 and FR04C0007) on July 2014 in both the UK and France.

Fig. 49: Key regional patents for Herceptin

Herceptin	Patent Title	Submission Date	Estimated Patent Expiry
JP4124480	Method for Making Humanized Antibodies	Jun-15-1992	2012
EP0590058	Humanized Heregulin Antibody	Jun-15-1992	2014
US5821337	Immunoglobulin Variants	Aug-21-1992	2015
US6407213	Method for Making Humanized Antibodies	Jun-15-1992	2019

Source: Nomura, EUPTO, JPO, USPTO

Fig. 50: Patient Population Estimate: Herceptin

Herceptin Sales (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
Herceptin ($, US)	1,525	1,559	1,664	1,786	2,094	2,115
Herceptin (€, Europe)	1,500	1,462	1,476	1,491	1,489	1,504
Herceptin (¥, Japan)	25,242	25,765	27,667	30,260	34,583	36,313
Herceptin ($, ROW)	1,403	1,565	1,724	1,875	1,927	1,979
Herceptin Total						

Annual cost per treatment (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
	(Adjuvant AC + TH regimen, 60kg, 240mg on day 1, 120mg subsequent, JP Only: AC					
Herceptin ($, US)	35,217	35,217	35,217	35,217	35,217	35,217
Herceptin (€, Europe)	26,400	26,400	26,400	26,400	26,400	26,400
Herceptin (¥, Japan)	1,514,970	1,514,970	1,439,222	1,439,222	1,367,260	1,367,260
Herceptin (INR, ROW, India)	957,273	957,273	957,273	957,273	957,273	957,273
Herceptin (Yuan, ROW, China)	263,864	263,864	263,864	263,864	263,864	263,864
Herceptin (ROW, USD, India)	20,969	20,810	20,810	20,810	20,810	20,810
Herceptin (ROW, USD, China.)	38,981	39,383	39,383	39,383	39,383	39,383
Herceptin (ROW, USD, est.)	20,000	20,000	20,000	20,000	20,000	20,000

Est. Number of Patients (# of Patients)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
Herceptin (US)	43,300	44,300	47,200	50,700	59,500	60,000
Herceptin (Europe, UK)	56,800	55,400	55,900	56,500	56,400	57,000
Herceptin (Japan)	16,700	17,000	19,200	21,000	25,300	26,600
Herceptin (ROW, est.)	70,100	78,200	86,200	93,800	96,400	99,000

Source: Nomura, Japanese government prices, Red Book 2010, MIMS (India Prices), China prices courtesy of Gideon Lo (Nomura HK)

Data Exclusivity: JP gastric cancer will expire in April 2011
Because the EU clinical trial is already initiated, by definition the data exclusivity for Herceptin has expired. We assume the same with the US. In Japan, Chugai was not granted an additional period of data exclusivity for the gastric cancer indication approved on March 2011, because dosage for gastric cancer was identical to that of breast cancer. As it stands, all data exclusivity for Herceptin will expire in April 2011. Thus, we believe that Celltrion and partner Nippon Kayaku will also be able to add gastric cancer to the list of biosimilar indications. This is a very important point in a region where effective treatment to gastric cancer is highly sought-after.

Patient demographics: predominantly price sensitive elderly women
In all areas of the world, patients are predominantly women over 50-60 years old. Prevalence is much higher in the US (83 per 100,000) and Europe (80-90 per 100,000) than in Japan (43 per 100,000) or in other parts of Asia. In the US every year about 200,000 patients are diagnosed with breast cancer, over 300,000 in Europe and 50,000 in Japan. We believe that the patient demographics point to a very price-sensitive population, since (1) patients are nearing retirement or have retired, (2) women in certain regions such as Asia in this age group are generally unemployed.

Patient population estimate
We have estimated the patient population of each biologic assuming year-long adherence to a treatment regimen from publicly available data. Some caution is necessary when interpreting the calculated population number, since it is a “ballpark” estimate based on assumptions of indication distribution and may well deviate from the actual number. We do believe, however, this could be a good way of estimating sales from assumptions of biosimilar penetration rates in each region.

Celltrion’s CT-P06 Forecast

Global clinical trials: patient enrollment to be complete by June 2011
The list of clinical trials for submission of CT-P06 biosimilar is shown in the table below. According to Celltrion sources, other clinical trials are under way in regions that have not been disclosed. These clinical trials were designed through extensive discussions with authorities in each country, with particular focus on EMEA requirements. We focus on the clinical trials registered in the EudraCT database 2009-016197-33. We believe that all of the clinical trials underway focus on the HER2 overexpressing metastatic breast cancer indication; none are designed for the adjuvant breast cancer or gastric cancer indication. The European trial targets enrollment of 84 patients in Europe. According to Celltrion, the global target is 536 patients. We expect patient enrollment to be complete globally by June 2011.

Fig. 51: Clinical trials in progress for CT-P06

NCTID/EUDRACT/Japan	Compound	Country	2010				2011				2012				2013				2014			
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
2009-014463-39	CT-P6	UK		PIII				EC			S											
2009-016197-33	CT-P6	AT	PIII					EC			S											
		BG	PIII					EC			S											
NCT01084863	CT-P6	KO	PI/II					EC		S	A											
NCT01084876	CT-P6	RO		PIII				EC			S											
-	CT-P6	SG	PIII					EC			S											
CTRI/2010/091/001181	CT-P6	IN		PIII				EC		S												
-	CT-P6	PH	PIII					EC		S												

PI/II = Start of Phase I/II
PIII = Start of Phase III
PI = Start of Phase I
EC = Enrollment Complete
S = Submission
A = Approval
○ = Start of Sales

Source: DART publication, EudraCT (EU), Clinicaltrials.gov (US), Nippon Kayaku (Japan)

Data extrapolation should be possible for adjuvant setting

Even though the existing clinical trials are evaluating the bioequivalence between biosimilar CT-P06 and original Herceptin solely in metastatic breast cancer patients, we believe that the data can be extrapolated to cover the adjuvant breast indications. Metastatic breast cancer comprises at most 30% of sales in any region; the number of cases is vastly outnumbered by patients in the adjuvant setting. Therefore, it would not make much business sense for Celltrion to miss out on the adjuvant opportunity. Note that dosage is similar in either setting: initial dose of Herceptin 4mg/kg, followed by Herceptin 2mg/kg every week maintenance dose. Since the clinical trials were designed in close consultation with EMEA, we think that the EMEA authorized Celltrion to conduct trials only in metastatic breast cancer patients, and afterwards extrapolated to cover the adjuvant indication.

Fig. 52: Comparison of Clinical Trial Design : CT-P06

	H0648g Trial (2001)	CT-P06
Inclusion Criteria	Women with HER2 overexpressing cancers who had not received prior chemotherapy	Women with HER2 overexpressing cancers who had no prior Herceptin/chemotherapy treatment or **as adjuvant/neoadjuvant discontinued >12 months** before trial
	-	Have at least 4 weeks since last surgery or radiation therapy
	-	AST and ALT < 2.5x ULN
Exclusion Criteria	Received prior chemotherapy	Received prior chemotherapy (for metastatic breast cancer)
	Brain metastases	Brain metastases
	-	Receiving concurrent hormonal therapy or immunotherapy
	-	**CHF patients in any NYHA class, LVEF < 50%**
	Have received treatment with any other investigational drug in the last 30 days	Have received treatment with any other investigational drug in the last 30 days
Dosage	Loading dose 4mg/kg, maintenance dose 2mg/kg once a week	Loading dose 4mg/kg, maintenance dose 2mg/kg once a week
Primary Endpoint	Time to Disease Progression	ORR at 6 months by Response Evaluation Criteria in Solid Tumours RECIST 1.1
Secondary Endpoint	ORR, Duration of response, time to treatment failure, OS	Comparable safety, pharmacokinetic bioequivalence in CtroughSS
Sample Size	469	84 (Europe) 536 (global)
Primary Endpoint Results	Median Time To Progression: 7.2 (Herceptin) 4.5 (Chemotherapy)	-
Secondary Endpoint Results	**ORR 50% (Herceptin) 38% (Chemotherapy)**	-
PK	t1/2 = 6days, **CtroughSS = 79mcg/mL**, CpeakSS = 123mcg/mL	-
Adverse Events	Infection 47% (Herceptin + Chemo) 29% (Chemo alone) **18 patients in the trastuzumab subgroup discontinued due to cardiac dysfunction**	-
Immunogenicity	Among 903 women with metastatic breast cancer, only 1 tested positive to HAHA (human anti-human antibody)	-

Source: Clinicaltrials.gov, EUdraCT

Data extrapolation to gastric cancer: a strong possibility

Since gastric cancer is one of the top cancers in the Far East region, Japan and ROW sales projections can vary considerably depending on the assumption made on sales for this indication. Gastric cancer dosage is very different from the metastatic/adjuvant indication: the initial dose is 8mg/kg and the maintenance dose is 6mg/kg every three weeks instead of every week. Ordinarily this would require a separate clinical trial. Though it remains to be seen whether EMEA and PMDA would allow extrapolation to gastric cancers, past examples with first-generation biosimilars have seen extrapolation to indications with very different dosages. For example, “Epoetin Alfa BS1500IU,” a

biosimilar erythropoietin approved by the Japanese PMDA in 2010, had conducted clinical trials for anemia in dialysis patients (3,000IU three times a week). Data was extrapolated to include indication for neonatal anemia, where the dosage is 200IU/kg twice a week.

Comparison of clinical trials: H0648g pivotal trial vs. Celltrion's study

Clinical design of the original pivotal study for use of Herceptin in metastatic breast cancer patients (H0648g Trial) and Celltrion's European clinical study (2009-016197-33) is contrasted in the table on the previous page. The disadvantage of Celltrion's trial is that there are very few naïve metastatic patients remaining due to the successful penetration of Herceptin in the adjuvant setting worldwide. Thus, the inclusion criteria for Celltrion's trial admit patients who have been treated for adjuvant treatment as opposed to the original trial which enrolled only naïve patients. Although a washout period of greater 12 months is in place, this may affect the comparison of efficacy. The advantage of Celltrion's trial is that cardiotoxicity of Herceptin has been studied extensively since the original pivotal trial. To exclude adventitious cardiac dysfunction, Celltrion's trial screens for cardiac function. Furthermore, cardiotoxicity arising from the concurrent use of anthracyclines and Herceptin is now well understood. Thus, cardiotoxicity adverse events should be no greater or possibly less than the pivotal trial. We believe the trial is adequately powered with n=536, where the original trial had n=469.

What is needed for EMEA/PMDA acceptance?

Due to persistent doubts about the quality of biosimilars in developed countries, clinical outcome data of biosimilars will be placed under rigorous scrutiny, almost on par with the attention to detail lavished on innovative drugs. We believe the clinical trial results must show the following for approval by EMEA/PMDA:

- Efficacy: Assuming the trial uses anthracyclin + cyclophosphamide + Herceptin regimen, we would expect ORR to be within statistical equivalent to the results from the original trial. The original trial showed ORR of 50%, with 42-58% being the 95% confidence interval.
- Pharmacokinetics: Similar half life of six days, concentration at trough at stable state of 79mcg/mL
- Adverse Events: ～50% infection rate but cardiotoxicity not worse than the original trial
- Immunogenicity: very low or almost undetectable as with the original

It is of paramount importance for the biosimilar CT-P06 to show bioequivalence in efficacy. For approval by EMEA/PMDA/FDA, it is absolutely essential that non-inferiority to original is proven with statistical significance. Pharmacokinetics may show some variation from the original, but in past cases (e.g. erythropoietin biosimilars in Europe/Japan) changes in PK was acceptable to authorities, so long as the efficacy is proven. Pronounced difference in immunogenicity will be of significant issue to EMEA/PMDA if neutralizing antibodies are produced in excess of what was found in the original. Also, cardiotoxicity must be below or equal to the original for Europe/Japan/US approval. In short, CT-P06 will have to demonstrate: 1) non-inferiority in efficacy; 2) similar immunogenicity; and 3) similar adverse events with a particular emphasis on cardiotoxicity.

Approval timeline: 2012 in Emerging countries, 2014 for Japan and Europe

The forecasted approval timeline is given in the table on the previous page. After patient enrollment, the trial duration is six months, and with two months work up of clinical data, we expect submission in 1Q12 or 4Q11. Celltrion is hoping for a submission in 4Q11. The earliest launch will be in Korea where the KFDA is actively encouraging the development of biosimilars by allowing for a rolling BLA. Thus, somewhat conservatively, we expect approval by 2Q12 and launch in 2H 2012. Celltrion has not specified the timing of launch in emerging markets. Based on interviews with EGIS, the Eastern Europe launch is expected in 2013. Because of the aforementioned patents, marketing in Western Europe cannot start until July 2014 at the earliest. Finally, according to Nippon Kayaku, approval of CT-P06, at the earliest, will be in 2014.

Fig. 53: Approval timeline for CT-P06

Region	Compound	2010				2011				2012				2013				2014			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Korea	CT-P6						EC			S	A	○									
SE Asia/LatAm/CIS	CT-P6						EC			S	A	○									
Eastern Europe	CT-P6						EC			S				A	○						
Western Europe	CT-P6						EC			S				A						○	
Japan	CT-P6								PI		PIII					S				A	○
Other Regions	CT-P6						EC			S				A						○	

PI/II = Start of Phase I/II
PIII = Start of Phase III
PI = Start of Phase I
EC = Enrollment Complete
S = Submission
A = Approval
○ = Start of Sales

Source: Nomura research

Base assumptions for CT-P06 forecast

Forecast for CT-P06 biosimilar is based on two main assumptions:

- The penetration Rate in Japan is Not at Saturation: We believe that in Western Europe and the US, the penetration of Herceptin in adjuvant/metastatic breast cancer setting is at saturation. Chugai Pharmaceuticals also claims that the Japanese penetration rate is near saturation at >90%. However, from interviews with companies in Japan, we believe that the penetration rate is lower than it is claimed. The estimated number of patients is inflated by the fact that: 1) patients who had received trastuzumab in the adjuvant setting then advance to the metastatic setting in some cases; and 2) some doctors prescribe Herceptin to non-HER2 positive breast cancer patients. We estimate the actual penetration rate in Japan to be 70-80%.
- Assumes Gastric Cancer Indication will be approved (or used off-label in ROW): As noted above, there are some doubts as to whether the gastric cancer indication will also be included for biosimilar CT-P06. At this point, we believe that the European/Japanese authorities would tend towards allowing extrapolation of data to gastric cancer indication, if the clinical data shows sufficient bioequivalence. In any case, we also believe that the gastric cancer indication will be used off-label in Far East Asia where the disease is most prevalent.

Biosimilar penetration assumption in ROW

As discussed in Chapter III, ROW is the largest driver of biosimilar growth. When a biosimilar is introduced in the market at 50% of the originator's price, biosimilars are able to access untapped markets. This "market creation effect" is expected to increase over the years with increasing affluence in emerging nations. As shown in the above table, our forecast contains three scenarios: 1) Scenario A where the introduction of biosimilars expands the user base by 100% in 2020; 2) Scenario B 200% in 2020; and 3) Scenario C 400%. Note that the percentage levels of population using Herceptin for all scenarios are well below those of the developed nations.

We believe that CT-P06 will take at most 20% by volume of the expanded Herceptin patient base. Although Celltrion expects a 50% market share by volume in ROW, we have not incorporated their forecast because: 1) Roche will probably adjust prices to about 70% of the current level; this would siphon off a large share of more affluent patients; and 2) extremely cheap and low-quality antibody therapeutics from other countries are likely to flood the market. Note that we assume the patient base using Herceptin would expand threefold over 10 years. The market share of 20% in the expanded patient volume is actually equivalent to 50% in the non-expanded patient set.

Taking Scenario B as our scenario of choice, we forecast that ROW sales to Celltrion will reach KRW140bn by 2015 before reaching a peak of near KRW400bn in 2020, despite losing share in the last three years of the decade due to competitive pressure.

Biosimilar Penetration Assumption in Japan

As discussed in the summary, we believe the Japanese market will behave like the ROW region to a limited extent. The Japanese pharmaceutical pricing system will allow only a 30% cut to the originator price. At this price differential, we believe that the "market creation effect" will be limited to a 30% increase of the market from the baseline in 2020. Note that the 30% increase also includes expansion of patients from gastric cancer. Because of Nippon Kayaku's known strength in the oncology area, we forecast a bullish 30% peak market share. Still, we forecast Celltrion sales of KRW5bn in 2015, and peak sales of KRW28bn in 2017-2018, almost negligible amount. Should Nippon Kayaku decide to lower prices even further to 50% of the originator price or lower, we believe that the market share would expand to as much as 50% by volume.

Biosimilar Penetration Assumption in Europe

Since automatic substitution of biologic agents with biosimilars is not allowed in the major European markets (UK, France, Germany), we believe that biosimilar penetration in Europe will be limited to at most 10% by volume. Unfortunately, competitive entries from Teva-Lonza or Sandoz are highly likely within couple years of Celltrion's launch. Because Hospira's European operations are somewhat limited compared to Teva or Sandoz, our forecast only assumes a peak 10% share by volume in 2017, and rapidly falling afterwards due to competitive pressure. Note that 10% may appear large, but we are assuming at most two products on the market. Thus, we estimate European sales will reach only KRW14bn in 2015, and then increases to peak sales of around KRW48bn in 2017. Considerable upside is possible only if governments in Western Europe actively encourage biosimilars. We believe that this will require few years of experience in the market to establish confidence in the safety of biosimilars. We estimate that serious expansion of biosimilars will only be considered in Europe in 2015 or later.

US launch possible only in 2019

According to our research, Herceptin does not expire until 2019 in the US. Unless Hospira can challenge the patent effectively in the US, we assume that the launch would be delayed until 2019.

Fig. 54: CT-P06 Forecast

Expanded Patient from Biosimilars (Patients)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	43,300	44,300	47,200	50,700	59,500	60,000	60,000	60,000	60,000	60,000	60,000
Expansion (none, no biosimilar)	0	0	0	0	0	0	0	0	0	0	0
Europe	56,800	55,400	55,900	56,500	56,400	57,000	57,000	57,000	57,000	57,000	57,000
Expansion (none)	0	0	0	0	0	0	0	0	0	0	0
Japan	16,700	17,000	19,200	21,000	25,300	26,600	28,000	28,000	29,400	29,400	31,000
Expansion (2020: 30% expansion)	0	0	0	0	500	1,000	1,600	2,500	3,900	6,100	9,300
ROW (Scenario A)	70,100	78,200	89,200	101,800	109,400	119,000	129,000	142,500	160,500	185,000	218,600
ROW (Scenario B)	70,100	78,200	91,200	108,800	126,400	149,000	168,100	193,300	226,300	270,000	327,900
ROW (Scenario C)	70,100	78,200	94,200	113,800	146,400	199,000	235,200	283,400	347,300	432,600	546,500
ROW (2020 Scenario A: 100% expansion)	0	0	3,000	8,000	13,000	20,000	28,100	39,500	55,500	77,900	109,300
ROW (2020 Scenario B: 200% expansion)	**0**	**0**	**5,000**	**15,000**	**30,000**	**50,000**	**67,200**	**90,300**	**121,300**	**162,900**	**218,600**
ROW (2020 Scenario C: 400% expansion)	0	0	8,000	20,000	50,000	100,000	134,300	180,400	242,300	325,500	437,200
ROW (Potential)											

Prevalence by population (basis point, women only)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	2.8	2.9	3.0	3.2	3.7	3.7	3.7	3.7	3.6	3.6	3.6
Europe	3.4	3.3	3.3	3.4	3.3	3.4	3.3	3.3	3.3	3.3	3.3
Japan	2.6	2.7	3.0	3.3	4.0	4.2	4.5	4.5	4.7	4.7	5.0
ROW (Scenario A)	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3
ROW (Scenario B)	**0.1**	**0.1**	**0.1**	**0.2**	**0.2**	**0.2**	**0.3**	**0.3**	**0.3**	**0.4**	**0.5**
ROW (Scenario C)	0.1	0.1	0.1	0.2	0.2	0.3	0.4	0.4	0.5	0.6	0.8

Biosimilar Penetration Rate (%)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (Expiry 2018-19)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Europe (Expiry 2013/4)	0.0	0.0	0.0	0.0	1.0	3.0	7.0	10.0	9.0	8.0	7.0
Japan (Expiry 2012)	0.0	0.0	0.0	0.0	1.0	5.0	15.0	30.0	30.0	30.0	30.0
ROW (Scenario I)	0.0	0.0	5.0	10.0	15.0	20.0	25.0	25.0	15.0	13.0	10.0
ROW (Scenario II)	**0.0**	**0.0**	**5.0**	**10.0**	**15.0**	**20.0**	**25.0**	**25.0**	**15.0**	**13.0**	**10.0**
ROW (Scenario III)	0.0	0.0	5.0	10.0	15.0	20.0	25.0	25.0	15.0	13.0	10.0

End market size (mn) (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US ($, 20% discount)	0	0	0	0	0	0	0	0	0	0	0
Europe (€, 20% discount)	0	0	0	0	12	36	84	120	108	96	84
Japan (¥, 20% discount)	0	0	0	0	277	1,455	4,364	8,729	8,707	8,707	8,722
ROW ($, 50% discount, Scenario I)	0	0	45	102	164	238	323	356	241	241	219
ROW ($, 50% discount, Scenario II)	**0**	**0**	**46**	**109**	**190**	**298**	**420**	**483**	**339**	**351**	**328**
ROW ($, 50% discount, Scenario III)	0	0	47	114	220	398	588	709	521	562	547

Celltrion's sales (mn) (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	0	0	0	0	0	0	0	0	0	0	0
Europe	0	0	0	0	4	11	25	36	33	29	25
Japan	0	0	0	0	83	436	1,309	2,619	2,612	2,612	2,616
ROW (Scenario I)	0	0	22	51	82	119	161	178	120	120	109
ROW (Scenario II)	0	0	23	54	95	149	210	242	170	176	164
ROW (Scenario III)	0	0	24	57	110	199	294	354	260	281	273

Celltrion's sales (mn) 20% Discount (Korean Won)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	0	0	0	0	0	0	0	0	0	0	0
Europe	0	0	0	0	5,000	14,000	34,000	48,000	43,000	39,000	34,000
Japan	0	0	0	0	1,000	5,000	14,000	28,000	28,000	28,000	28,000
ROW (Scenario I)	0	0	20,000	45,000	72,000	105,000	142,000	157,000	106,000	106,000	96,000
ROW (Scenario II)	**0**	**0**	**20,000**	**48,000**	**83,000**	**131,000**	**185,000**	**213,000**	**149,000**	**154,000**	**144,000**
ROW (Scenario III)	0	0	21,000	50,000	97,000	175,000	259,000	312,000	229,000	247,000	240,000
Total (Scenario I)	0	0	20,000	45,000	78,000	124,000	190,000	233,000	177,000	173,000	158,000
Total (Scenario II)	**0**	**0**	**20,000**	**48,000**	**89,000**	**150,000**	**233,000**	**289,000**	**220,000**	**221,000**	**206,000**
Total (Scenario III)	0	0	21,000	50,000	103,000	194,000	307,000	388,000	300,000	314,000	302,000

Source: Nomura estimates

Understanding Market Dynamics of TNF-α Inhibitors: Fierce Competition among the Innovators

CT-P13 and CT-P05: much more complicated picture

CT-P13, the biosimilar of Remicade (infliximab) and CT-P05 biosimilar of Enbrel (etanercept) present a more complex marketing as well as approval challenge. Excluding pediatric indications, Remicade has six major non-pediatric indications in Europe, US, and Japan, while Enbrel has five. Unlike Herceptin, multiple TNF-alpha inhibitors have been approved such as Humira (adalimumab), Cimzia (certolizumab pegol), and Simponi (golimumab). Principal differences among the TNF alpha inhibitors

are shown in the table above. Additionally, Remicade also competes, to a much more limited extent, with other second-line biologics possessing different mechanisms, such as Actemra/RoActemra (tocilizumab, a IL-6R inhibitor), Orencia (abatacept, T cell activation), and Rituxan/MabThera (rituximab, CD20 inhibitor). It may also compete in the future with Pfizer's highly anticipated oral JAK3 inhibitor tofacitinib (CP-690,550) as well as others in Phase III trials such as Celgene's apremilast and AstraZeneca/Rigel Pharmaceuticals' fostamatinib, all of which are oral small molecule drugs. Added to the complication is the fact that CT-P13 and CT-P05 may very well compete with each other if it is distributed by separate partners.

Fig. 55: Comparison of TNF-alpha Inhibitors: Remicade, Enbrel, Humira, Simponi

	Remicade	Enbrel	Humira	Simponi
Approval	○	○	○	**○ (US/EP ONLY)**
Type	**Chimeric** mAb	Fusion protein	Fully human mAb	Fully human mAb
Indications	Rheumatoid Arthritis	Rheumatoid Arthritis	Rheumatoid Arthritis	Rheumatoid Arthritis
	Crohn's Disease	PJIA	Crohn's Disease	Psoriatic Arthritis
	Ulcerative Colitis	Ankylosing Spondylitis (US/EP)	Juvenile Idiopathic Arthritis (PJIA in EP, not approved in JP)	Ankylosing Spondylitis
	Ankylosing Spondylitis	Psoriatic Arthritis (US/EP)	Ankylosing Spondylitis	
	Psoriatic Arthritis	Plaque Psoriasis (US/EP)	Psoriatic Arthritis	
	Plaque Psoriasis (Psoriasis in EP/JP)	Pediatric Plaque Psoriasis (EP)	Plaque Psoriasis (Psoriasis in EP)	
	Pediatric Crohn's Disease			
	Refractory Uveitis from Behcet's Disease (JP Only)			
Formulation	Vial 100mg Lyophilized	Vial 25/50mg Lyophilized **(JP: 10/25/50mg)**	HUMIRA pen 40mg (US/EP Only)	SmartJect 50mg
		Syringe 25/50mg	Syringe 40mg (US: 20/40mg)	Syringe 50mg
Administration	**IV ONLY**	Subcutaneous (self-injection)	Subcutaneous (self-injection)	Subcutaneous (self-injection)
Dosage	RA: 3mg/kg on week 0, 2, 6 and at 8wk intervals with MTX	RA, AS, PsA: 50mg weekly (EP/JP: 25mg twice weekly also)	RA, AS, PsA: 40mg biweekly	RA: 50mg monthly with MTX
	Others: 5mg/kg on week 0, 2, 6, and at 8wk intervals (**6-8 for AS in JP/EP, 6 for US**)	Adult PsO: 50mg twice weekly for 3months, followed by weekly 50mg dose	JIA: For 15-30kg 20mg biweekly, for >30kg 40mg biweekly	Others: 50mg monthly with or without MTX or DMARDS
		PJIA: For >63kg 50mg weekly, For < 63kg 0.8mg/kg weekly	Crohn's: 160mg day 1, 80mg 2week, maintenance biweekly 40mg	
			Ps: 80mg day 1, maintenance biweekly 40mg	
Inhibiting Structural Damage	Yes (EP/US, not approved in JP)	Yes (RA and PsA, EP/US, not approved in JP)	Yes (RA and PsA EP/US, not approved in JP **though Phase III**)	No (Filed in US/EP, see below)
Clinical Remission (US ONLY)	UC, Crohn's	RA	RA, Crohn's	-
Most Common Side Effects	Infections, **Infusion reactions (20%)**, Headache	Infections, Injection site reactions, headache	Infections, Injection site reactions, headache	Upper respiratory tract infection, Nasopharyngitis
Serious Side Effects	**Infusion reactions**, Hepatotoxicity, Malignancy, Heart Failure	Infections, Malignancies, Allergic reactions (<2%), Heart Failulre	Infections, Malignancies, Hypersensitivity (1%), Heart Failure	Serious infections (1%), Malignancies, Heart Failure
Clinical Trials in Progress	US: Pediatric UC Filed	US: None	US: None	US: Phase III for PA and RA (IV), Structural Damage for RA and PsA Filed, Phase III for UC
	EP: Pediatric UC Filed	EP: None	EP: None	EP: Phase III for PA and RA (IV), Structural Damage for RA and PsA Filed, Phase III for UC
	JP: Crohn's (change in dosage) Filed	JP: None	JP: PJIA Filed, PIII for Structural Damage, PII/III for UC	JP: **RA Filed (June 2010)**

Note: RA = Rheumatoid arthritis, UC = Ulcerative Colitis, PJIA = Paediatric Juvenile Idiopathic Arthritis, PsA = Psoriatic Arthritis, PsO = Psoriasis, AS = Ankylosing Spondylitis
Source: Nomura research, based on Roche presentation data

Fierce competition between TNF-alpha inhibitors

Remicade's primary competitors are Enbrel and Humira, followed to a much lesser extent by Cimzia and Simponi. Remicade has three well-known major disadvantages compared to these competitors.

- Remicade must be slowly administered as an IV infusion over two hours, by a doctor in a clinical setting. On the other hand, Enbrel, Humira, Cimzia, and Simponi are all self-injectable and are superior to Remicade in ease-of-use.
- Remicade is a chimeric antibody composed of both murine and human antibodies as opposed to antibodies that have been humanized (Cimzia), and fully human antibodies (Enbrel, Humira, and Simponi). Remicade has a comparatively higher incidence of

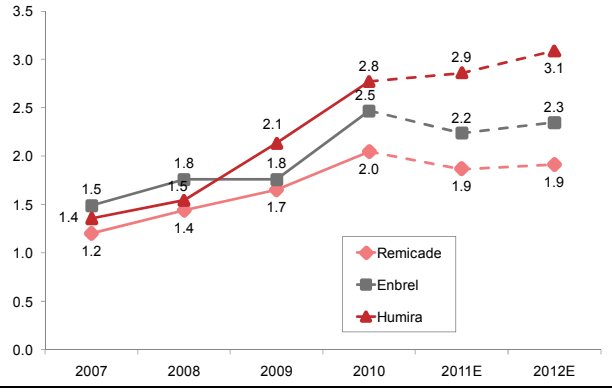
infusion reactions that include potentially fatal anaphylactic shock. Anaphylactic shock is a grave concern for administering physicians in any country, although it can be effectively mitigated by prior injection of steroids.

- Remicade has not demonstrated maintenance of clinical remission to the same extent that Enbrel and Humira have shown. There is a risk in our view that Remicade itself may not be favoured much compared to other TNF-alphas, which would also impact the use of infliximab biosimilars.

Advantages of Remicade do not counteract its major disadvantage in the US

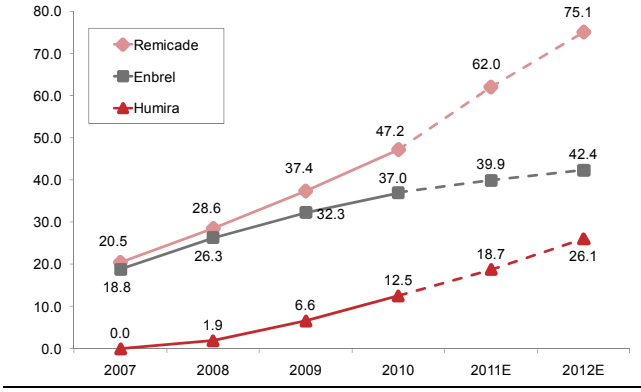
Remicade does have two major advantages. First, it has been on the market the longest, and the safety data is well-established. Second, Remicade is administered in week 0, 2, 6 and every 8 weeks afterwards. This is less frequent compared to all other TNF-alpha inhibitors; Simponi administration is once a month, while Humira and Cimzia is once every two weeks, and once or twice a week for Enbrel. However we do not believe that the advantages are enough to counteract the inferiority in ease-of-use. As shown in the table above, the implied price of Remicade in the US has declined relative to two years ago, while the price of the two main competitors Enbrel and Humira continues to rise. Thus, we believe that the market potential of biosimilar CT-P13 is more limited compared to CT-P05, assuming that both drugs are available in the market.

Fig. 56: Europe & ROW Sales of TNA-alpha inhibitors, USDbn



Source: Nomura, based on JNJ, Amgen, Abbott data

Fig. 57: Japan Sales of TNA-alpha inhibitors, JPYbn



Source: Mitsubishi Tanabe, Takeda, Eisai

Self-injection not a large factor in Japan/Europe

Above charts show Europe + ROW and Japan sales trend of TNF-alpha inhibitors. Note that these figures are based on market consensus figures that do not account for significant market share erosion by biosimilars. Remicade sales in the US (not shown) have been falling mostly due to increased competition with Enbrel and Humira. We believe that Humira will gain more market share at the expense of other TNF-alpha inhibitors primarily because of its ease-of-use and its less frequent dosage (compared to Enbrel).

The same holds true for Europe + ROW, where presumably self-injectability of Humira and Enbrel are not as much a competitive factor as it is in US, as shown in the comparable market share of the three competing biologics. We also believe that Remicade in Japan will maintain growth potential until 2015 due to recently approved indications. Penetration of Remicade in non-RA autoimmune diseases is at an earlier stage in Japan than in EP/US. Additionally, competition in Crohn's disease and ankylosing spondylitis is limited to Humira, and potentially Cimzia in 3-4 years. In our opinion, Japanese also tend to favour IV administration over self-injection more so than in US/Europe, because doctor consultation fees are much more affordable (e.g. IV administration in Japan costs only JPY470, of which 30% (JPY141) is out-of-pocket).

Crohn's disease and ankylosing spondylitis are major indications in EU and US

Merck has disclosed the sales distribution by indication for Remicade in Europe. According to data presented on Merck's R&D Day in March 2010, the two largest indications by sales are rheumatoid arthritis and Crohn's disease, which both combined represent about 60% of European sales. The third largest indication is ankylosing

spondylitis. Although ankylosing spondylitis is a less common disease, the recommended regimen is 5mg/kg every six weeks in the US after three initial infusions, as opposed to eight weeks for all other indications. Thus, the annual cost per treatment can double that of rheumatoid arthritis. Other indications such as psoriatic arthritis, psoriasis, and ulcerative colitis represent around 25% of Remicade sales, though it should be noted that ulcerative colitis is growing very rapidly (2007-9 CAGR 23%).

Johnson & Johnson has not publicly disclosed the US Remicade sales breakdown by indication. For the purpose of calculation, we hypothesize that it is similar to that of Europe. Mitsubishi Tanabe Pharmaceuticals claims that about 40% of sales of Remicade in Japan are from Crohn's disease and about 10% from other non-Rheumatoid Arthritis indications. Although the incidence of non-RA autoimmune diseases is rarer in Japan, the contrast between Japan and Europe indicates that a relatively large number of untreated patients remains in Japan.

Enbrel: Less affected than Remicade but ceding growth to Humira in EU and US
We believe that Enbrel would be less affected by competitive pressure compared to Remicade. Since Enbrel is self-injectable like Humira, has shown clinical remission in RA, and has indication for inhibiting structural damage, we expect US sales of Enbrel to be stable until 2015. The same applies to Europe. In Japan, Enbrel has only two indications, of which PJIA (pediatric juvenile idiopathic arthritis) is rare. Enbrel is sold by Takeda Pharmaceuticals in Japan, whose pipeline does not contain clinical trials for additional indications of Enbrel. Although growth is limited compared to Remicade or Humira, we believe that Enbrel will grow in Japan primarily because of the marketing strength of Takeda: the premier pharmaceutical company in Japan.

Patent Expiration: Remicade expires earlier in the EU/Japan, Enbrel earlier in US
Key regional patents of Remicade and Enbrel are outlined in the table below. Because US Patents for early biologics were filed prior to the Uruguay Round Agreements Act in 1995, the patent expiry is calculated by adding 17 years after the registration date of the patent. Since patents for most of these biologics were granted after product launch, extension of patent protection is limited, as shown in the table. Thus we believe that Remicade US patent expiry is 2018, while Enbrel's US patent expiry is in October of 2012. In Europe, the SPC expiry date (Supplementary Protection Certificate) of the key patent is assumed to be the most important for generic launch. Accordingly, Remicade expires in 2014, and Enbrel expires in 2015 both in the UK and Japan. Variations exist in other European countries.

In Japan, to the best of our knowledge, the patent for Remicade has not been granted. The original application and the subsequent split applications (Unexamined Patent Application Publication 1992-506120, 2004-180686, 2007-197457, 2007-254477) have all been rejected. Even if the patent is granted, it would face expiry in 2012. Since Enbrel was launched in 2005 in Japan, we believe that the maximum period of patent extension should apply. Thus, the Enbrel Japan patent expires only in 2015. Substance patents for the other TNF-alpha competitor, Humira, do not expire until 2016 in the US, and 2018 in Europe/Japan.

Fig. 58: Key patents for the TNF-alpha inhibitors: Remicade, Enbrel, and Humira

Remicade	Patent Title	Submission Date	Estimated Patent Expiry
US5656272	Methods of Treating TNF-alpha-mediated Crohn's Disease Using Chimeric Anti-TNF Antibodies	Feb-4-1994	2014-2015
US5698195	Methods of Treating Rheumatoid Arthritis Using Chimeric Anti-TNF Antibodies	Oct-18-1994	2014-2015
US6284471	Anti-TNFa Antibodies and Assays Employing anti-TNFa Antibodies	Feb-4-1994	2018
EP0610201	Monoclonal and Chimeric Antibody Specific for Human Tumor Necrosis Factor	Mar-18-1992	2014
JP2008-156371	Monoclonal and Chimeric Antibody Specific for Human Tumor Necrosis Factor	Mar-18-1992	-
JP2008-195724	Monoclonal and Chimeric Antibody Specific for Human Tumor Necrosis Factor	Mar-18-1992	-

Enbrel	Patent Title	Submission Date	Estimated Patent Expiry
US5395760	DNA Encoding Tumor Necrosis Factor-Alpha and Beta Receptors	May-10-1990	2012
RE36755	DNA Encoding Tumor Necrosis Factor-Alpha and Beta Receptors	Aug-31-1998	Oct-23-2012
US7648702	Stable Aqueous Formulation of a Soluble TNF Receptor and Arginine	Feb-27-2003 (Original Filing Date)	Feb-27-2023
EP0418014	Tumor Necrosis Factor-Alpha and -Beta Receptors	Sep-10-1990	2015
EP0464533	Fusion Proteins with Parts of Immunoglobulins, Their Production and Use	Jun-22-1991	2015
JP2721745	Tumor Necrosis Factor-alpha and -Beta Receptor	Sep-5-1990	2015
JP2960039	Tumor Necrosis Factor-alpha and -Beta Receptor	Sep-5-1990	2015

Humira	Patent Title	Submission Date	Estimated Patent Expiry
US6090382	Human Antibodies That Bind Human TNF Alpha	Feb-9-1996	Dec-31-2016
EP0929578	Human Antibodies That Bind Human TNF Alpha	Feb-10-1997	2018
JP3861118	Human Antibodies That Bind Human TNF Alpha	Feb-10-1997	2018

Source: JPO, EPO, USPTO

Fig. 59: Data Exclusivity Period: Japan, Europe, US

	Remicade		
Data Exclusivity	US	Europe	Japan
Rheumatoid Arthritis	Oct-04	Jun-10	May-09
Crohn's Disease	Aug-01	Jun-10	Jan-12
Ankylosing Spondylitis	Dec-07	Jun-10	**Apr-20**
Ulcerative Colitis	Oct-13	Jun-10	Jan-12

	Enbrel		
Data Exclusivity	US	Europe	Japan
Rheumatoid Arthritis	Nov-03	Feb-10	Jan-13
Psoriatic Arthritis	Jan-05	Feb-10	N/A
Ankylosing Spondylitis	Jul-06	Feb-10	N/A

Source: JPO, EPO, USPTO

Fig. 60: Patient Population Estimate: TNF alpha inhibitors

Sales of TNF Alphas (Regional Currency, mn)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
US	8,018	8,126	8,332	8,397	8,271	8,184
Remicade ($, JNJ)	1,612	1,486	1,452	1,397	1,321	1,284
Enbrel (US and Canada, $, Amgen)	3,534	3,540	3,480	3,400	3,300	3,200
Humira ($, Abbott)	2,872	3,100	3,400	3,600	3,650	3,700
Europe	5,327	4,939	5,040	4,988	4,841	4,627
Remicade (€, MSD, Nomura est.)	1,535	1,383	1,378	1,325	1,181	1,012
Enbrel (€, Amgen, Nomura est.)	1,852	1,611	1,621	1,611	1,587	1,520
Humira (€, Abbott, Nomra est.)	1,940	1,946	2,041	2,053	2,074	2,095
Japan	96,700	120,600	143,600	161,800	165,300	171,300
Remicade (¥, MTP)	47,200	62,000	75,100	83,800	92,400	92,600
Enbrel (¥, Takeda)	37,000	39,900	42,400	44,100	38,300	39,000
Humira (¥, Eisai)	12,500	18,700	26,100	33,900	34,600	39,700
ROW	2,600	3,082	3,520	3,737	3,895	3,931
Remicade ($, MSD, Nomura est.)	679	738	815	905	1,009	1,026
Enbrel ($, Amgen, Nomura est.)	819	952	1,107	1,152	1,188	1,190
Humira ($, Abbott, Nomura est.)	1,103	1,392	1,598	1,680	1,698	1,715

Annual Cost of TNF Alpha Drugs (Regional Currency, mn)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
US						
Remicade ($, average including AS, Crohn's)	24,975	24,545	24,773	24,958	25,035	24,942
Enbrel ($)	26,520	27,316	28,135	28,135	28,135	28,135
Humira ($)	26,000	26,780	27,583	28,411	29,263	30,141
Europe						
Remicade (€, average including AS, Crohn's)	20,109	20,167	20,354	20,506	20,569	20,493
Enbrel (€)	23,400	23,400	23,400	23,400	23,400	23,400
Humira (€)	23,400	23,400	23,400	23,400	23,400	23,400
Japan						
Remicade (¥, average including AS, Crohn's)	1,851,717	1,887,718	1,828,711	1,851,290	1,773,046	1,787,940
Enbrel (¥)	1,584,752	1,584,752	1,553,057	1,553,057	1,521,996	1,521,996
Humira (¥)	1,848,522	1,848,522	1,811,552	1,811,552	1,775,321	1,775,321
ROW						
Remicade ($)	22,000	22,000	22,000	22,000	22,000	22,000
Enbrel ($)	18,000	18,000	18,000	18,000	18,000	18,000
Humira ($)	20,000	20,000	20,000	20,000	20,000	20,000

Est. Number of Pooled Patients (Sales / Average Annual Cost)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
US	308,300	305,900	305,600	303,500	294,800	288,000
Remicade	64,500	60,500	58,600	56,000	52,800	51,500
Enbrel	133,300	129,600	123,700	120,800	117,300	113,700
Humira	110,500	115,800	123,300	126,700	124,700	122,800
Europe	238,300	220,600	224,200	221,100	213,800	203,800
Remicade	76,300	68,600	67,700	64,600	57,400	49,400
Enbrel	79,100	68,800	69,300	68,800	67,800	64,900
Humira	82,900	83,200	87,200	87,700	88,600	89,500
Japan	55,600	68,100	82,800	92,400	96,800	99,800
Remicade	25,500	32,800	41,100	45,300	52,100	51,800
Enbrel	23,300	25,200	27,300	28,400	25,200	25,600
Humira	6,800	10,100	14,400	18,700	19,500	22,400
ROW	131,000	156,000	178,000	189,000	197,000	199,000
Remicade	30,800	33,600	37,000	41,100	45,900	46,600
Enbrel	45,500	52,900	61,500	64,000	66,000	66,100
Humira	55,100	69,600	79,900	84,000	84,900	85,800
Total	733,200	750,600	790,600	806,000	802,400	790,600

Source: Nomura, IMS data, Company data, Red Book 2010, Japanese government prices

Enbrel: More than meets the eye

In their 2010 fiscal year 10-K, Amgen claims that Enbrel is further protected by an aqueous formulation patent until 2023. This means that the biosimilar will be forced to use a lyophilized powder formulation unless the biosimilar company can come up with an aqueous formulation that does not infringe Amgen's patents. Our research suggests that US patent number 7,915,225 assigned to Immunex Corporation (who was acquired by Amgen) expires in 2023, and describes the use of a common amino acid arginine or cysteine as an aggregation inhibitor. Lyophilized proteins are problematic since rehydration may result in protein denaturation or aggregation. Aggregation is especially important since it has a possibility to cause immunogenicity. In our view, overcoming this formulation patent may be difficult.

Possible problems with misfolding proteins

Furthermore, because Enbrel is an unnatural fused protein unlike monoclonal antibodies, the 3D structure of the protein may not always be the same. US patent number 7,294,481 describes how Enbrel has three forms: the therapeutically active form, a truncated protein from proteolytic cleavage, and a misfolded form. The patent describes how alkanoic acid can be introduced into the bioreactor to reduce the formation of misfolded proteins. We believe this patent expires in 2022. It is presumed that other patents exist that will present additional issues. In summary, we believe that the development of biosimilar Enbrel may be more difficult than Rituxan, Herceptin, or Remicade.

Data exclusivity: ankylosing spondylitis off-limits in Japan

In Japan, data exclusivity is generally 8-10 years for additional indications. Longer data exclusivity periods are awarded to NCEs with novel indications (such as Crohn's in 1998), and additional indication for rare diseases (such as Ankylosing Spondylitis). Thus, biosimilars are barred from penetrating the Japanese Ankylosing Spondylitis market. We think that the exclusion of Ankylosing Spondylitis will have a limited impact on the uptake of biosimilars, since it comprises considerably less than 10% of Remicade sales in Japan, although the share is growing.

In the developed markets, we do not believe that biosimilars will be used off-label for indications still protected by data exclusivity. Since US data exclusivity is five years for CE, and three years for additional indications, data exclusivity will have expired by the date of patent expiry. In Europe, we assume the data exclusivity is 10 years for a drug approved by the EMEA through a centralized procedure, two years for the first additional indication, and one year for the second indication. In both regions, we believe the data exclusivity will also have expired by the date of patent expiry.

Patient demographics: again catering to a cost sensitive population

According to the Arthritis Foundation, the prevalence of Rheumatoid Arthritis is estimated to be around 1% of the adult population in the US (1.3mn). The disease afflicts women three times more than men, where fully 70% of patients are women. The European prevalence is expected to be similar to that of the US, though generally the disease is less prevalent in South Europe. The prevalence of RA in Asia is slightly less (about 0.5%) than North America or Europe. Age of onset is often between 30 and 60 years old. We believe that the patient demographics point to a very price sensitive population, since: 1) patients are nearing retirement or have retired; and 2) women in certain regions, such as Asia, in this age group are generally unemployed (see ILO Study, http://www.ilo.org/public/libdoc/jobcrisis/download/story113_women_asia.pdf).

Patient population: all combined over 700,000 patients in the world

From the distribution of indications in Europe, we calculate that the average annual cost of Remicade for all indications in 2010 is about EUR20,000 and JPY1.9mn in Japan. From the regional sales, we estimate the number of patients using Remicade to be about 76,000 in Europe, 29,000 in ROW, and 25,000 in Japan. The same calculation has also been performed for Enbrel and Humira as shown in the table on the previous page. The combined number of patients who are being treated with the three main TNF-alpha inhibitors throughout the world is about 730,000 patients. We believe that the patient pool will shrink from 2010 to 2015 in US/Europe due to attrition from other newer TNF-alpha inhibitors and, possibly, from oral molecules (see tofacitinib, below). The

patient base is expected to increase in Japan through addition of indications. The ROW regions are expected to increase to about 150% of 2010 levels by 2015. This represents the baseline patient population without accounting for the “market creation effect” induced by the entry of biosimilars.

Celltrion’s CT-P13/CT-P05 Forecast

Focus on European clinical trial

The list of clinical trials for submission of CT-P13 biosimilar is shown in the table below. We focus on the clinical trials registered in the EudraCT database 2010-018636-31. The European trial targets enrollment of 11 patients in Italy, 18 in Austria, 53 in Spain, and 30 in Latvia. Total target in East/West Europe is 260. According to Celltrion, the global total target is 830 patients.

Fig. 61: List of Clinical Trials for CT-P13

NCTID/EUDRACT/Clinical Trial Identifier	Compound	Country	2010				2011				2012				2013				2014			
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
2010-018636-31	CT-P13	Italy			PIII			EC			S											
		Austria			PIII			EC			S											
		Spain			PIII			EC			S											
		Latvia			PIII			EC			S											
-	CT-P13	Philippines	PIII					EC			S											
-	CT-P13	Colombia			PIII			EC			S											
-	CT-P13	Portugal			PIII			EC			S											
-	CT-P13	Bulgaria				PIII		EC			S											
-	CT-P13	Mexico				PIII		EC			S											
-	CT-P13	Slovakia				PIII		EC			S											
-	CT-P13	Ukraine				PIII		EC			S											
-	CT-P13	India				PIII		EC			S											
-	CT-P13	Lithuania				PIII		EC			S											
-	CT-P13	Romania				PIII		EC			S											
NCT01217086	CT-P13	Korea				PIII		EC			S											
NCT01220518	CT-P13	Korea				PIII		EC			S											

Source: DART publication, EudraCT (EU), Clinicaltrials.gov (US)

Two clinical trials for RA and ankylosing spondylitis

Celltrion is currently conducting two clinical trials for CT-P13 in Korea, PLANETRA for rheumatoid arthritis and PLANETAS for ankylosing spondilytis. PLANETRA is evaluating CT-P13 in 584 rheumatoid arthritis patients. The primary endpoint is PK equivalence to Remicade at week 30. PLANETAS is evaluating CT-P13 in 246 ankylosing spondilytis patients.

Extrapolation to other indications possible from the two clinical trials

According to the European guideline on biosimilars containing monoclonal antibodies, “it is not generally required to investigate the pharmacokinetic profile” in all indications, and that data from one indication can be extrapolated to others. However, the guideline states that for a particular antibody with indications in distinct therapeutic areas, such as auto-immune disease and oncology, separate PK studies may need to be conducted. Since the six indications for Remicade are all auto-immune diseases, we believe that the two clinical trials should be sufficient for approval in all indications. Guidelines for monoclonal antibodies do not exist elsewhere in the world, but we expect that similar reasoning to apply in Japan and ROW.

Clinical trial design: What is ACR20?

The primary endpoints for the European trials are ACR20 improvement at week 30. Secondary endpoints are long term efficiency, pharmacokinetics, pharmacodynamics, and safety up to week 30. ACR20 is the standard measure of clinical effectiveness for improvement of rheumatoid arthritis devised by the American College of Rheumatology. ACR20 is 20% improvement in number of tender or swollen joints, with improvement in three of additional five parameters: 1) patient’s assessment of pain using VAS; 2) patient global assessment of disease; 3) physician global assessment of disease; 4)

questionnaire concerning physical ability and functionality; and 5) clinical measure of inflammation (serum CRP concentration or blood cells sedimentation rate).

Clinical trial comparison: ATTRACT pivotal trial vs CT-P13

A comparison of the clinical trial design for the pivotal Remicade trial (ATTRACT trial), and CT-P13 biosimilar infliximab is shown in the table below. Unsurprisingly, the clinical trial design is based on the ATTRACT trial with some minor differences in the inclusion criteria. The exclusion criteria are similar for both studies, excluding patients with hepatitis, infections, malignancies, etc. We believe the patient sample size is adequately powered in comparison to the pivotal trial.

Fig. 62: Comparison of Clinical Trial Design

	ATTRACT Trial (1999)	CT-P13
Inclusion Criteria	6 or more swollen and tender joints and at least two of the following: 1. morning stiffness for 45 minutes, 2. sedimentation rate > 28mm/h, 3. CRP >2.0mg/dL	6 or more swollen and tender joints and at least two of the following: 1. morning stiffness for 45 minutes, 2. sedimentation rate > 28mm/h, 3. CRP >2.0mg/dL
	Must have received MTX for at least 3 months, > 12.5mg/week for at least 4 weeks prior to screening	Must have received MTX for at least 3 months, > 12.5mg/week for at least 4 weeks prior to screening
	Serum creatinine < 150μmol/L	Serum creatinine < 1.7x ULN
	ALP, AST < 2x ULN	ALT, AST < 2x ULN
Dosage	3mg/kg for week 0, 2, 6, and every 8weeks subsequent	(Presumably the same)
Primary Endpoint	ACR20 at week 30	ACR20 at week 30
Sample Size	428 (only 86 for 3mg/kg q 8wks)	260 (Europe) 830 (global)
Result at wk30	3mg/kg q 8wks ACR20 in 50% of patients	-
PK	At week 30, 3mg/kg q 8wks showed average serum concentration of infliximab at 1.5μg/mL (SD 1.6), t1/2 8-12 days	-
Other results	Response rapid: Of the responders >50% attained ACR20 response by the second week, 90% by 6 week evaluation	-
Immunogenicity	Of 27 patients who discontinued treatment, 3 tested positive for human antichimeric antibodies	-

Source: Remicade Full Prescribing Information (US/EU/JP), EudraCT Database

What is required for EMEA/PMDA acceptance?

We believe the clinical trial results must show the following for approval by EMEA:

- Efficacy: ～50% of patients should attain ACR20 improvement to prove bioequivalence
- Phamacokinetics: Similar average serum concentration of 1.5μg/mL (though the error is large here)
- Immunogenicity: generally about 10% of patients developed antibodies to infliximab

As was described in CT-P06, proof of safety and efficacy is of paramount importance for approval. Thus, CT-P13 must demonstrate 50% of patients with ACR20 improvement and not more than 10% of patients with antibodies to infliximab. In short, CT-P13 will have to demonstrate: 1) non-inferiority in efficacy; 2) similar immunogenicity; and 3) tolerably similar PK profile.

Approval timeline: 2012 for emerging countries, 2014 for Europe and Japan

The forecasted approval timeline is given in the table overleaf. After patient enrollment, the trial duration is seven months, and with two months work up of clinical data, we expect the submission to be in 1Q 2012 or 4Q 2011. Celltrion is hoping for a submission in 4Q 2011 Q4. Again, Celltrion has not specified the timing of launch in emerging markets but based on interviews with EGIS, the Eastern Europe launch is expected in 2013. Because of the aforementioned patents, marketing in Western Europe cannot start until 1H 2014 at the earliest. Finally, according to Nippon Kayaku, Japanese clinical trials are expected to proceed such that approval, at the earliest, will be in 2014.

Fig. 63: Approval Timeline: CT-P13

Region	Compound		2010				2011				2012				2013				2014			
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Korea	CT-P13							EC			S	A	○									
SE Asia/LatAm/CIS	CT-P13							EC			S	A	○									
Eastern Europe	CT-P13							EC			S				A	○						
Western Europe	CT-P13							EC			S				A					○		
Japan	CT-P13									PI		PIII				S			A	○		
Other Regions	CT-P13							EC			S				A	○						

PI/II = Start of Phase I/II
PIII = Start of Phase III
PI = Start of Phase I
EC = Enrollment Complete
S = Submission
A = Approval
○ = Start of Sales

Source: Company, Nippon Kayaku, EGIS, Hikma Pharmaceuticals, Nomura Assumptions

Four base assumptions for CT-P13/CT-P05 forecast

Forecast for CT-P13 and CT-P05 biosimilar is based on four main assumptions:

- Infusion Reactions Are Not a Problem: Remicade's well-known disadvantage is the relative frequency of infusion reactions. Unlike other TNF-alpha inhibitors, infusion reactions have been observed in patients who had tolerated Remicade for many years. Prior injection with corticosteroids or antihistamines can mitigate the risk of infusion reactions. Slowing the rate of infusion is also known to sometimes improve the risk of reactions. Risks associated with Remicade are now well understood by rheumatologists worldwide.
- Self-Injectability is not a big advantage in Europe/ Asia: As noted above, self-injectability is not as large an advantage in Europe/Asia as it is in the US. This is particularly evident in the sales trend of Remicade in Japan, where it leads the other TNF-alpha inhibitors. We believe that patients in much of Asia including Japan are culturally averse to self-injection, and prefer administration in a clinic setting where infusion reactions can be monitored.
- CT-P13 will compete with ALL TNF-Alpha inhibitors: From (1) and (2), it follows that CT-P13 should be competitive, not only with the original Remicade, but also with the other TNF-alpha inhibitors such as Enbrel and Humira, especially in Asia and in ROW. In Europe, where patients bear very little financial burden of biologics, share erosion from the launch of biosimilar CT-P13 is likely limited to Remicade. But in Asia where the cost of treatment is borne to a larger part by the patients themselves, the market share of all expensive treatments is likely to be eroded.
- CT-P05 for the Emerging Markets: It follows from the above that biosimilar etanercept CT-P05 will have limited appeal to many patients in Europe and Japan where self-injection is not strongly favored, and where access to clinics is readily available. However, we believe that CT-P05 is more appealing in some emerging regions where access to clinics is very limited due either to scarcity of doctors or to geographic expanse. In these regions, sales potential of CT-P13 may be limited by the lack of medical access.

CT-P-5: Approval timeline

According to Celltrion's timeline, the IND filing and approval in EMEA/Asia is planned for the second half of 2011. If we assume that Phase III trials commence (note that in many cases Phase I is conducted concurrently) usually 1-3 months after IND approval, and that Phase III trial is similar to Enbrel's pivotal trial which enrolled 234 patients, patient enrollment should be completed by late 2012 and early 2013. The Enbrel pivotal trial lasted six months, and with an additional two months of data workup, we expect to see CT-P05 launch in early 2014 for Korea and some emerging regions, followed by approval in Western Europe around the end of 2014 or beginning of 2015. Note that sales partners in Japan have not yet been determined.

Fig. 64: Approval Timeline: CT-P05

Region	Compound	2010				2011				2012				2013				2014			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Korea	CT-P05								I	PIII			EC			S	A	○			
SE Asia/LatAm/CIS	CT-P05								I	PIII			EC			S	A	○			
Eastern Europe	CT-P05								I	PIII			EC			S				A	○
Western Europe	CT-P05								I	PIII			EC			S				A	○

PI/II = Start of Phase I/II
PIII = Start of Phase III
PI = Start of Phase I
EC = Enrollment Complete
S = Submission
I = IND Submission
A = Approval
○ = Start of Sales

Source: Company, Nomura estimates

Biosimilar penetration assumption in ROW

We believe that CT-P13 and CT-P6 can only take at most 18% by volume of the total TNF alpha inhibitor patient base, because of increasing competition post-2017 with other biosimilars. Taking Scenario B as our scenario of choice, we forecast that ROW sales to Celltrion will reach KRW205bn by 2015, and a peak of KRW320bn in 2020, despite losing share in the last three years of the decade due to competitive pressure.

Biosimilar penetration assumption in Japan

As discussed in the summary section, we believe the Japanese market will behave like ROW to a limited extent. According to the Japan Medical Association, the RA incidence in Japan is estimated to be around 700,000 patients a year. Yet, we estimate the total number of patients receiving TNF alpha is calculated to be about 55,000. Anecdotal evidence from doctors suggests that many patients, usually in the 50s and 60s, eschew antibody treatment because of the economic burden imposed. From our analysis there is substantial untapped demand remaining.

Unfortunately, the Japanese pharmaceutical pricing system will allow only a 30% cut to the originator price. At this price differential, we believe that the "market creation effect" will be limited to a 30% increase of the market from the baseline in 2020. Even then, we forecast Celltrion sales of KRW20bn in 2015, and peak sales of KRW71bn in 2018.

Biosimilar penetration assumption in Europe

Biosimilar penetration in Europe will be limited to at most 7% by volume. Thus, we estimate European sales will reach only KRW35bn in 2015, which then increases to peak sales of around KRW2bn in 2017-18. Considerable upside is possible only if governments in Western Europe actively encourage biosimilars.

Biosimilar penetration assumption in US

According to Johnson & Johnson, Remicade does not expire until 2018 or 2019. This leaves only Enbrel, whose substance patent apparently expires in 2012. The development of Enbrel is entirely dependent on Hospira. At present, there are no indications that Hospira will be starting a clinical trial in the US for Enbrel. The table overleaf shows what would happen if a US FTF is obtained for Enbrel in 2016. We calculate that about USD1bn in revenue may result. This is not included in our forecast because many aspects of US biosimilar guidelines remain vague.

Fig. 65: Forecast Details: CT-P13 and CT-P05

Expansion of Patient Size From Biosimilars (# of Patients)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	308,300	305,900	305,600	303,500	294,800	288,000	288,000	288,000	288,000	288,000	288,000
Expansion (None, no biosimilar entry assumed)	0	0	0	0	0	0	0	0	0	0	0
Europe	238,300	220,600	224,200	221,100	213,800	203,800	203,800	203,800	203,800	203,800	203,800
Expansion (None)	0	0	0	0	0	0	0	0	0	0	0
Japan	55,600	68,100	82,800	92,400	97,800	101,800	105,800	111,800	117,800	123,800	129,800
Expansion (2020: 30% expansion)	0	0	0	0	1,000	2,000	6,000	12,000	18,000	24,000	30,000
ROW (Scenario A)	131,000	156,000	188,000	209,000	237,000	252,000	272,700	299,200	333,300	377,300	434,400
ROW (Scenario B)	131,000	156,000	198,000	229,000	257,000	282,500	318,500	367,500	434,300	525,800	651,600
ROW (Scenario C)	131,000	156,000	208,000	249,000	287,000	330,300	394,000	485,600	617,700	808,800	1,086,000
Expansion (2020 Scenario A: 100% expansion)	0	0	10,000	20,000	40,000	53,000	70,300	93,200	123,600	163,900	217,200
Expansion (2020 Scenario B: 200% expansion)	0	0	20,000	40,000	60,000	83,500	116,100	161,500	224,600	312,400	434,400
Expansion (2020 Scenario C: 400% expansion)	0	0	30,000	60,000	90,000	131,300	191,600	279,600	408,000	595,400	868,800

% of total population receiving TNFalpha (Basis points)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	10.0	9.9	9.8	9.6	9.3	9.0	8.9	8.8	8.8	8.7	8.6
Europe	7.2	6.6	6.7	6.6	6.3	6.0	6.0	6.0	5.9	5.9	5.9
Japan (with 30% expansion)	4.4	5.4	6.5	7.3	7.8	8.1	8.5	9.0	9.5	10.0	10.5
ROW (Scenario A)	0.2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.5	0.6	0.6
ROW (Scenario B)	0.2	0.3	0.3	0.4	0.4	0.4	0.5	0.6	0.6	0.8	0.9
ROW (Scenario C)	0.2	0.3	0.3	0.4	0.4	0.5	0.6	0.7	0.9	1.2	1.6

CT-P05 and CT-P13 Penetration Rate (%)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	0.0	0.0	0.0	0.0	0.0	0.0	10.0	8.0	6.0	6.0	6.0
US (FTF)	0.0	0.0	0.0	0.0	0.0	0.0	20.0	8.0	6.0	6.0	6.0
Europe	0.0	0.0	0.0	0.0	0.5	3.0	5.0	7.0	7.0	6.0	6.0
Japan	0.0	0.0	0.0	0.0	0.1	5.0	10.0	14.0	16.0	15.0	14.0
ROW	0.0	0.0	5.0	9.0	10.0	15.0	16.0	18.0	13.0	9.0	6.0

End market size (mn) (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US ($, 50% discount)	0	0	0	0	0	0	359	287	215	215	215
US (FTF, $, first year 30%, 50% discount)	0	0	0	0	0	0	1,006	287	215	215	215
Europe (€, 30% discount)	0	0	0	0	15	88	146	205	205	175	175
Japan (¥, 30% discount)	0	0	0	0	121	6,370	13,241	18,610	22,410	19,871	19,446
ROW ($, 50% discount, Scenario A)	0	0	103	207	261	416	480	592	477	374	287
ROW ($, 50% discount, Scenario B)	0	0	109	227	283	466	561	728	621	521	430
ROW ($, 50% discount, Scenario C)	0	0	114	247	316	545	693	961	883	801	717

Celltrion's sales (mn) 20% Discount (Korean Won)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (50% discount)	0	0	0	0	0	0	59,300	47,400	35,600	35,600	35,600
US FTF (80% discount)	0	0	0	0	0	0	66,400				
US Average	0	0	0	0	0	0	62,900	47,400	35,600	35,600	35,600
Europe	0	0	0	0	6,000	35,000	59,000	82,000	82,000	70,000	70,000
Japan	0	0	0	0	0	20,000	42,000	59,000	71,000	63,000	62,000
ROW (Scenario A)	0	0	45,000	91,000	115,000	183,000	211,000	261,000	210,000	164,000	126,000
ROW (Scenario B)	0	0	48,000	100,000	124,000	205,000	247,000	320,000	273,000	229,000	189,000
ROW (Scenario C)	0	0	50,000	108,000	139,000	240,000	305,000	423,000	389,000	352,000	315,000
Total (Using Scenario A)	0	0	45,000	91,000	121,000	238,000	374,900	449,400	398,600	332,600	293,600
Total (Using Scenario B)	0	0	48,000	100,000	130,000	260,000	410,900	508,400	461,600	397,600	356,600
Total (Using Scenario C)	0	0	50,000	108,000	145,000	295,000	468,900	611,400	577,600	520,600	482,600

Source: Nomura estimates

Understanding Market Dynamics of MabThera/Rituxan

What is MabThera/Rituxan

MabThera/Rituxan (rituximab) is a chimeric anti-CD20 monoclonal antibody that was developed by IDEC Pharmaceuticals (now Biogen-Idec). The antibody attaches to B-cells with CD20 and induces cell lysis through ADCC (antibody dependent cell-mediated cytotoxicity) or CDC (complement dependent cytotoxicity) or induces apoptosis. The drug is the predominant biologic for diseases that increase the number of B-cells, such as B-cell lymphoma, or leukemia. MabThera/Rituxan's main indication is Non-Hodgkin's Lymphoma, an aggressive form of cancer in the lymphatic system. Since February 2009 in Europe and February 2010 in the US, MabThera/Rituxan is also indicated for first-line treatment of CLL (chronic lymphocytic leukemia). Very recently, MabThera/Rituxan was also approved for first-line maintenance treatment of follicular lymphoma. The drug is also used as a second-line biologic for Rheumatoid Arthritis.

At least two clinical trials needed to cover all indications

MabThera/Rituxan has one of the broadest indications of all biologics. Indications span both oncology (NHL, CLL, FL) and autoimmune diseases (Rheumatoid Arthritis). This presents special challenges to the clinical development of biosimilars, since oncology and autoimmune diseases are two distinct therapeutic areas. The draft "Guideline on Similar Biological Medicinal Products Containing Monoclonal Antibodies" published on November 26th 2010 states that "… if distinct therapeutic areas are involved for one particular mAb (e.g. autoimmunity and oncology), separate pK studies may be recommendable as a support for extrapolation between these two indications". Thus, at least two clinical trials are required for the biosimilar rituximab to cover all indications. We believe that the drug regimen for NHL and CLL are significantly different; NHL is used with CHOP therapy (see below), while CLL is indicated for use with FC therapy (fludarabine/cyclophosphamide). Since Celltrion already covers rheumatoid arthritis with Remicade and Enbrel, we think that only two clinical trials (NHL and CLL) are likely to be performed.

Non-Hodgkin's Lymphoma

Lymphomas consist of a group of cancers in the lymphatic system. Non-Hodgkin's Lymphomas (NHL) are further distinguished by cancers originating in B-lymphocytes, T-lymphocytes, and Natural Killer lymphocytes. 80-85% of cases in the US are B-cell lymphomas, the remainder being T-cell lymphomas. Incidence is similar in Europe and Japan. Most common type of Non-Hodgkin's Lymphomas is Diffuse Large B-Cell Lymphoma (DLBCL), constituting around 40% (US) to greater than 50% (Japan) of cases, followed by Follicular Lymphomas (FL) constituting about 25% worldwide.

Rituxan: First-line choice for NHL

R-CHOP (rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisone) is the first-line therapy of choice for Diffuse Large B-Cell Lymphoma. A detailed description of the regimen using Japanese prices is shown in the table below. The estimated annual price assumes eight cycles of R-CHOP therapy for maximum annual pricing. Annual price for R-CHOP therapy is about JPY2mn in Japan, USD30mn in the US, of which MabThera/Rituxan constitutes greater than 80% of the cost.

Fig. 66: R-CHOP Therapy: Annual cost calculation

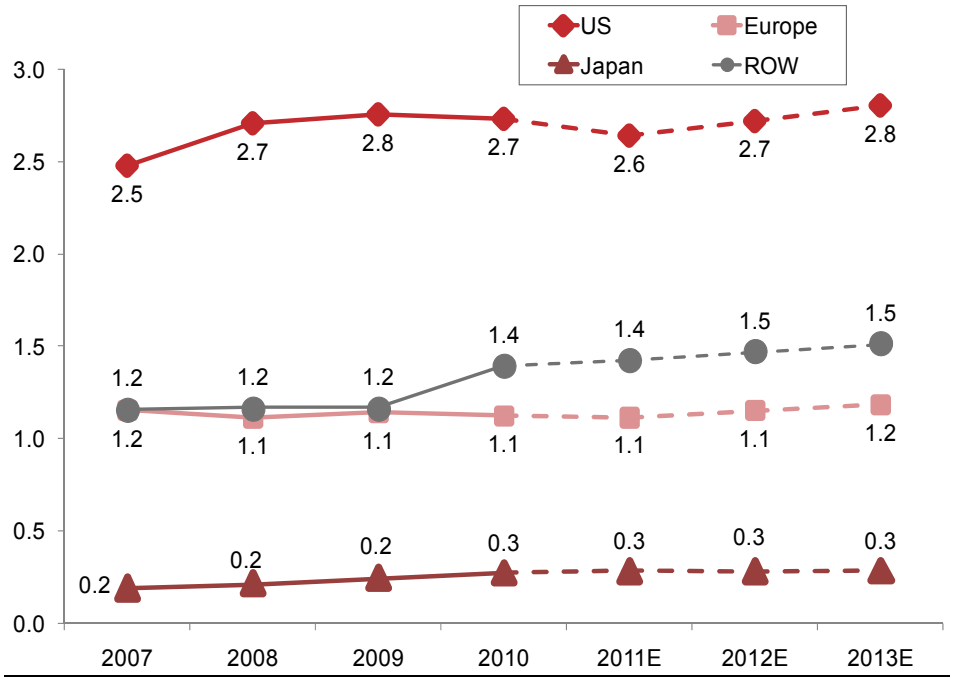
1 Course is 3wks, repeat to maximum x8				
Day 1			Day 2-5	Day 6-20
Rituximab 375mg/m2		Cyclophosphamide 600mg/m2		
214,160		698		
Adriamycin 50mg/m2		Vincristine 1.4mg/m2		
18,608		6,504		
Prednisolone 60mg/m2			Prednisolone 60mg/m2	Rest
1,020			1,020	
Total Cost per Course - JP				245,070
Total Cost per Course - US				3,608
Annual Maximum Cost - JP				**1,960,563**
Annual Maximum Cost - US				**28,863**
Rituxan Cost - JP				**1,713,280**
Rituxan Cost - US				**26,573**

Source: Japanese Drug Prices, Red Book, Nomura

Expanded indication has little implication for growth

Despite the new indications in CLL and follicular lymphoma, Nomura forecasts little growth in either the US or Europe. Roche has commented that in the US, MabThera/Rituxan is already being used off-label for follicular lymphoma and the patient share has reached 95% prior to FDA approval. Same applies in Europe, where CLL is already treated with rituximab to a large extent. No clinical trials are planned for CLL or FL in Japan, presumably because of a particularly diminutive patient pool. Thus, Nomura believes that MabThera/Rituxan sales will be relatively constant in the foreseeable future.

Fig. 67: Rituxan Oncology Sales



Source: IMS Health

Patent expiration: 2013 in Japan and Europe, 2018 in US

Biogen Idec, the originator of MabThera/Rituxan, claims in their most recent 10-K that the principal patent expiry in the US is 2015-2018, while patents in ROW will expire in 2013, although additional patents may extend the period. In Japan and Europe, the substance patent expires around 2013, although an SPC for EP2000149 has been filed recently in some countries. In the US, some patents were filed a day or two – presumably not by coincidence – before the Uruguay round cutoff date of Jun 8th, 2005, after which patents would expire 20 years from the first filing date. Because these were filed on June 6th and 7th, barring exceptions, patents should expire 17 years from patent registration, meaning that they may very well extend to 2020 in some cases. Thus, we do not include the launch of US biosimilar launch in Celltrion's forecasts.

Fig. 68: Key Patents for MabThera/Rituxan

Rituxan	Patent Title	Submission Date	Estimated Patent Expiry
JP3095175	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-12-1993	2014
JP4091235	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-12-1993	2013
JP4203080	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-12-1993	2013
EP0669386	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-12-1993	2013
EP1005870	Therapeutic Application of Chimeric Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-12-1993	2013
EP2000149	Chimeric Anti-CD20 Antibody	Nov-12-1993	2013
US5595898	Modular Assembly of Antibody Genes, Antibodies, Prepared Thereby and Use	Aug-18-1994	2014
US5693493	Modular Assembly of Antibody Genes, Antibodies, Prepared Thereby and Use	May-25-1995	2015
US5736137	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Nov-3-1993	2015
US5776456	Therapeutic Application of Chimeric and Radiolabeled Antibodies to Human B Lymphocyte Restricted Differentiation Antigen for Treatment of B Cell Lymphoma	Jun-7-1995	2015
US7648702	Stable Aqueous Formulation of a Soluble TNF Receptor and Arginine	Feb-27-2003 (Original Filing Date)	Feb-27-2023

Source: JPO, EPO, USPTO

Patient demographics: 60 years or older

According to the American Cancer Society estimates, about 66,000 people will be diagnosed in 2010 with Non-Hodgkin's Lymphoma. Patients are most often diagnosed when they are in their 60s. Incidence of NHL has risen in the past years, presumably due to increased longevity and decreasing mortality from other causes.

Patient population

From the average annual cost of Rituxan treatment, the number of patients in each region is calculated as below. Based on our calculation, the number of NHL patients using Rituxan in 2010 is estimated, for the purpose of calculating biosimilar penetration, to be 93,000 in the US, 48,000 in Europe, and 13,000 in Japan. We emphasize that the calculation is a rough estimate; we are assuming that all oncology indications are DBCLC patients for the purpose of estimation.

Fig. 69: Patient Calculation: MabThera/Rituxan

Rituxan Sales (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
Rituxan (US)	2,901	3,057	3,155	3,249	3,347	3,447
Oncology	2,616	2,750	2,833	2,918	3,005	3,096
Rheumatoid Arthritis	285	307	322	332	341	352
Rituxan (Europe)	1,185	1,133	1,181	1,224	1,261	1,299
Oncology	811	765	787	811	835	860
Rheumatoid Arthritis	374	368	394	414	426	439
Rituxan (Japan)	22,971	24,480	24,376	24,684	24,579	24,893
Oncology	22,971	24,480	24,376	24,684	24,579	24,893
Rheumatoid Arthritis						
Rituxan (ROW)	1,359	1,512	1,558	1,605	1,654	1,703
Oncology	1,336	1,486	1,530	1,576	1,624	1,672
Rheumatoid Arthritis	23	26	28	29	30	31
Rituxan Total						

Annual cost per treatment	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
Rituxan (US, NHL)	$28,000	$28,000	$27,440	$26,891	$26,353	$25,826
Rituxan (US, RA)	$28,000	$28,000	$27,440	$26,891	$26,353	$25,826
Rituxan (Europe, NHL)	16,800 €	16,800 €	16,464 €	16,135 €	15,812 €	15,496 €
Rituxan (Europe, RA)	16,800 €	16,800 €	16,464 €	16,135 €	15,812 €	15,496 €
Rituxan (Japan, NHL)	¥1,713,280	¥1,713,280	¥1,627,616	¥1,627,616	¥1,546,235	¥1,546,235
Rituxan (Japan, RA)						
Rituxan (ROW, India, NHL)	640,000	640,000	640,000	640,000	640,000	640,000
Rituxan (ROW, China, NHL)	¥152,800	¥152,800	¥152,800	¥152,800	¥152,800	¥152,800
Rituxan (ROW, USD, India)	$14,019	$13,913	$13,913	$13,913	$13,913	$13,913
Rituxan (ROW, USD, China.)	$22,573	$22,806	$22,806	$22,806	$22,806	$22,806
Rituxan (ROW, USD, est.)	$20,000	$20,000	$20,000	$20,000	$20,000	$20,000
Rituxan (ROW, USD, RA)	$20,000	$20,000	$20,000	$20,000	$20,000	$20,000

Est. Number of Patients	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY
Rituxan (US, NHL)	93,442	98,221	103,239	108,506	114,042	119,860
Rituxan (US, RA)	10,169	10,948	11,730	12,328	12,957	13,618
Rituxan (Europe, NHL)	48,281	45,506	47,818	50,252	52,815	55,510
Rituxan (Europe, RA)	22,247	21,913	23,926	25,635	26,942	28,317
Rituxan (Japan)	13,407	14,288	14,977	15,166	15,896	16,099
Rituxan (ROW, NHL)	66,824	74,294	76,524	78,820	81,184	83,620
Rituxan (ROW, RA)	1,150	1,292	1,382	1,451	1,495	1,540

Source: Nomura Europe Forecast, Nomura estimates

Fig. 70: CT-P10 Forecast

Expansion of Patient Size From Biosimilars (# of patients)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (NHL)	93,400	98,200	103,200	108,500	114,000	119,900	126,000	132,400	139,200	146,300	169,600
US (RA)	10,200	10,900	11,700	12,300	13,000	13,600	14,300	15,000	15,800	16,600	17,000
Europe (NHL)	48,300	45,500	47,800	50,300	52,800	55,500	58,300	61,300	64,400	67,700	70,900
Europe (RA)	22,200	21,900	23,900	25,600	26,900	28,300	29,800	31,300	32,900	34,600	34,600
Japan (NHL)	13,400	14,300	15,000	15,200	15,900	16,100	17,200	17,400	18,600	19,800	20,800
Japan (RA)											
ROW (NHL)	66,800	74,300	76,500	78,800	81,200	83,600	86,100	88,700	91,400	94,100	96,900
ROW (RA)	1,200	1,300	1,400	1,500	1,500	1,500	1,600	1,600	1,700	1,700	1,700
ROW (Scenario A)	68,000	75,600	77,900	80,300	84,700	90,100	96,700	106,600	122,600	149,200	195,500
ROW (Scenario B)	68,000	75,600	77,900	80,300	86,700	95,100	105,800	123,000	152,300	202,900	292,400
ROW (Scenario C)	68,000	75,600	77,900	80,300	90,700	105,100	123,900	155,800	211,600	310,200	486,200
Expansion (2020 Scenario A: 100% Expansion)	0	0	0	0	2,000	5,000	9,000	16,300	29,500	53,400	96,900
Expansion (2020 Scenario A: 200% Expansion)	0	0	0	0	4,000	10,000	18,100	32,700	59,200	107,100	193,800
Expansion (2020 Scenario A: 400% Expansion)	0	0	0	0	8,000	20,000	36,200	65,500	118,500	214,400	387,600

% of total population receiving rituximab (Basis points)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US	3.4	3.5	3.7	3.8	4.0	4.2	4.3	4.5	4.7	4.9	5.6
Europe	2.1	2.0	2.1	2.3	2.4	2.5	2.6	2.7	2.8	3.0	
Japan	1.1	1.1	1.2	1.2	1.3	1.3	1.4	1.4	1.5	1.6	1.7
ROW (Scenario A)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.3
ROW (Scenario B)	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.3	0.4
ROW (Scenario C)	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.3	0.5	0.7

Biosimilar Penetration Rate (%)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (Expiry 2014-5)	0.0	0.0	0.0	0.0	0.0	0.0	10.0	8.0	5.0	5.0	5.0
US FTF (Expiry 2014-5)	0.0	0.0	0.0	0.0	0.0	0.0	40.0	8.0	5.0	5.0	5.0
Europe (Expiry 2013/4)	0.0	0.0	0.0	0.0	0.0	3.0	5.0	7.0	5.0	3.0	3.0
Japan (Expiry 2012)	0.0	0.0	0.0	0.0	0.0	5.0	10.0	25.0	25.0	25.0	25.0
ROW (Scenario A)	0.0	0.0	0.0	0.0	10.0	15.0	20.0	19.0	18.0	15.0	12.0
ROW (Scenario B)	0.0	0.0	0.0	0.0	10.0	15.0	20.0	19.0	13.0	13.0	10.0
ROW (Scenario C)	0.0	0.0	0.0	0.0	10.0	15.0	20.0	19.0	18.0	15.0	12.0

End market size (mn) (Regional Currency)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (50% discount)	0	0	0	0	0	0	159	131	85	87	99
US FTF (First year 30% discount, 50% thereafter)	0	0	0	0	0	0	893	131	85	87	99
Europe (30% discount)	0	0	0	0	0	18	31	45	33	20	21
Japan (30% discount)	0	0	0	0	0	871	1,769	4,473	4,542	4,594	4,584
ROW (Scenario A, 60% discount)	0	0	0	0	68	108	155	162	177	179	188
ROW (Scenario B, 60% discount)	0	0	0	0	69	114	169	187	158	211	234
ROW (Scenario C, 60% discount)	0	0	0	0	73	126	198	237	305	372	467

Celltrion's sales (mn) 20% discount (Korean Won)	2010FY	2011FY	2012FY	2013FY	2014FY	2015FY	2016FY	2017FY	2018FY	2019FY	2020FY
US (50% discount)	0	0	0	0	0	0	26,300	21,700	14,000	14,400	16,300
US FTF (90% discount)	0	0	0	0	0	0	29,500				
US Average	0	0	0	0	0	0	27,900	21,700	14,000	14,400	16,300
Europe	0	0	0	0	0	12,000	21,000	30,000	22,000	14,000	14,000
Japan	0	0	0	0	0	5,000	9,000	24,000	24,000	24,000	24,000
ROW (Scenario A, 70% discount)	0	0	0	0	30,000	48,000	68,000	71,000	78,000	79,000	83,000
ROW (Scenario B, 70% discount)	0	0	0	0	31,000	50,000	74,000	82,000	70,000	93,000	103,000
ROW (Scenario C, 70% discount)	0	0	0	0	32,000	55,000	87,000	104,000	134,000	164,000	205,000

Source: Nomura estimates

Appendix II: Competition vs Innovation

This section summarizes the counterstrategy of brand-name makers against biosimilar incursion and also competition between biosimilar and next generation innovative antibody therapeutics and/or oral molecules being developed by Roche and others as a bulwark against biosimilar encroachment.

Bio-betters: not as easy as it looks

Next-gen antibody therapeutics does not show compelling improvement
Innovative brand-name companies' response to biosimilars center around two themes. One is the promotion of entirely new molecules with different mechanisms (e.g. Roche's pertuzumab) and the other is the development of bio-betters. Focusing on the latter, Roche is currently developing two bio-betters: T-DM1, an armed antibody linked to a cytotoxic drug, GA-101 that has a glycoengineered Fc portion that improves ADCC activity. The results, discussed below, are decidedly mixed: T-DM1 shows less hair loss at the expense of liver toxicity, GA-101 shows good response but also infusion reactions and serious infection. A humanized antibody ocrelizumab has shown a significant rate of infusion reactions. Other bio-betters have been developed that was quietly dropped because of lack of efficacy or safety issues.

Stark warning to all companies developing bio-betters
If Roche/Biogen-Idec cannot successfully develop bio-betters that have convincingly better value, then it is reasonable to assume that biosimilar companies with much less experience in working with biotechnology would have less of a chance of developing bio-betters. If the development of bio-betters is just as risky as any innovative antibody, companies might eschew bio-betters altogether and tackle innovation head-on.

CT-P06: Roche's biosimilar counter-strategy likely to be of limited effect

Roche's line of defense #1: Threat of flexible pricing in the ROW
Foremost among Roche's defense strategy against biosimilar is the concept of flexible pricing. At the 14 April 2011 conference call, Roche commented that it is currently working on flexible pricing in Brazil and Eastern Europe to ensure greater access to the drug. Roche is also negotiating in China. The incentive, initiated in 2010, and will go forward in 2011. Roche does not disclose the details of its strategy but some adjustment in pricing is probably unavoidable. Overall, Roche has been very cautious in approaching the subject of price reduction.

You have to make up what you lose
We believe that it is not in the best interest of Roche and its shareholders to indiscriminately lower prices, even in the ROW countries. First, in order to maintain growth in ROW - the only growth region for Herceptin – Roche must make certain that whatever is lost from reducing prices, will be compensated by increased volume. Except in regions like India and Peru where price sensitivity is extremely high, Roche and other brand-name biologics makers are very cautious in lowering prices. Second, biosimilars will always respond by lowering their price even further. At some point it is not beneficial for companies.

Futility of price wars when the competitor has 60% OP margin
Celltrion's operating profit margin of approximately 60% (FY10) will also be a factor in considering price adjustment. Celltrion and its partner would be more than capable of lowering prices to whatever level necessary, in our view.

Roche's line of defense #2: Subcutaneous formulation
Roche, during its conference call presentation of 2010 fiscal year results on 4 February 2011, outlined three additional lines of defense against Herceptin biosimilar encroachment. First, Roche is currently working on a subcutaneous formulation of Herceptin in collaboration with Halozyme, which is currently undergoing a Phase III trial. The new formulation utilizes Halozyme's proprietary Enhanze technology. Enhanze

technology uses Halozyme's proprietary rHuPH20 enzyme, which is a human synthetic version of hyaluronidase, an enzyme that breaks down hyaluronan (an oligosaccharide abundant in tissues). By digesting hyaluronan in tissues, this facilitates the penetration and diffusion of antibodies that are usually too large to penetrate via a subcutaneous formulation. Patient enrollment is already completed, and Roche is planning to provide results by the end of 2011, and ultimately filing for subcutaneous formulation in 2012.

From 90 minutes in a hospital to 5 minutes at home

Halozyme, during its fiscal year 2010 conference call on 11 March 2011, outlined the benefits of using the Enhanze technology with Herceptin. Halozyme noted that Herceptin would require 30 to 90 minutes in a hospital setting on an IV regimen but a subcutaneous administration would shorten the time required to five minutes at home. Moreover, the dosage would be constant for subcutaneous treatment, as opposed to the weight-based dosage for IV, thereby improving the clinical ease-of-use.

Subcutaneous formulation would improve therapy compliance

Additionally, Roche believes that a subcutaneous formulation would improve drug therapy compliance. The average duration of Herceptin treatment is 48-50 weeks. A follow-up study to the HERA pivotal study is testing the effectiveness of 12 months of trastuzumab treatment vs a 24-month treatment. Roche believes that if a benefit is observed with a 24-month regimen, the average duration of Herceptin treatment would lengthen by 20-30%. The subcutaneous formulation would help in lengthening the duration by its ease of use, which would encourage patient adherence to the recommended drug regimen.

Fig. 71: Clinical Trials Exploring Longer or Shorter Duration of Herceptin Therapy

Trial Name	Country	# of patients	Data Est.	Duration
FinHer	Finland	232	2009	12 months vs 9 weeks
HERA Study	International	3,404	2012	24 vs 12 months
PHARE	France	3,400	2012-3	12 vs 6 months
PERSEPHONE	UK	4,000	2014-5	12 vs 6 months
SOLD	International	3,000	2014-5	12 months vs 9 weeks

Source: Clinicaltrials.gov, Nomura research

Patients may prefer subcutaneous formulation particularly in US

It is clear that patients would most probably prefer self-administration at home to 90 minutes in a hospital. However, we believe that one factor is the cost of treatment. Although the subcutaneous formulation of Herceptin has not been approved yet, the recombinant hyaluronidase has been approved as Hylenex for pediatric dehydration. According to Baxter's website (Baxter markets Hylenex), the list price of one vial of Hylenex is USD360. Although the amount of recombinant hyaluronidase may differ significantly between Hylenex and subcutaneous Herceptin, one would assume that the already expensive Herceptin price would increase significantly. Despite its ease of use, Nomura believes that the penetration of subcutaneous formulation of Herceptin will likely be limited even in Europe and Japan due to its prohibitive pricing.

Another threat: shortening the duration of Herceptin

Note that clinical trials that explore a shorter duration of Herceptin treatment are currently underway in multiple countries. The biggest concern in the use of Herceptin is cardiac failure, which is seen in 1-4% of patients in adjuvant treatment. Thus, a shorter duration would likely mitigate the risk of adverse cardiac events.

FinHER trial showed shortened duration not effective

To date, the FinHER (Finland Herceptin) trial is the only trial that tested a shorter duration of Herceptin. The results showed that in the subgroup of patients with HER2 positive disease, chemotherapy (either docetaxel/FEC or vinorelbine/FEC) with nine weeks of Herceptin showed no statistically significant improvement when compared to chemotherapy alone. However, patients who were treated with docetaxel/FEC/ trastuzumab showed an unexpectedly favourable DDFS (distant disease-free survival).

We think that the FinHER trial is not the final word on the topic, since its main limitation is the small number of patients who were assigned to Herceptin (n = 116).

All eyes on the SOLD trial

The SOLD (Synergism or Long Duration) trial that is currently underway will be adequately powered with expected patient enrollment of 3,000. If the results show that disease-free survival with nine-week Herceptin/docetaxel is equivalent to a one-year treatment of docetaxel/CEF/trastuzumab, we believe that duration of Herceptin treatment could be curtailed in all regions of the world. The same will likely apply to the use of biosimilars, which may affect Celltrion's sales. Although the final data of the SOLD clinical trial will not be available until 2015, we believe that presentation of any interim results should be followed with caution. If the FinHER trial serves as a guide, Nomura believes that the potential for statistically significant efficacy from the nine-week Herceptin treatment is limited.

Roche's line of defense #3: Pertuzumab + Herceptin

Roche's second line of defense is a combination with pertuzumab, an investigative monoclonal antibody currently in a Phase III trial. Like trastuzumab, pertuzumab is also HER2-directed. Pertuzumab binds to a site distinct from trastuzumab and prevents the heregulin-induced HER2-HER3 dimerization. On 10 December 2010, Genentech announced the result of NEOSPHERE Phase II trial which considered various combinations of docetaxel, trastuzumab, and pertuzumab in early-stage HER2 positive breast cancer patients. The results revealed that docetaxel combined with trastuzumab and pertuzumab showed pCR (pathological complete response) of 46%, which is among the highest ever seen in HER2 positive breast cancer. It is also worthy of note that the high response rate was achieved after only 12 weeks of neoadjuvant treatment. Currently, the Phase III trial (CLEOPATRA trial) evaluating the efficacy and safety of pertuzumab and trastuzumab plus chemotherapy has completed patient enrollment in 2Q10. Data is expected by the end of 2011.

One antibody = expensive, two antibodies = VERY expensive

We do not believe that pertuzumab will present a significant barrier to biosimilar entry, even if the CLEOPATRA trial replicates the favorable results seen in NEOSPHERE. In order to cover sales erosion from Herceptin biosimilars, Roche would most likely request a premium pricing for pertuzumab. Japan has one of the lowest drug prices in the developed world. Even in Japan, a full year treatment of AC + T (anthracycline + trastuzumab) regimen costs JPY3mn, of which about 30% is copayment or paid out of pocket. If pertuzumab is added on top of this, a year long adjuvant treatment could be well above JPY5mn. Even if pertuzumab combination treatment proves very effective, the drug caters to an entirely different subset of the patient population.

Roche's line of defense #4: Conjugate antibody T-DM1

Roche's most important defense against biosimilars is the next-generation conjugate antibody T-DM1. T-DM1 is a monoclonal antibody that binds to HER2, much like Herceptin, with a linked chemotherapy drug called emtansine (DM1). T-DM1 is being developed by Roche using ImmunoGen's technology. On 7 April 2011, Roche announced the results of a 137-patient Phase II trial showing significant improvement in progression free survival (PFS) compared to patients treated with Herceptin and docetaxel. Detailed results are scheduled to be presented at a future medical congress.

T-DM1 clinical trials

T-DM1 is currently being studied in a number of clinical trials. The most important phase III clinical trials are EMILIA, which evaluates T-DM1 in second-line setting for metastatic breast cancer against comparators Tykerb and Xeloda, and MARIANNE, which evaluates T-DM1 in first-line metastatic breast cancer against Herceptin and taxanes. EMILIA clinical trial results are expected in 2012 and MARIANNE after 2013.

Less hair loss …

A comparison of results from Phase II TDM4450g trial is shown in the table below. T-DM1 shows significantly lower hair loss, diarrhea, and neutropenia compared to Herceptin + Docetaxel. Significant reduction in hair loss is especially important for women undergoing treatment. However, Amit Roy Nomura Europe Research notes that

the rate of discontinuation were similar in both cases, 32.8% with T-DM1 and 35.7% with Herceptin + Docetaxel.

Fig. 72: Clinical Trials Exploring Longer or Shorter Duration of Herceptin Therapy

Adverse Event	T-DM1	Herceptin + Docetaxel
Hair Loss	1.5%	66.2%
Diarrhea	10.4%	45.6%
Neutropenia	7.5%	57.4%
Nausea	47.8%	39.7%
Fatigue	46.3%	46.2%
Pyrexia	35.8%	20.6%

Source: ESMO 2010 (abstract #LBA3), Nomura Europe research

… but more liver toxicity

Our European colleague, Amit Roy, also notes that benefits of T-DM1 must be weighed against increased risk of liver toxicity and thrombocytopenia. At the ESMO (European Society for Medical Oncology) conference in October 2010, preliminary Phase II data was presented which showed elevated liver toxicity in 40% of patients, compared to 13% on chemotherapy. Also, 22.4% of patients on the T-DM1 arm experienced thrombocytopenia compared with only 5.9% in the Herceptin + docetaxel arm. Furthermore, the number of patients on Stable Disease at six months of T-DM1 treatment was half that of the Herceptin + docetaxel arm. For more information on T-DM1 clinical trials, we refer the reader to Amit Roy's report dated 12 October 2010 "Avastin DOES work in 5% taxane-Triple Negatives".

Fig. 73: Main Clinical Trials for T-DM1

Disease Stage	Filing Expected	Expected launch date	Trial ongoing	Phase	Final data	# patients
1st line mBC	post 2013	2015	TDM4450g	II	2011	137
			MARIANNE	III	post 2013	1,092
2nd line mBC	2012-13	Mar-12	EMILIA	III	2012	980
3rd line mBC	2010	2011	TDM4374g	II	2009	110

Source: Nomura Europe

T-DM1 unlikely to provide much cover to biosimilar

Final data from extensive trials with more patients are necessary to make the final verdict. Also, the progression free survival curves from the final data set of Phase II TDM4450g clinical trial will need to be examined. But with the present information, there are already reasonable doubts that T-DM1 will significantly improve on Herceptin in terms of PFS, OS, or safety. Thus, we do not think that T-DM1 will provide much cover from biosimilar erosion, unless later Phase III data (EMILIA or MARIANNE) shows more significant improvement.

CT-P13/P05: Neither Simponi nor tofacitinib will stop the forward march of biosimilars

Simponi the most likely defense strategy against biosimilars

Neither Johnson & Johnson (US), nor Merck (ex-US, not including Japan), nor Mitsubishi Tanabe Pharmaceutical (Japan) has publicly outlined its defense strategy against biosimilar penetration. But we note that all three companies currently marketing Remicade have distributing rights in their respective regions to Simponi, a longer-lasting self-injectable TNF-alpha inhibitor. Thus, we believe that cannibalization of Remicade market share by Simponi is a strong candidate for the innovators' biosimilar defense strategy.

Simponi: once daily anti-TNFalpha

Unlike Remicade, Simponi is a fully-human monoclonal antibody. Therefore, it demonstrates much less incidence of infusion reactions compared to Remicade. It is also approved as a subcutaneous injection, much like Enbrel and Humira. The approval of Simponi was granted on 24 April 2009 in the US, making Simponi a late addition in the TNF-alpha inhibitor subclass. We believe Simponi is still positioned as a second-line biologic. Currently, Simponi does not have indication for inhibiting structural damage in Rheumatoid Arthritis or Psoriatic arthritis, though submission for these indications have been filed recently in Europe and the US. Simponi has been filed for submission in Japan in June 2010. We expect approval in Japan by late 2011.

Cannibalization limited in Europe or US

Currently, we note that there is little evidence of cannibalization of Remicade sales from Simponi in Europe or the US. According to Merck's 2010 R&D Day, 58% of Simponi sales is from naïve patients and 42% from patients switching to Simponi from other antibodies. Of the switching patients, Merck shows that 95% of the patients are those who have been using Humira, Enbrel, or Orencia and only 1% of patients have switched from Remicade. We believe that if biosimilar penetration becomes significant, all three companies may promote Simponi to maintain revenue. In the US, Johnson & Johnson commented that cannibalization of Remicade sales from Stelara (for Psoriasis) and Simponi were limited. According to Johnson & Johnson's 19 October 2010 conference call, about 25% of Simponi patients are biologic naïve, while the remaining 75% are patients that have switched from either Enbrel or Humira. Simponi seems to be well differentiated from Remicade in all regions where it is being marketed.

Simponi's second line status will hinder its biosimilar defense

Until the arrival of biosimilars, we assume that Johnson & Johnson, Merck, and Mitsubishi Tanabe would skillfully promote Simponi so that the cannibalization of Remicade sales is mitigated. This means that Simponi will necessarily be a second-line drug after treatment with either Enbrel or Humira. Because this drug will be promoted in this manner, we do not think that Simponi can be elevated to the first-line position within five years when the biosimilar threat materializes. Currently, we do not see any evidence that these companies are planning on gradually replacing Remicade with Simponi. Thus we believe that the use of Simponi as a bulwark against biosimilar erosion is somewhat limited.

Biggest threat is the rise of the oral small molecule drugs

The foremost threat is the rise of the oral small molecule drugs to treat autoimmune diseases. Orally administered drugs would clearly be a threat to injectable antibodies since they greatly improve patients' ease of use. If this is coupled with lower prices, these drugs may have a significant impact on TNF-alpha inhibitors and, by implication, penetration of biosimilars. Among the candidates, Pfizer's tofacitinib (CP-690,550) is closest to approval. Tofacitinib is a novel JAK3 kinase inhibitor that is being studied in Rheumatoid Arthritis, dry eye, Crohn's disease, plaque psoriasis, ulcerative colitis and solid organ transplant.

ORAL1045: Significant improvement in ACR20

Detailed results from the Phase III rheumatoid arthritis trial (ORAL 1045) have been presented at the ACR 2010 meeting. The study enrolled patients who showed inadequate response to disease modifying anti-rheumatic drug (DMARD), including traditional and biologics, such as TNF alpha inhibitors. The results showed significant increase in the percentage of patients achieving ACR20 (20% improvement in swollen joint counts and improvement in other parameters) against placebo. For tofacitinib administered twice daily, the percentage of patients achieving ACR20 after three months was around 60% for 5mg BID, 66% for 10mg BID, and 27% for placebo. The percentage of patients achieving ACR70, which represents clinical remission, was 20% for 10mg BID, 15% for 5mg BID, and 6% for placebo. Although it is not strictly comparable because the patient population is very different, it is interesting to note that both Humira and Remicade showed only 50-60% of patients improving to ACR20 in 30 weeks in their respective pivotal phase III trials. Serious adverse events were reported in 4.1% of patients. There were six cases of serious infection that was reported. Less serious adverse events included decrease in white blood cells, increase in LDL cholesterol, and

rise in liver enzymes in some patients. Tofacitinib holds great promise in advancing the cure of rheumatoid diseases if its clinical effectiveness can be sustained in subsequent longer studies.

ORAL 1044: Solid 2-year results

Results of another Phase III Rheumatoid Arthritis trial (ORAL 1044) were reported on 15 April 2011. The two-year study enrolled patients who had inadequate response to methotrexate (MTX) and randomized to receive 5mg or 10mg tofacitinib BID. The study met all primary endpoints at 10mg BID dose, showing statistically significant changes versus placebo in ACR20, reducing the progression of joint damage, and clinical remission as measured by DAS28-4(ESR) < 2.6 at six months. The study showed no new safety issues.

Four deaths reported in ORAL 1046 clinical trial result

Pfizer's ORAL Sync 1046 clinical trial data was released on the EULAR website on 26 April 2011 and it showed four deaths among patients as well as raised levels of LDL cholesterol in one-third the patient population. Pfizer subsequently stated that three of the deaths were not related to tofacitinib. According to Nomura Europe Analyst Bhanu Singhal, while Pfizer's Phase III clinical development programme (six trials) is heavily focused on the same patients that currently use anti-TNFs (like Cimzia), early clinical data (Phase II) showing Actemra-like increases in levels of bad cholesterol (LDL) may cause the FDA to grant Actemra-like, restricted approval to patients who have previously tried and failed anti-TNFs. Bhanu Singhal also does not rule out the possibility of further investigation into cardiovascular risk given the death from acute heart failure in the Phase III and the previous death from stroke seen in the Phase II "1035" trial. For more information on tofacitinib clinical trials, we refer the reader to Bhanu Singhal's report dated 27 April 2011"Pfizer's oral RA drug likely to compete with Roche's Actemra rather than UCB's Cimzia".

Fig. 74: CP-690,550 (tofacitinib) Rheumatoid Arthritis Clinical Trial

Trial Name	Months	n	Patient Type	Dosage	Primary Endpoints	Completion Date
ORAL Scan (1044)	24	750	Inadequate responders to MTX	5 or 10mg BID	Tests preservation of joint structure	Completed
ORAL Solo (1045)	6	652	Inadequate responders to DMARD (biologic or traditional)	5 or 10mg BID	ACR20, HAQ DI, DAS28-4(ESR)<2.6	Completed
ORAL Sync (1046)	12	750	Inadequate responders to DMARD (biologic or traditional)	5 or 10mg BID	ACR20, HAQ DI, DAS28-4(ESR)<2.6, Safety	Completed
ORAL Standard (1064)	12	700	Inadequate responders to MTX	5 or 10mg BID vs Humira	ACR20, HAQ DI, DAS28-4(ESR)<2.6, Safety	Mar-11
ORAL Step (1032)	6	400	Inadequate responders to TNF-alpha	5 or 10mg BID	ACR20, HAQ DI, DAS28-4(ESR)<2.6, Safety	Mar-11
ORAL Start (1069)	24	900	Inadequate responders to TNF-alpha	5 or 10mg BID	6 months radiographic change, ACR70, Safety (vital sign change)	Mar-13

Source: Clinicaltrials.gov

Other oral drugs hot on Pfizer's heels

There are other oral DMARDs for rheumatoid arthritis under development. The Syk inhibitor fostamatinib, developed by Rigel Pharmaceuticals and AstraZeneca, is currently in Phase III trials. The drug boasts an additional advantage of once-daily dosing. Eli Lilly (LY3009104) has a JAK1/JAK2 inhibitor, which it in-licensed from Incyte Corporation in Phase II clinical trials. Vertex (VX-509) also has a JAK3 inhibitor in the pipeline that is in phase II trial. The trial is expected to obtain results in 2011. We think that it is very likely that at least one of the compounds will reach commercialization.

Biosimilars will not compete with oral small molecules

We do not think that any of these oral compounds will compete with biosimilars. Based on the past few cases where a monoclonal antibody or recombinant protein treatment was followed by an oral small molecule drug, there was few, if any, evidence of a significant price reduction for a new oral drug. Tykerb is an oral EGFR/HER2 inhibitor approved for treatment of patients with HER2 positive metastatic breast cancer already exposed to anthracyclines, taxanes, and trastuzumab. The annual cost of treatment using lapatinib is not significantly different from treatments with anthracyclines,

trastuzumab, and Herceptin. Another recent example is the difference between Gilenya (fingolimod) versus Avonex (interferon beta-1a). The US annual treatment price for Gilenya recently reported (see Novartis report 29 March 2011) is USD48,000/year, at a 40-50% premium over current injectables such as Avonex or Copaxone.

CT-P10: GA101 and subcutaneous MabThera/Rituxan

Subcutaneous formulation for MabThera/Rituxan

On 16 February 2011, Roche announced the start of a phase III study to investigate a subcutaneous formulation of MabThera/Rituxan using Halozyme's proprietary Enhanze technology. The Enhanze technology uses an enzyme that facilitates the penetration and diffusion of antibodies via a subcutaneous formulation. Roche plans to launch the subcutaneous format in 2012.

Limited for the same reasons as subcutaneous Herceptin

For the same reasons outlined for subcutaneous Herceptin, we do not believe that the subcutaneous formulation of rituximab will present an entry barrier to Celltrion's biosimilars due to two main reasons: 1) the addition of Halozyme's technology is likely to increase the price per dose considerably, making the drug clearly cost prohibitive; and 2) as seen in the case of Remicade and Enbrel for the TNF alphpa inhibitors, subcutaneous formulation is not as significant an advantage in the geographic areas where biosimilar competition is expected (e.g. Europe and Japan).

GA-101 as the counterstrategy of choice

Roche also cites GA-101 (obinutuzumab) as a line of defense against biosimilar encroachment. GA-101 is a glycoengineered anti-CD20 fully-human monoclonal antibody that has a glycoengineered Fc portion capable of improving binding affinity to FcgR, which then increases ADCC of NHL cancer cells. Roche reported Phase II data from two studies investigating GA-101 on 6 December 2010. In one study, a third of the patients with aggressive NHL who had not responded well to prior treatments showed good response. In another study, patients with relapsed/refractory indolent NHL who had been pre-treated showed 55% response to treatment. However, adverse events were not infrequent, this included infusion reactions, cases of neutropenia, and one serious infection out of 40 patients.

Next-generation antibodies not a threat for biosimilars

As with pertuzumab for Herceptin and golimumab for Remicade, the next-generation antibodies under development thus far do not demonstrate convincing superiority over its predecessors. Thus, we do not believe that innovators can automatically switch the patient base of Herceptin/Remicade/Rituxan to pertuzumab/golimumab/obinutuzumab. Essentially, the similarity in approach of the three next-generation antibodies is that it shares a similar mechanism (HER2 dimerization inhibition, TNF-alpha inhibition, anti-CD20) but it is either humanized (suffix -zumab) or fully human (suffix -mumab) antibody. It is important to note that humanizing antibodies do not automatically confer a better safety profile. It is well known that fully-human adalimumab (Humira), for example, can show up to 90% HAHA (human anti-human antibodies) incidence, and that humanized ocrelizumab – another anti-CD20 antibody under development – shows a 30% infusion reaction rate. Unless, truly groundbreaking improvement in safety or efficacy is demonstrated, we do not think that innovator companies can defend against biosimilars through next-generation antibodies.

Other next-generation antibodies

There are many other anti-CD20 antibodies in the pipelines throughout the world. A representative selection is provided in the table below. Note that many third-generation engineered anti-CD20 antibodies have failed in clinical trials.

Fig. 75: Other Novel Anti-CD20 Antibodies

Brand/Code Name	INN	Target Indication	Developer	Details
Zevalin	Y90-Ibritumomab	NHL	Biogen Idec	US approval in 2002, rarely used because of expensive dosage
Arzerra	Ofatumumab	NHL, CLL, RA, MS	GSK	US approval in Oct 2009, higher CDC and ADCC
-	Ocrelizumab	NHL, RA	Roche	Phase II for RRMS, already failed for RA due to high risk profile, higher ADCC than rituximab
GA-101	Obinutuzumab	NHL, CLL	Roche	Phase II, glycoengineered with bisected non-fucosylated oligosaccharides, improves binding to FcgRIII and higher ADCC
-	Veltuzumab	NHL, CLL, RA, ITP	Immunomedics	Phase II, higher CDC activity, subcutaneous fomulation for RA
AME-133v	-	NHL	Eli Lilly	Terminated, showed binding to lower affinity variant FcgRIII
PRO131921	-	NHL, CLL	Genentech	Terminated in Phase I/II
TRU-015	-	RA	Trubion	Terminated in Phase II
LFB-R603	-	CLL	LFB	Phase I, higher ADCC and demonstrates better activity in CLL, obtained orphan status for CLL treatment from the FDA in Aug 2010

Source: Nomura Europe Forecast, Nomura Japan Calculation

Appendix III: Competition vs Biosimilars

This section examines Celltrion's global biosimilar competition and their pipeline in detail.

CT-P06: No significant threat on the horizon

List of companies developing biosimilar Herceptin

The table below shows a list of companies developing biosimilars/bio-betters of Herceptin. The list is primarily limited to companies in Korea and India. Our research does not indicate that any of these companies have received INDs from the three global regulated bodies, Europe (EMEA), Japan (PMDA) or US (FDA) which is required for acceptance in developed nations. Thus, we do not view these companies to be significant threats to Celltrion. Some players have regional marketing power which may hinder access for Celltrion's partner. In the case of CT-P06, the regional giant India may be a source of concern in the Indian market.

Fig. 76: Competitors developing biosimilar trastuzumab (Herceptin)

Company	Country	Clinical Stage	Active Region	Indication	Phase
ISU Abxis	Korea	Pre-clinical	Korea, some emerging markets	Breast Cancer	ISU103 Planning on IND submission by 1H 2012, company claims increased productivity of up to 6g/L
Biocon	India	Pre-clinical	**India, Global**	Breast Cancer	India's leading biosimilar company, Bmab200 pre-clinical trial stage, the company has partnership with Mylan for global distribution of antibody biosimilars, partnership with Pfizer for global distribution of insulin biosimilars
GTC Bio (LFB Biotechnologies)	France	Pre-clinical	**Global**	Breast Cancer	Biosimilar trastuzumab produced from the milk of transgenic goats, development status unknown
PlantForm Corporation	Canada	Pre-clinical	Europe	Breast Cancer	Novel antibody production using transgenic tobacco plants, can produce antibody drugs for as little as 5% of the cost of originators, animal safety and toxicology studies now under way, aiming for European launch in 2015-6

Source: ISU ABXIS presentation, company home pages

Competitor #1: ISU ABXIS

ISU ABXIS is a subsidiary of the Korean conglomerate ISU Group. ISU ABXIS was founded in 2001 with an aim of becoming a global player in monoclonal antibody therapeutics. The company was the first company in Korea to market monoclonal antibody biosimilars. Clotinab (biosimilar abciximab, brand name ReoPro) was approved by the KFDA in 2007. Clotinab currently generates annual revenue of around USD2mn. ISU ABXIS is developing biosimilars only as a source of short-term cashflow; the company remains primarily focused on the development of novel antibody therapeutics.

Biosimilar pipeline: main product is ISU302 and ISU303

ISU ABXIS has three biosimilar products in its pipeline: ISU302, ISU303, and ISU103. ISU302 and 303 are biosimilars of Cerezyme and Fabrazyme, respectively, both of which are used in enzyme replacement therapies of very rare lysosomal storage diseases. The company may be one of the earliest developers of biosimilars for these drugs globally although the target market is limited to Korea and emerging markets. The company is actively seeking global partners for regulated markets. On 4 May 2011, ISU ABXIS reported that the Argentinian authorities rejected approval of ISU302. Further details are not available.

ISU103

ISU103 is the Herceptin biosimilar, currently in the preclinical stage. ISU ABXIS acknowledges that it is behind Korean competitors but also claims that the production capacity is much higher than the originator, with a titer of 6g/L in the production process. Since the yield is so high, the company believes capex will be significantly mitigated. The company aims to file an IND in Korea by the end of 1H12. For ISU ABXIS to

become a significant competitor to Celltrion, we believe that it will have to partner with companies in the regulated areas such as Europe or the US to navigate regulations in the developed markets.

Competitor #2: Biocon

Biocon is India's leading biopharmaceutical company. It was established in 1978 as a manufacturer of enzymes. From its founding, the company has manufactured products using its cell cultivation technologies. It began making cholesterol-reducing statins in 1996, the APIs of which requires bioreactors. Biocon became the first company in Asia to develop human insulin on Pichia Pastoris (type of yeast) expression system in 2003. It then became the leading insulin manufacturer in Asia with the market release of Insurgen in 2004. Biocon's market share of insulin in India is 10-15%, ranking third after Novo Nordisk and Eli Lilly. Biocon has signed an agreement with US generics giant Mylan for co-development of biosimilars. The two companies will share development and certain other costs related to bringing products to market. Mylan will have exclusive commercialization rights in the US, Canada, Japan, Europe, Australia, and New Zealand through a profit sharing agreement with Biocon. In October 2010, Biocon also signed an agreement with Pfizer for exclusive global marketing rights of insulin biosimilars.

BMab200: clinical trial to start soon in India

Biocon is developing Bmab200, a biosimilar of Herceptin. Bmab200 is still in preclinical stages, although according to the Indian GMO Research Information System (IGMORIS), it has recently been recommended by RCGM for clinical trials to be conducted with the permission of Drug Controller General of India.

Competitor #3: GTC Biotherapeutics

US-based GTC Biotherapeutics is a subsidiary of LFB (Laboratoires Francais de Fractionnement et des Biotechnologies) is a leading producer of plasma-derived medicinal products. The company also specializes in biotechnology research, for which the company invests 20% of sales in R&D. Very little is known about the development of biosimilar trastuzumab.

Competitor #4: PlantForm

PlantForm is a Canadian bioventure that specializes in monoclonal antibody production from transgenic tobacco plants. Antibody DNA is introduced into tobacco cells, plants are grown and harvested, then processed to retrieve the target antibody. Through an unspecified process, the Fab regions of the antibody are replaced with appropriate Fab regions for human therapeutic use. Through this novel technology, the company claims to be able to produce biosimilar Herceptin at a cost of 5% of the brand-name product.

Targeting European launch in 2015-16

According to their April 2011 newsletter, Kentucky BioProcessing has successfully scaled-up their proprietary manufacturing process, producing three lots of GMP compliant trastuzumab. The company is currently conducting animal safety and toxicology studies. PlantForm hopes to launch plant-produced biosimilar Herceptin in Europe in 2015-16. If the company is successful, PlantForm's drugs would quickly erode the market for biosimilars.

Transgenic biosimilars … are they biosimilars or innovation?

We believe transgenic production of biosimilars carries a much higher risk profile since: 1) it is not entirely clear whether proteins produced from very different species qualifies as a biosimilar in the first place; and 2) production from transgenic sources were attempted in the past by innovator companies (e.g. Kyowa Hakko Kirin in Japan has a subsidiary called HemaTech in the US which makes polyclonal human antibodies from cattle) but nothing so far has been approved for use. Plant-produced protein therapeutic that is closest to approval is Protalix BioTherapeutics' taliglucerase alfa, a biosimilar of Genzyme's Cerezyme. More details on Protalix are found at the end of Appendix III, section on CT-P13.

Watch the usual suspects: Teva and Sandoz

Excluding the companies pursuing novel antibody production platforms, the only biosimilars in development are Biocon and ISU ABXIS. The most significant threat, in our opinion, is Biocon's Bmab200. It appears that Bmab200 will undergo clinical trials in

India. If Biocon, in association with Mylan, were to obtain EMEA IND approval, the likelihood of European EMEA approval within 3-5 years of Celltrion's launch would become feasible. We also think that Teva-Lonza and Sandoz are likely to develop and launch biosimilar Herceptin within three years of Celltrion's launch.

CT-P13/P05: Many competitors but very few high quality biosimilars

The table below shows companies developing biosimilars/bio-betters of the TNF alpha inhibitors. The competition is largely of Asian provenance, with Korea, China, and India representing the bulk. Very few companies appear to be targeting the developed world market.

Fig. 77: Competitors developing biosimilar etanercept (Enbrel) and infliximab (Remicade)

Manufacturer	Country	Clinical Stage	Active Region	Details
Etanercept				
Shanghai CP Guojian	China	Approved	China, Brazil	Markets Etanercept in China since 2005, Agreement with Brazil EMS SA for production and marketing in Brazil, pipeline contains what is presumed to be Herceptin, Rituxan, and Remicade, recently started marketing Zenapax (daclizumab) biosimilar
Shanghai Celgen	China	Awaiting Approval	China	Etanercept expected to be approved and start manufacturing in 2011
3S Bio	China	Preclinical	China, Some Emerging Markets	SSS07, an anti-TNF monoclonal antibody being developed in collaboration with Epitomics, currently developing NuEPIAO, a biosimilar of 2nd generation erythropoietin, expecting to push into emerging markets such as Turkey, South America
Avesthagen	India	Phase I	India	Phase I trials for AVDESP (darbepoetin alfa biosimilar) started in India on Mar 2011, received etanercept technology patent in India, hopes to start clinical trials for AVENT (biosimilar etanercept)
Zenotech	India	Phase I	India	Clinical trial being initiated by the CRO Clinsys, received approval from DCGI.
Cipla	India	Phase III	India	Phase III initiated in India
Protalix Biotherapeutics	Israel	Preclinical	Global	PRX-106 is a plant cell-expressed recombinant anti-TNF fusion protein, the company has recently received a complete response letter from the FDA for their first biosimilar product taliglucerase alfa (biosimilar of Cerezyme)
Hanwha	Korea	Phase III	Korea, Brazil, Turkey	HD203, Phase I completed in Korea, currently in Phase III, commercial production planned in 2012, signed a distribution agreement with Bergamo in Brazil, DEM Pharmaceuticals in Turkey
LGLS	Korea	Phase I	Korea, Emerging Markets	LBEC0101, Phase I completed in Korea, start of Phase III in 2011 planned
Green Cross	Korea	Preclinical	Korea	
Genexine	Korea	Preclinical	Korea	GX-PO4, biobetter of Enbrel, immunofusion protein consisting of p40 and Genexine's hybrid Fc, supposedly decreases the side effects by targeting IL-23-Th17 pathway
Mycenax	Taiwan	Phase II	Taiwan, Korea, Japan	TuNEX (etanercept biosimilar): Phase III in Korea, Phase III in Taiwan, Announced sales partnership agreement with Macter in Pakistan and Sollievo in Colombia for distribution in Middle East and South America
Remicade				
Aprogen	Korea	Preclinical	Korea, Japan	GS071 is a biosimilar of Remicade
LGLS	Korea	Preclinical	Korea, Emerging Markets	-
Adalimumab				
GTC Biotherapeutics	USA			Acquired by LFB France
PharmaPraxis	Brazil			Part of Axis Biotec, Brazil

Source: Clinicaltrials.gov

Celltrion's primary strength is experience with authorities in developed nations

Celltrion's strength compared to all other biosimilar producers is its quality, in our view. To the best of our knowledge, Celltrion is the only biosimilar manufacturer in ex-Japan Asia to have obtained an IND approval from authorities in the developed world for biosimilars of the TNF-alpha inhibitor class. Thus, we do not envision most of the other biosimilar companies in Korea, China, or India as a threat in the developed markets. In the more distant future beyond 2015, Aprogen-Nichi Iko may enter the Japanese market with a Remicade biosimilar, and Protalix may compete in Europe or the US with an Enbrel biosimilar. Lastly, we also believe that Sandoz and Teva-Lonza are also likely to launch biosimilars in EU and Japan.

Competition in developed markets more limited

The principal characteristic of almost all companies listed in the table above is that the clinical development is entirely confined in the company's country of origin. We believe that for proper development of drugs targeting the developed world, consultation with the relevant authorities (FDA/EMEA/PMDA) must start well before preclinical studies are performed. The principal weakness of biosimilar companies in the developing world is

lack of experience in dealing with foreign regulatory authorities, who are often much more demanding in chemical and manufacturing data, animal pharmacology and toxicology studies, and protocols for clinical studies. We believe that companies whose consultation was restricted to authorities in their respective countries are likely to face considerable difficulty when filing in the US/Europe/Japan. We think it's highly likely that many of these companies would need to re-establish their CMC (chemistry, manufacturing, and control) and safety process. After safety and manufacturing is assured, these companies will then proceed to Phase I clinical trials.

Both infliximab and etanercept present unique challenges in manufacturing and quality assurance

First, because both proteins are by nature cytotoxic and can affect the cells in the bioreactor themselves, optimal production is said to be challenging compared to other antibodies.

Second, according to the EPAR Scientific discussion made public in the EU, infliximab is manufactured by continuous perfusion cell culture. Perfusion is a type of cell culture where reagents and media are added to the bioreactor continuously, unlike the more popular fed batch cell culture, where media is supplied intermittently at designated time intervals. GMP requires proper oversight over each manufacturing process. Perfusion cell culture is notorious for its difficulty in GMP compliance since a strict differentiation between the production cell culture process, and the purification process is not delineated by the nature of the process. Although companies can overcome the difficulty, it requires sophisticated controls that are widely understood to be complicated and costly. Thus, even pharmaceutical companies in the developed world with extensive experience in antibody production studiously avoid using perfusion culture. The challenge is more daunting for aspiring biopharmaceutical companies in the developing world. This also means that substantial research in process engineering is required to produce Remicade in a fed batch mode. We believe that Celltrion may have a head start in development and production methods.

Third, etanercept is an unnatural fusion-protein made from TNF receptor p75 and Fc portion of IgG1. This is likely to invite a closer scrutiny of its three-dimensional molecular structure since it is not as established as monoclonal antibodies. A rigorous analysis of solution-phase three-dimensional molecular structure is challenging even for most developed world companies.

Because of the three points above, we believe that biosimilar etanercept and infliximab faces higher hurdles than other biosimilars. We believe that Celltrion is the most likely candidate to develop it successfully, due to its: 1) experience in commercial size production; and 2) rigorous quality assurance. It remains to be seen whether other companies can produce antibodies with quality acceptable for marketing in developed markets.

The rise of the Chinese biosimilars #1: Shanghai CP Guojian

There are currently three Chinese companies manufacturing biosimilars of TNF alpha inhibitor. Shanghai CP Guojian Pharmaceutical is a joint venture between Hong Kong CITIC Pacific and Shanghai Lansheng Group. The company specializes in monoclonal antibody production and has been marketing Yisaipu, a biosimilar of Enbrel (etanercept). According to Simcere Pharmaceuticals, a rival Chinese company, the annual sales of Shanghai CP Guojian is estimated to be around 250-300 million CNY. Pipeline contains compounds that are similar to Rituxan, Herceptin, Zenapax (daclizumab), and Remicade. The company has announced collaboration with EMS SA in Brazil. EMS is one of the largest generics makers in Brazil. According to EMS S.A., the market for rheumatoid arthritis in Brazil is estimated to be BRL160mn (approximately USD100mn). The estimated number of rheumatoid arthritis patients is 850,000.

The rise of the Chinese biosimilars #2: Shanghai Celgen

Shanghai Celgen is also focused on developing and producing biosimilars. The company's leading product is biosimilar etanercept called Qiangke. In May 2009, Simcere Pharmaceuticals acquired a 34% stake in Shanghai Celgen. Simcere, during its 19 May 2009 conference call, said it believed that the product would require two years of marketing and promotion period to become profitable. Originally, the company expected

its biosimilar etanercept to be approved by the SFDA in 2010, but it only got approved on 9 May 2011. The company does not appear to have plans to sell etanercept overseas.

The rise of the Chinese biosimilars #3: 3SBio

3Sbio (Shenyang Sunshine Pharmaceutical) is a Nasdaq-listed biopharmaceutical company with long experience in biologics. The company's principal products are EPIAO (erythropoietin), TPIAO (thrombopoietin), INTEFEN (Intereferon Alpha), and INLEUSIN (Interleukin-2). The company's pipeline contains Anti-TNF mAb SSS07, a biosimilar of etanercept in preclinical stages. During its 16 May 2011 conference call, the company announced that it would be exploring the global biosimilar space for growth. In 2011, the company is aiming for approval in larger developing markets such as Malaysia, Turkey, or South Africa. The company hopes to get approval in these countries, and then target the European or US markets in the future.

Limited potential for Chinese competition in overseas markets, though this may change

Of the three companies above, only Shanghai CP Guojian can be a serious competitor to Celltrion, in our view. Shanghai CP Guojian has an arguably solid position in Brazil, but little evidence of activity in other countries. 3SBio appears to be contemplating an aggressive push into ex-Chinese markets. Even in the case of 3SBio, overseas sales have constituted only 3-4% of total sales in the past years. The product portfolio consists of protein therapeutic agents such as erythropoietin, and is still at preclinical stage for biosimilar etanercept.

Indian biosimilars #1: Avesthagen

Avesthagen is a life science company in India, focusing on integrated approach to biological discovery. The company announced in March 2011 that it started a clinical trial in India for AVDESP, a biosimilar darbepoetin alfa. AVDESP is being manufactured by Inno Biologics of Malaysia. The company's second target is AVENT, a biosimilar etanercept. This product will also be manufactured by Inno Biologics. Again, there is no indication that Avesthagen will be aiming at the developed market.

Indian biosimilars #2: Zenotech

Zenotech focuses on developing and manufacturing generic biopharmaceuticals. Zenotech's early phase clinical trial for biosimilar etanercept was being conducted by Jubilant ClinSys,. Through their prior TOB agreement with Ranbaxy, Daiichi Sankyo acquired 20% of Zenotech shares on 4 August 2010.

Indian biosimilars #3: Cipla

Cipla, a multinational generic giant, is currently conducting Phase III trials in India for biosimilar etanercept (CTRI/2009/091/000399). Cipla had acquired biologic technology through an earlier USD65mn investment in Hong Kong-based BioMab and Mabpharm based in Goa, India.

Protalix Biotherapeutics: making biosimilars from carrots

Protalix Biotherapeutics specializes in biosimilars produced from plants cell culture technology. The company's ProCellEx is a novel recombinant protein expression system that uses carrot and tobacco cell culture technology to produce human proteins. Cells produced by the ProCellEx technology are produced in disposable bags, which aids scalability of production. Production of plants also precludes the chance of mammalian virus transmission. The disadvantage is that proteins made from plant cells are not strictly biosimilar and would raise some new concerns from regulators.

PRX-106 is still at preclinical stage

Protalix's leading candidate product is biosimilar Cerezyme (taliglucerase alfa) used in enzyme replacement therapy for Gaucher's disease. This compound is currently being developed with Pfizer. Gaucher's disease patients lack an enzyme called glucocerebrosidase. The enzyme requires high concentration of mannose containing glycosylated enzymes to be effective. Because carrot cells naturally yield high mannose-content glycoproteins, Protalix's technology is advantageous. The company recently received a complete response letter from the FDA for taliglucerase alfa. The product is awaiting approval in Israel, EU, and Brazil, among others. The company is also developing PRX-106, a biosimilar of Enbrel, although it is in the preclinical stage.

Korean competition #1: Hanwha Chemical's HD-203

Hanwha Chemical is currently at the forefront of competition among Korean pharmaceutical companies for the launch of Enbrel biosimilar HD-203. Currently, the company is conducting phase III clinical trials in Korea, with an expected launch in 2011. The company announced on 9 November 2010 that it had signed sales agreements with Dem Pharmaceuticals in Turkey, and Bergamo in Brazil. Bergamo was subsequently acquired by Amgen on 8 April 2011. Since Amgen is the originator of Enbrel, we expect that the sales agreement, at the very least, to be renegotiated.

Korean competition #2: LG Life Sciences' LBEC0101

LG Life Sciences' LBEC0101 is currently in Phase III clinical trial in Korea. LG Life Sciences has subsidiaries in India, Poland, Jordan, China, and the US. LG commented during an interview that the companies' etanercept biosimilars are made using the perfusion system. In perfusion culture, the bioreactor is supplied with media and reagents continuously, while spent media and byproducts are removed. The advantage of perfusion culture is that it removes toxic byproducts and etanercept, which in itself is cytotoxic. Higher cell density can be reached so that per volume productivity would increase. However, compared to the standard fed-batch culture, where the media and reagents are added at fixed intervals, the perfusion culture is not widely used in the biopharmaceutical industry because of its operational complexity. Therefore, the development, manufacturing, and regulatory hurdles are higher. We believe that a switch to fed-batch production would be desirable for approval in developed markets.

Korean competition #3: Genexine

Genexine is a bioventure founded by Y.C. Sung in 1999. Genexine specializes in developing therapeutic vaccines and next-generation antibody fusion protein drugs. An antibody that utilizes Genexine's proprietary hybrid Fc technology removes antibody dependent cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC) by creating a hybrid Fc region consisting of a mixture of IgD and IgG4. The antibody is also designed in such a manner that it improves the steric hindrance of the antibody, thereby increasing the receptor affinity and hence its efficacy. The result is a long-lasting antibody that shows higher bioactivity. The company is currently developing GX-PO4, a biobetter of Enbrel. The product is a fusion protein of p40 and Genexine's hybrid Fc technology.

Korean competition #4: Aprogen

Aprogen is a biopharmaceutical venture company founded for the development of innovative drugs. The company has experience in developing biosimilars. Aprogen has developed biosimilars of Reopro (licensed to ISU ABXIS) and idulsulfonase alpha for enzyme replacement therapy of Hunter's syndrome (licensed out to Green Cross). Japanese generics maker Nichi-Iko acquired a 34% stake in the company for the development and manufacturing of biosimilars. Aprogen is currently developing GS-071, a Remicade biosimilar. Dr. Jaeseob Kim, the CEO of the company commented that Aprogen has developed an improved vector expression technology, such that the yield is increased threefold relative to the originator. Aprogen is currently building a 1,200L perfusion bioreactor in Songnam. The bioreactor should be ready after validation for production by the end of 2011. The target approval date is late 2013 in Korea and presumably somewhere around 2015 in Japan.

Lone Taiwanese Challenger: Mycenax Biotechnology

Mycenax is a Taiwanese bioventure founded by Dr. Hwang. Mycenax is currently developing two biosimilar products TuNEX (biosimilar of Enbrel) and GranNEX (biosimilar of G-CSF). TuNEX is currently in phase III trial in Taiwan and Korea. The company also has an agreement with an anonymous Japanese company for co-development in the Japanese market. Mycenax hopes to start clinical trials in Japan by the end of 2011. On March 18, Mycenax announced that it had signed a distribution agreement with Macter (Pakistan) for sales in the Middle East, and Sollievo Ltda. (Colombia) for sales in Central and South America.

CT-P10: First Battleground of the Biosimilars

For companies developing biosimilars/bio-betters of rituximab (Rituxan/MabThera), the competition is very different from other biosimilars where small companies from the emerging region are predominant. We understand that many companies are targeting Europe if not the US for biosimilar development.

Fig. 78: Competitors developing biosimilar rituximab (Rituxan)

Manufacturer	Country	Clinical Stage	Active Region	Indication	Indication
Teva-Lonza	Europe	Phase I/II	Czech Republic Hungary Italy Spain United Kingdom	Non-Hodgkin's Lymphoma	TL011 for Severe, Active Rheumatoid Arthritis Patients Primary Endpoint: PK comparison betw een MabThera and TL011 after 1yr, enrollment **60 patients** Secondary Endpoint: Safety and tolerability for 1.5 years, PK, PD, preliminary efficacy
	Europe	Phase I	Belgium Estonia Hungary Italy Latvia Poland Russia Spain Ukraine	Rheumatoid Arthritis	TL011 for CD20-positive Diffuse B Cell Non-Hodgkin's Lymphoma Subjects Administered w ith CHOP and others Primary Endpoint: AUC during dosing interval (21 w eeks) Secondary Endpoint: PK and PD paramaeters Estimated **Enrollment of 200 patients**
Sandoz	Europe, Asia, South America	Phase I/II	Argentina Austria Brazil France Germany India Italy Spain Turkey	Rheumatoid Arthritis	GP2013 in the Treatment of RA Patients Refractory to or Intolerant of Standard Therapy Primary Endpoint: PK comparison of GP2013 and rituximab over 24 w eeks, compares AUC(0-infinity) and Cmax Secondary Endpoint: Additional PK, PD, and efficacy over 1.5 years, AUC(0-24), clearance, t1/2 and volume distribution are measured. Estimated Enrollment of **164 patients**
Zenotech	India	Phase III	India	Non-Hodgkins' Lymphoma	Evaluate the Safety and Efficacy of Rituximab (Zenotech) in Non Hodgkin's Lymphoma (CTRI/2010/091/001195) Primary Endpoint: ORR at end of study (3 years) Secondary Endpoint: PFS **Patient Sample Size = 50** First Patient Enrollment = Feb 11 2009
Biocon	India	Phase I/II	India	Non-Hodgkins' Lymphoma	BVX20: Developed w ith US company Vaccinex
Dr. Reddy's	India, Latin America and Asia	Marketing	India, Peru, Russia, emerging nations	Non-Hodgkins' Lymphoma/Rheu matoid Arthritis	Marketed since April 2007, w orld's first monoclonal antibody biosimilar, currently marketed in India, Peru, Vietnam, and Middle Eastern Countries
Aprogen	Korea	Pre-clinical	Korea	-	AP052 Under development to be sold in Korea in 2014 and in Japan through major shareholder Nichi-Iko Pharmaceuticals, plan to complete Phase III clinical trials in 2013
Biocad	Russia	Phase I	Russia, CIS	Non-Hodgkins' Lymphoma	On February 11 2011, Biocad received approval from the Roszdravnadzor to initiate Phase I clinical trials
Samsung-Quintiles	Korea	Phase I	Global	-	SAIT101 under development, KFDA approval of Phase I clinical trials in March, Samsung to invest 266 million USD to construct a 30,000L facility in Incheon, expects full-operation in 2013, biosimilar commercial production in 2016
Viropro-Spectrum	US	Pre-clinical	US	Presumably Non-Hodgkins' Lymphoma	On January 5th, Spectrum signed an agreement w ith Viropro to develop rituximab biosimilar, target launch date not disclosed, good sales synergy w ith Spectrum's leading product Zevalin
GTC Bio	France	Pre-clinical	Global	-	TG20 is an anti-CD20 monoclonal antibody produced from the milk of transgenic goats, designed for high ADCC, high-level production announced on May 2010

Source: Clinicaltrials.gov, Company data, Nomura research

Why is everyone on the rituximab bandwagon?
Aside from the fact that rituximab is one of the first large biologics to go off patent in the US, we also suspect that rituximab is a monoclonal antibody with the most straight-forward production and development. According to the European EPAR Scientific Discussion, rituximab is produced by a CHO cell line (Chinese Hamster Ovary), in a standard fed-batch mode, then subsequently purified using standard Protein A and anion exchange chromatographic columns (for further details of antibody production, we refer the reader to Section 3 of Report No. 10-236).

Teva-Lonza: Meticulous approach to biosimilar approval
Teva-Lonza is developing TL011, biosimilar Rituxan, for both autoimmune (Rheumatoid Arthritis) and oncology (Non-Hodgkins' Lymphoma) indications. Clinical trial number NCT01123070 ("TL011 in Severe, Active Rheumatoid Arthritis Patients") is a Phase I/II clinical trial evaluating the PK bioequivalence of TL011 with MabThera in 60 patients. The clinical trial is scheduled for completion by August 2011. Note that Teva-Lonza's clinical trial lasts one year, considerably longer than Celltrion's Phase III trials for both drugs to date.

Clinical trial number NCT01205737 ("A Double-blind, Randomized Controlled Study in CD20-Positive Diffuse B Cell Non-Hodgkin's Lymphoma Subjects") is a Phase I trial for TL011 in combination with CHOP in naïve diffuse large B cell lymphoma patients. The primary endpoint is AUC during dosing interval for Rituximab after 21 weeks. The planned enrollment is 200 patients, making it the largest clinical trial for biosimilars to date. The clinical trial completion is planned for November 2012.

Targeting Europe and ROW first?
The Rheumatoid Arthritis clinical trial design is probably the most meticulous trial conducted on biosimilars to date. However, the clinical trial is entirely European, and it would require bridging studies in the US or Japan for launch in individual countries. We surmise that Teva may be primarily targeting ROW expansion. Phase III trials must be conducted for both these trials. If we assume another year for clinical trials, we believe that if the clinical trial proceeds on plan, Teva's biosimilar would be approved by European patent expiry of 2014.

Sandoz: Targeting only the RA population?
Sandoz is developing GP2013, biosimilar rituximab, for Rheumatoid Arthritis. Sandoz is conducting Phase I/II clinical trials (EudraCT number 2010-021184-32) in Europe (Austria, France, Germany, Italy, Spain), South America (Brazil, Argentina), India and Turkey. Primary endpoints for the clinical trial are PK comparison between GP2013 and rituximab over week 24. PK bioequivalence is defined by the standard AUC(0-infinity) and Cmax of blood concentrations. Secondary endpoints measure PK, PD, and efficacy over 1.5 years. Patients who have failed prior treatment with DMARDs (disease modifying anti-rheumatic drugs) including MTX and TNF-alpha inhibitor are included in the trial. The clinical trial is scheduled for completion in 2012-13. Sandoz announced in January 11 that it had built a large scale process explicitly for the production of biosimilar rituximab at its facilities in Schaftenau, Austria.

Korean rituximab biosimilar competitors: Aprogen
Currently, there are two Korean pharmaceutical companies developing biosimilar rituximab. Aprogen is developing AP052 in Korea. The target approval date is 2014 and currently at the preclinical stage. Presumably, AP052 will be co-developed with Nichi-Iko Pharmaceuticals of Japan, for Japanese launch in 2015 or thereafter.

Korean rituximab biosimilar competitors: Samsung Electronics
The other Korean company is Samsung Electronics. On 15 February 2011, Samsung Electronics announced its plan to invest KRW300bn (USD266mn) to establish a joint venture with US CRO Quintiles towards the manufacturing of monoclonal antibodies. Quintiles will own 10% of the JV, while Samsung Electronics, Samsung Everland, and Samsung C&T will hold each 40%, 40%, and 10%, respectively. Samsung divides the business initiation into three stages. In the first stage, construction of a 30,000L facility in Incheon is slated to begin in 2011 and completed by 1H13. The plant will then start operation as a CMO for overseas companies. In stage 2, Samsung will start commercial production of biosimilars, notably rituximab, in time for patent expiry in major markets. In

stage 3, Samsung will use the cashflow gained from the biosimilar business to develop innovative antibodies.

Samsung, a long-term threat

Both of these Korean competitors may become a threat in the long term. In terms of technical prowess and experience in biologic production, we believe that Aprogen stands out from the crowd in Korea. The employees at Aprogen have either extensive experience in life sciences research (Dr. Jae Seop Kim) or have previously held positions in leading biologic companies. Aprogen's weakness is lack of a large-scale production plant and lack of experience with foreign regulatory authorities. The current scale of production is not sufficient for global production. Together with its shareholder, Nichi-Iko Pharmaceuticals of Japan, we believe the company may be able to navigate the complicated path to biosimilar approval. In the end, Aprogen's impact is very limited to Celltrion's sales.

Samsung, under the tutelage of Quintiles, is very likely to become a formidable competitor for Celltrion's rituximab in the future. However, the company will need to have a validated and fully-operational large-scale production facility to start clinical trials in developed nations such as Europe or the US. Even though scale-up production after Phase I clinical trials are routinely performed in the case of innovative antibodies, regulatory authorities in developed nations are very reluctant to allow clinical trials of biosimilars without demonstrating quality already at a large mass-production scale (note that the quality of antibodies can change considerably after scale-up). Seen in this light, the timeline offered by Samsung is ambitious and delays in the production is not unlikely.

Biocon is developing humanized biobetter of rituximab

The company is developing BVX20, a humanized version of rituximab. BVX20 targets CD20 as in the original rituximab with similar ADCC activity, but off rate CDC activity is higher than rituximab, suggesting higher efficacy in CLL. The company has been approved for Phase I/II clinical trial in India for relapse/refractory Non-Hodgkin's Lymphoma. The trial is scheduled to start sometime in 2011. The company is also planning on US IND submission in 3Q11. Because the molecule is a biobetter, it would go through Phase II and Phase III trials as an innovative drug not as a biosimilar.

Spectrum Pharmaceuticals

Spectrum Pharmaceuticals is an American company specializing in oncology drugs. The company currently markets Zevalin (ibritumomab tiuxetan), a radioactive biologic for use in Indolent Non-Hodgkin's Lymphoma, and Fusilev, a high-dose methotrexate rescue therapy in Osteosarcoma. On 5 January 2011, Spectrum Pharmaceuticals signed an agreement with Viropro for the development of rituxan biosimilar. Viropro specializes in contract research and manufacturing services for the biopharmaceutical industry. An expected launch date was not disclosed.

Spectrum markets Zevalin, a mouse monoclonal antibody similar to rituximab with a chelator called tiuxetan attached. Tiuxetan binds a radioactive isotope either yttrium-90 or indium-111. The antibody binds to CD20 on the surface of B cells, much like rituximab. The combined effect of ADCC, CDC, apoptosis, and radiation kills the B cell. The drug has not sold successfully in the US, and was acquired by Spectrum in 2008. Since then, the sales of Zevalin rebounded from USD12mn in 2008 to USD29mn in 2010. The company believes that the drug may eventually claim a market size of couple hundred million US dollars in the future. Since Zevalin is used with Rituxan, the sales synergy is significant. The company does not have any marketing force outside of the US, and is unlikely to market the product overseas, in our view.

GTC Biotherapeutics

US-based GTC Biotherapeutics is a subsidiary of LFB (Laboratoires Francais de Fractionnement et des Biotechnologies) is a leading producer of plasma-derived medicinal products. The company also specializes in biotechnology research, for which the company invests 20% of sales in R&D. it is also developing an anti-CD20 biobetter of rituximab produced from transgenic goats called TG20. TG20 has a 10-fold higher ADCC activity compared to rituximab. Since the product is a biobetter with a very different manufacturing process, we believe that TG20 will be treated much like an innovative drug. Therefore, we do not expect TG20 to be launched in the near term.

Dr. Reddy's Reditux: Aiming for penetration in Russia

Dr. Reddy's has an established presence in Russia dating back to 1991. The company currently is the leading Indian generic player in Russia and derives over 14% of its global revenues from Russia. Dr. Reddy's is targeting Reditux expansion in Russia as the basic Rituxan patent is expected to expire in 2012. The company is currently preparing for conducting clinical trials in Russia and other countries. In its earnings conference call held on 13 May 2011, Dr. Reddy's said that is was building a biologics facility which would address its capacity requirements as well as matter of manufacturing of clinical trial batches for regulated markets.

Available in six countries

Reditux is currently available in six countries globally including Peru, Chile and Vietnam and is pending approval in another eight countries. Dr. Reddy's partner, CFR Pharmaceuticals, has launched the biosimilar in three Latin American countries and is awaiting approval in another two countries. According to CFR, Reditux has achieved a market leadership position in Peru and has received a vote of confidence from the medical community. The company also claims that after the launch of Reditux, the price of Rituxan has been lowered by up to 50%.

Potential competition in Russia

According to our research, Russia's lone biosimilar player is a biotech company called Biocad. It was founded in 2001 by Dmitry Morosov and has since launched a series of first-generation biosimilars in Russia. In 2005, the company launched its first product, called Genferon, a biosimilar interferon alpha-2b. The company claims that the biosimilar is used by over 44,000 doctors across the country. Biocad launched Russia's first domestically manufactured biosimilar filgrastim called Leukostim in 2006. The company currently operates in oncology, urology and neurology segments, and markets eight drugs including interferon beta-1b, gemcitabine and paclitaxel. Recently, Biocad received a grant of RUB145mn (USD5mn) in subsidies from the federal budget for the development of monoclonal antibody biosimilars. The government decree, signed by Prime Minister Putin in February 2011, aims to reduce the import of expensive biologics such as Rituxan, Herceptin and Avastin. According to the government, the price of biosimilars produced in Russia would be 40-50% lower than the original biologics. Biocad is currently in the process of initiating Phase I clinical trials of biosimilar rituximab in approximately 120 patients with non-Hodgkin's Lymphoma, after having received approval from the Roszdravnadzor (Russian FDA) in February 2011. The company already has conducted pre-clinical studies to establish equivalence with Rituxan. According to the company's website, Biocad claims to have a foundation in the domestic and neighbouring markets of CIS countries such as Ukraine, Azerbaijan and Armenia. However, we do not expect it to become a significant competitor outside these regions because of higher regulatory hurdles and stringent quality requirements.

ISU Abxis

ISU Abxis is a Seoul-based biotech company that is a listed subsidiary of ISU Chemical and a part of the South Korean conglomerate ISU Group. ISU Abxis was founded in 2004 after the consolidation of ISU Chemicals with Petagen. The company's two main businesses areas are monoclonal antibody therapeutics and medical services, with the former contributing 60% of overall revenues. The antibody therapeutics pipeline includes biosimilar molecules such as ISU302 (Cerezyme) and ISU 103 (Herceptin) and ISU 303(Fabrazyme). ISU Abxis' novel drug pipeline includes a molecule for Asthma/Sepsis (ISU 201) and a monoclonal antibody for metastatic cancer (ISU 102).

In 2007, the company launched Clotinab – a biosimilar of Eli Lilly's ReoPro, thereby becoming the first Korean company to manufacture and market biosimilar monoclonal antibodies. Clotinab has been approved in Korea, India, Pakistan, Paraguay and Chile while it is under marketing and sales registration in over 33 countries globally. In 2009, Clotinab revenues accounted for over 50% of Abxis' overall sales. By using a different manufacturing process, ISU claims to have achieved significantly higher productivity levels than the originator. Despite being difficult to produce molecule, the biosimilar antibody has shown comparability to the branded product. Another key biosimilar product in the pipeline is ISU103, an HER2+ biosimilar that is currently in preclinical trials for which the company aims to submit the IND application by 1H12. While competition in the Herceptin biosimilar market is expected to be strong, ISU aims to leverage this experience to develop a cost competitive technology.

The lead candidate in the company's novel drug portfolio is ISU201, a recombinant Fc fusion protein that is indicated for severe asthma (sepsis), asthma refractory to steroids. It was discovered through an in-house target discovery programme and has gone on to show significant efficacy in asthma murine models. ISU201 acts as an antagonist for the highly over-expressed Fc-Bst2 fusion molecule by blocking intracellular adhesion and thereby obstructing critical pathways of inflammation. If successful, ISU201 could compete with Genetech's and Novartis's Xolair. Discussions with the US FDA regarding clinical trials are currently ongoing and the company is seeking global co-development and out-licensing partners for ISU201.

In 2009, the company invested KRW430mn to upgrade its 100L CHO cell fermentation capacity to 200L and thereby increase its batch capacity from 1,500 vials to 3,800 vials. The fermentation capacity can be increased multiple times if the company faces an increase in demand. However, given the company's 30x high productivity process, a very large capacity tank is not required by Abxis.

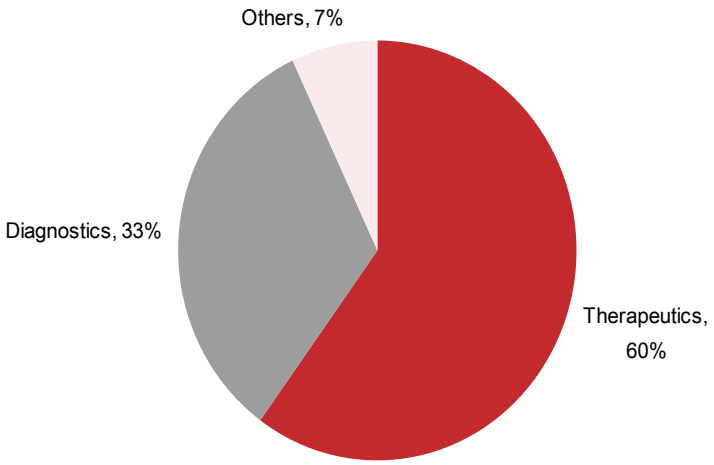
ISU Abxis's steady expansion in emerging markets can be seen by its evolving global footprint:

Fig. 79: ISU Abxis' Global Partnerships

Country	Details
Jordan	Received Jordan FDA approval for Clotinab (2009)
Sri Lanka	Received Sri Lankan FDA's approval for Clotinab (2009)
Mexico	Supply contract with Tecnofarma (2009)
Turkey	Supply contract with DEM Pharmaceuticals (2009)
Ukraine	Received approval for Clotinab from Ministry of Health, Ukraine (2010)
US	Strategic alliance with MabPrex to provide proprietary technology (2011)

Source: Company data, Nomura

Fig. 80: ISU Abxis' Sales Forecast for FY11 is USD4.3mn



Source: ISU Abxis

Aprogen

Aprogen was established in 2000 as a biotechnology company that developed and produced monoclonal antibodies through its advanced antibody, protein and animal cell engineering technologies. In 2009, Schnell Biopharmaceuticals acquired a 100% stake in Aprogen. The company's key business area consists of biosimilar development and its pipeline comprises four molecules, namely, GS071 (Remicade), AP032 (Aranesp), AP052 (Rituxan) and AP062 (Herceptin). GS071 is the most advanced molecule in the pipeline and is currently in phase I clinical trials while the other molecules are in pre-clinical stages.

Fig. 81: Aprogen's Pipeline

Biosimilar	2011	2012	2013	2014	2015
GS071 (Remicade	Ph I	Ph III	Ph III, Approval		
AP032 (Aranesp)	NCT	IND, Ph I	Ph III	Ph III	Approval
AP052 (Rituxan)	NCT	IND, Ph I	Ph III	Approval	

Source: Company data

In October 2010, Japan's Nichi-Iko acquired a 33.4% stake in Aprogen for JPY1bn, thereby gaining immediate access to its Remicade and other biosimilars. Through the deal, Nichi-iko received exclusive development and marketing rights for products made using Aprogen's technologies for the Japanese market. In May 2010, Sanofi Aventis bought a 4.66% stake in the Japanese generics company. The two companies may explore the US biosimilar market using Aprogen's pipeline of drugs.

In 2010, the company reported the following costs of developing its biosimilar pipeline and conducting clinical and preclinical trials:

Fig. 82: Detailed costs of developing biosimilars

Molecule	Process	Process Cost (KRW Mn)
GS071 (Remicade)	Cost of Phase 1 Clinical Trial Center	293
	- Clinical trials, the total funding agencies (Labor + Direct)	-250
	- Development costs (12%)	-30
	- Medical Expenses (5%)	-13
	CRO organizations related to clinical testing service fees	150
	Clinical sample specimens PK / immunogenicity GLP Authority	200
	Purchase of comparator (620,000/vial)	45
	Process validation	400
	Total	**1,088**
AP032 (Aranesp)	R&D Process	250
	Preclinical costs	100
	Preclinical animal tests	350
	Total	**700**
AP052 (Herceptin)	R&D Process	400
	Preclinical costs	100
	Cost of building evaluation model	50
	Total	**550**

Source: DART filings, Nomura

Apart from biosimilars, Aprogen is also working on developing novel biotherapeutic molecules and has three leading candidates in its pipeline – AP102 (COMP-Ang1), AP202 (DAAP) and AP302 (DIVB). AP102 is an angiogenesis protein that helps damaged tissues regenerate faster without having any negative effects on VEGF. The efficacy of the drug has been demonstrated in pre-clinical animal studies. Aprogen received the US patent in 2005, the EU patent in 2008 and the Japanese patent in 2009. AP202 is a double anti-angiogenic protein (DAAP) that simultaneously binds VEGF-A and angiopoietins, and blocks their actions. It effectively suppresses tumor angiogenesis, metastasis and vascular leakage and is superior to VEGF-Trap plus Tie2-Fc in blocking tumor growth and metastasis. The patent for AP202 has been filed in the US, EU, Japan, Korea, China, Israel and Canada

One of the company's key technologies is its SDR (Specificity Determining Residues) grafting technology. Murine antibodies are humanized by grafting their Complementarity Determining Regions (CDRs) and these often evoke immunogenic response in patients. In order to minimize immunogenic responses, a process to map the amino acids and transpose only certain specific amino acids has been developed by Aprogen. The humanized antibody thus maintains affinity and specificity of the original murine monoclonal antibody and minimizes human anti-mouse antibody response. The company has filed patents of this technology in the US, EU, Korea, China and Australia.

CrystalGenomics

CrystalGenomics was founded by Dr. Joong Myung Cho in 2000 as a structural biology and novel drug developing company. It is one of the few South Korean biotech companies that operates a US subsidiary for clinical development (CrystalGenomics Inc., located in Emeryville, California). CrystalGenomics has multiple novel drug candidates in its pipeline and boasts of a number of drug development partnerships with global companies such as AstraZeneca, Daiichi Sankyo, Hanmi, etc. CrystalGenomics' proprietary platform technology consists of three components - Soluble Protein Solution (SPS), Structural Chemo Proteomics (SCP) and Structure-based Drug Factory (SDF) Technologies. The scaffold based technologies are applied to structure determination of target proteins, lead generation and lead optimization, respectively.

The most advanced molecule in the company's pipeline is CG100649, a first-in-class next generation non-steroidal anti-inflammatory drug (NSAID) which inhibits COX-2 in the inflammatory joint. CG100649 does not inhibit COX-2 in the cardiovascular and

gastrointestinal systems and is therefore highly efficacious in the control of inflammation and pain without showing typical side effects of other NSAIDs. Such tissue specific inhibition was demonstrated in preclinical and clinical studies. If developed successfully, the drug aims to compete with Pfizer's Celebrex, a USD30mn drug whose US patent expires in 2015. CG100649 is being developed for the treatment of osteoarthritis, rheumatoid arthritis, CNS diseases (e.g. Alzheimer's, Huntington's, etc), and colon cancer. Phase IIa clinical trials were recently completed in the EU and further development plans are currently underway.

Another leading molecule in CGX's pipeline is CG400549, a novel Fab I (Enoyl-[Acyl-Carrier-Protein] Reductase) inhibiting antibiotic for multi-drug resistance of Staphylococcus spp (MRSA, VISA, VRSA) infection. The drug inhibits an essential enzyme in fatty acid synthesis, a process that is critical for the survival of bacteria. It can be administered orally or intravenously, and has shown a good safety profile in the ongoing IND enabling toxicity studies. CG400549 is equivalent to Pfizer's blockbuster drug Zyvox and its phase I Single Ascending Dose (SAD) study was recently completed in the EU.

CrystalGenomics' oncology portfolio consists of CG200745, an anti-cancer agent that deactivates HDAC, an enzyme that catalyzes the histone deacetylation. During a series of anti-cancer efficacy tests, the molecule has shown a better profile than other compounds in the same class such as Merck's Zolinza. Animal pharmacokinetic studies have shown that CG200745 is highly soluble and orally available. Phase I studies are currently underway for the treatment of multiple cancer types including colon cancer, breast cancer and stomach cancer.

In January 2010, CrystalGenomics tied up with AstraZeneca to develop antibiotics. The research for an anti-infective would be funded by Astrazeneca for two years and CrystalGenomics would receive milestone payments and royalty from Astrazeneca. The goal of the collaboration was to generate optimized lead compounds against a pre-agreed bacterial target, furthering AstraZeneca's ability to progress targets in this therapeutic area.

Fig. 83: List of global and local partnerships

Country	Partner Company	Partnership details
Japan	Daiichi Sankyo	Anticancer research
	SBI Biotech	Molecular targeted anticancer research
	Carna Biosciences	Inflammatory drug research
	Onco Therapy Science	Strategic alliance for molecular targeted anticancer research
	Kissei	Research and development
UK	AstraZeneca	Research collaboration to develop novel anti-infective treatments
US	ProQuest Investments	Formation of a JV called Palkion, for the development of drugs that modulate the HIF Prolyl Hydroxylase enzyme system
Korea	Hanmi	Molecular targeted anticancer research
	ASAN Medical Centre	Molecular targeted anticancer research
	Amore Pacific	Inflammation and obesity research and development
	Yuyu Pharma	Diabetes drug research and development

Source: Company data

Fig. 84: Global clinical trials for CG100649 for osteoarthritis

Phase	Study Type	Trial Size	Location	Status
I	Escalating dose study	24	UK	Completed
I	Safety and Pharmacokinetic Study	16	UK	Completed
Ib	5 day Pharmacokinetic study	48	US	Completed
IIa	21 day PoC study for efficacy	248	EU	Completed
I	Pilot biomarker study	24	US	Completed
I	Drug-drug interaction (DDI) study	26	Korea	Completed
I	Pilot Multiple Ascending Dose Study	48	Korea	Completed
IIb	Pivotal Ph IIb Study for efficacy & safety	132	Korea	Ongoing
III	Multi-centered study in Korea & China	Planning	Korea, China	Planning

Source: CrystalGenomics

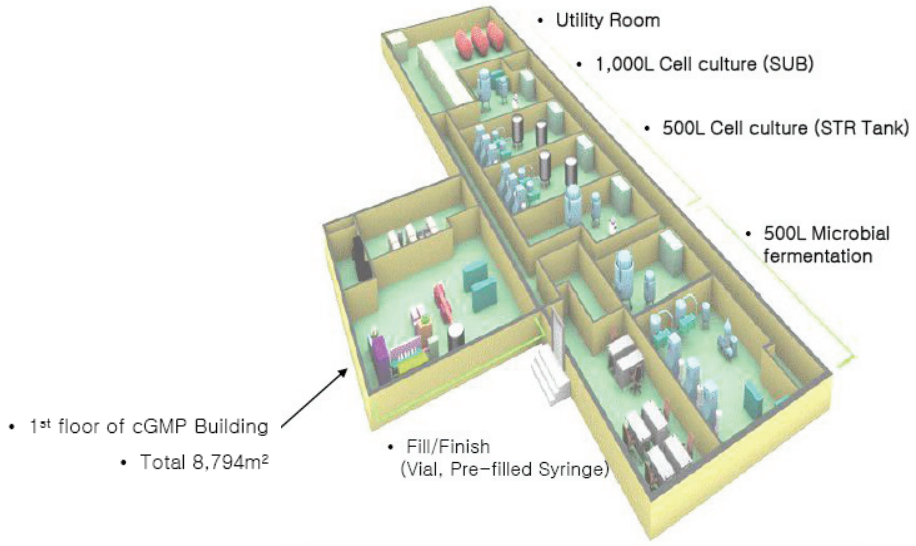
Binex

Binex was established in 1957 under the name Soonchudang as a company focused on generic drugs. In 1994, the company received KGMP approval for its manufacturing facility and it established a cell therapy manufacturing facility in 2003. After gaining critical experience in developing anti-cancer cell therapies such as TK Cell Therapy and Onco-Vac Cell Therapy, Binex signed an agreement with KITECH (Korea Institute of Industrial Technology) in 2009 for the contract management of KBCC (Korea Biotechnology Commercialization Center) in order to sharpen its expertise in contract manufacturing and development services.

KBCC was established by KITECH in 2000 as South Korea's first multi-purpose, cGMP contract manufacturing facility that offered a full range of services including providing cell banks, process and analytical method development and scaling-up, regulatory support and manufacturing services. The government-backed venture has received an investment of approximately USD100mn over the years and boasts of global and local clients such as Novartis, Sanofi Aventis, BMS, Pfizer Korea, Samsung, Celltrion, Aprogen, ISU Abxis, etc.

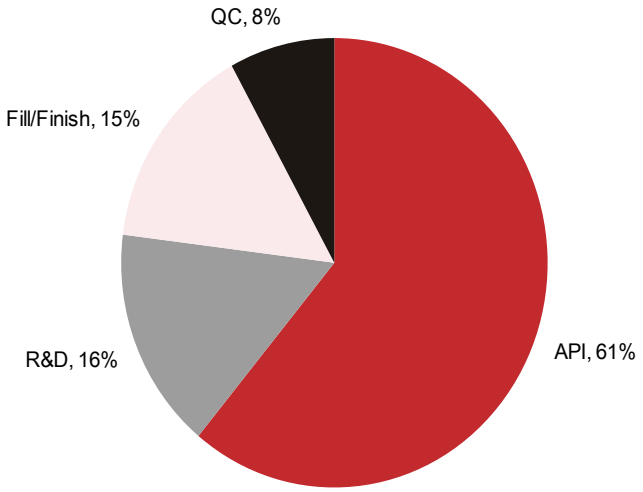
KBCC’s strength lies in its high quality and cost efficient manufacturing facility and the vast expertise that its senior management has to offer. As a government-built facility, KBCC faces comparatively lower regulatory hurdles and offers to be a reliable and stable partner that can be used by companies for a long term basis. Its production capacity consists of a 500L (SUS) and a 1,000L (SUB) mammalian cell culture capacity and the company is expected add an additional 2,000L (SUS) capacity by 2012. The company also has a 500L microbial facility along with a liquid vial, freeze-dried and a pre-filled syringe facility that is currently in operation.

Fig. 85: An overview of the manufacturing facility



Source: Binex

Fig. 86: Breakdown of KBCC's FY10 Sales



Source: Binex

Appendix A-1

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Issuer name	Ticker	Price	Price date	Stock rating	Sector rating	Disclosures
Celltrion Inc	068270 KS	33,200 KRW	19-May-2011	Buy	Not rated	

Previous Rating

Issuer name	Previous Rating	Date of change
Celltrion Inc	Not rated	30-May-2011

Rating and target price changes

	Ticker	Old stock rating	New stock rating	Old target price	New target price
Celltrion Inc	068270 KS	Not rated	Buy	N/A	50,000

Celltrion Inc (068270 KS) **33,200 (19-May-2011)**

Chart Not Available

Valuation Methodology We use a DCF methodology using a risk-free rate of 3.5%, risk premium of 8% and beta of 0.9 to arrive at WACC of 8.7%. Using FCF calculated from a projection going to 2020, and using a terminal growth rate assumption of 1.8%, we arrive at our target price of KRW50,000.

Risks that may impede the achievement of the target price First, the most important risk is the failure to achieve equivalence in Phase III clinical trials currently being conducted for CT-P06 and CT-P13. Should this be the case, our valuation would be significantly revised downward. Second, penetration rates of biosimilars in Europe, ROW, and/or Japan may be significantly less than proposed due to patient pushback or lack of physician acceptance. Third, innovators such as Roche may significantly lower prices in response to biosimilar introduction. This may trigger a price war. Finally, rival companies with global-level expertise may launch products faster than we have expected.

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Explanation of Nomura's equity research rating system for Asian companies under coverage ex Japan published prior to 30 October 2008

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A '**Reduce**' recommendation indicates that downside is between 10% and 20%.
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