PITT STREET RESEARCH

Biocure Technology (CSE:CURE, OTCQB:BICTF)

Share Price: C$0.21

Curing with its bio-engineering expertise

Biocure Technology, publicly listed on the Canadian Securities Exchange (CSE: CURE) and dual listed in the US (OTCQB: BICTF), is a biopharmaceutical company based in South Korea that is engaged in the development and potential commercialisation of biosimilars and CAR-T cell products. The company is developing its CAR-T cell therapy for leukaemia and is targeting conducting Phase I clinical trials before the end of 2021. Biocure is also in preclinical trials of three biosimilar products in South Korea, including Interferon beta-1b (for the treatment of Multiple Sclerosis), Ranibizumab (for macular degeneration) and Filgrastim (for neutropenia).

Frontrunner in cost-efficient CAR-T in Korea

Biocure is developing its 'BCP401' CAR-T cell therapy for Acute Lymphoblastic Leukaemia (ALL) in Korea. BCP401 therapy has demonstrated encouraging results in the preclinical stages and Biocure is currently awaiting approval from Korean regulatory agencies to initiate Phase I clinical trials. BCP401 is scheduled for market launch in Korea by the end of 2022 and we believe that upon commercialisation of the product, Biocure will be able to tap a huge addressable market, which will likely be worth over US$8bn by 2028. Notably, Biocure plans to offer a much more cost-efficient therapy as compared with existing FDA-approved products, and this should support its upside potential.

Emerging player in attractive biosimilars market

Biocure is well placed to capitalise on the high-growth global biosimilars market with a pipeline of low-cost biosimilars targeting diverse therapeutic areas. We believe that the markets being targeted by Biocure are multi-billion dollar opportunities with higher growth coming from the emerging markets where the price of biological drugs has been traditionally prohibitive. Interferon beta-1b, the lead product in Biocure's pipeline, is likely to be the first product to be commercialised, with preclinical trials in progress since 2020.

Valuation range of C$0.49–0.93 per share

We value Biocure at C$0.49 per share base case and C$0.93 in an optimistic case using the risk-adjusted DCF methodology. Key risks that we see are (1) delays in receiving regulatory approvals for BCP401; (2) clinical risk; and (3) funding challenges.

CSE: CURE, OTCQB: BICTF

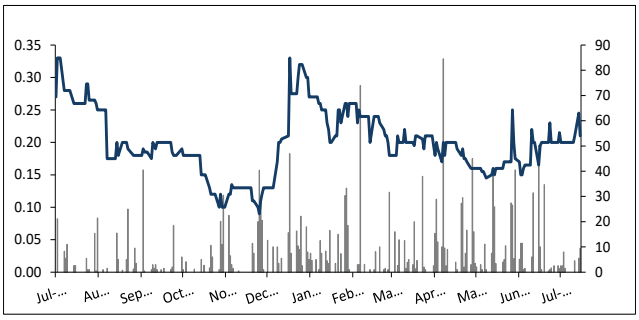
Sector: Healthcare

29 July 2021

Market Cap. (C$ m)	21.0
# shares outstanding (m)	99.9
# shares fully diluted (m)	108.0
Market Cap Ful. Dil. (C$ m)	22.7
Free Float	73.8%
52-week high/low (C$)	0.33 / 0.09
Avg. 12M daily volume ('1000)	7.4
Website	www.biocuretech.com

Source: Company, Pitt Street Research

Share price (C$) and avg. daily volume (k, r.h.s.)



Source: Refinitiv Eikon, Pitt Street Research

Valuation metrics	
DCF fair valuation range (C$)	0.49–0.93
WACC	14.6%
Assumed terminal growth rate	None

Source: Pitt Street Research

Analysts: Stuart Roberts, Cheng Ge

Tel: +61 (0)447 247 909

stuart.roberts@pittstreetresearch.com

cheng.ge@pittstreetresearch.com

Disclosure: Pitt Street Research directors own shares in Biocure Technology.

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Introducing Biocure Technology, CSE: CURE, OTCQB: BICTF

Biocure Technology (CSE: CURE, OTCQB: BICTF), a biopharmaceutical firm based in South Korea, is engaged in the development and potential commercialisation of biosimilars and CAR-T cell products. Biocure's in-house expertise in bio-engineering has enabled low-cost biosimilars to be developed, along with the novel CAR-T products. The company is planning to conduct Phase I clinical trials for its CAR-T product in the second half of 2021.

Forerunner in CAR-T cell therapy in Korea

CAR-T cell therapy is a novel scientific approach that utilises the body's own immune system to fight cancer. It works by extracting T cells from the patient's blood and then genetically engineering them to produce 'Chimeric Antigen Receptors' on their surface. Subsequently, the patient receives the CAR-T cell therapy in an infusion that can target and destroy cancer cells. This therapy is showing promising results in cancer patients worldwide, and the global CAR-T market is estimated to grow from US$734m in 2019 to ~US$8.3bn in 2028[1].

Biocure is a front-runner in commercialising CAR-T cell therapy in Korea

Biocure is developing its 'BCP401' CAR-T cell therapy for Acute Lymphoblastic Leukaemia (ALL) in Korea. With solid preclinical data and plans to commence Phase I clinical trials by the end of 2021, BCP401 is scheduled for market launch in Korea by the end of 2023. Biocure expects to make significant inroads in the Korean market post the launch of BCP401. Further, it aims to expand in Asia and Europe by offering cost-efficient CAR-T cell therapy. Biocure believes it can provide BCP401 at a price point that is 30–40% lower than that of existing FDA-approved products, including Kymriah and Yescarta. The company also plans to extend its CAR-T product pipeline and has started working on the development of a second CAR-T product to treat Chronic Lymphocytic Leukaemia (CLL).

Strong pipeline to tap lucrative biosimilars opportunity

The global biosimilars market is expected to grow at a healthy CAGR of 24.6% during 2020–2026

With several blockbuster biologics set to lose their patent protection in the next decade, the global biosimilars market is estimated to grow from US$11.9bn in 2020 to US$44.5bn in 2026, registering a healthy CAGR of 24.6%. We believe Biocure has a strong pipeline of low-cost biosimilars targeting diverse therapeutic areas, which should allow it to capitalise on the lucrative growth opportunities in the biosimilars space. Currently, preclinical trials of five biosimilar products, including Interferon beta-1b (for the treatment of Multiple Sclerosis), Ranibizumab (for macular degeneration) and Filgrastim (for neutropenia), are ongoing in South Korea. Interferon beta-1b is expected to be the first product in Biocure's kitty to be commercialised and the preclinical trials are in progress this year. Notably, the global Multiple Sclerosis medication market is expected to grow from US$16.3bn in 2016 to US$27.8bn in 2025[2].

Why is Biocure undervalued?

We believe that despite the strong catalysts for Biocure's growth, it is undervalued mainly because of the early stages of development of its biosimilar and CAR-T products. We foresee the stock being re-rated with the company's pipeline products advancing into clinical trials, starting with the

[1] Research and Markets, Coherent Market Insights.
[2] V.M. Biosimilar Drugs for Multiple Sclerosis: An Unmet International Need or a Regulatory Risk?; Neurol Ther; 2019; 8; 177–184.

CAR-T product, which is on track to commence Phase I clinical trials in late 2021.

Ten reasons to look at Biocure

1) **Biocure's expertise in bio-engineering has enabled the development of low-cost biosimilar pharmaceutical products.** The company possesses know-how related to the production of biological molecules at low cost and is a rapidly-emerging player in the large market for biosimilars. Its strong research capabilities will act as a stiff barrier for new entrants.
2) **Biocure is in the process of developing several large-market biosimilars.** In the near term, it is gearing up for the clinical trial of three major biosimilar products – Interferon beta-1b (Multiple Sclerosis), Ranibizumab (macular degeneration) and Filgrastim (neutropenia for cancer patients).
3) **Biocure is a forerunner in developing the CAR-T cell therapy in Korea.** The company demonstrated encouraging results during preclinical trials in 2018, where the data established the safety and efficacy of its CAR-T cell therapy in the treatment of cancer.
4) **The company plans to extend its CAR-T cell product pipeline** as it is working on the development of a second CAR-T cell product, which is expected to treat Chronic Lymphocytic Leukaemia (CLL). Further, Biocure has joint venture partners in Asia and Europe which will aid in exploring international opportunities such as ongoing JV discussion to implement a Clinical Trial at the University of Cologne Medical Center in Germany to make progress on CAR-T therapy for CLL.
5) **It has access to a third-party Good Manufacturing Practice (GMP) facility** in Korea, and this allows it to minimise capital requirements and investment risks.
6) **The opportunity in biosimilars is significant**, with many blockbuster biological drugs now off-patent or losing market exclusivity. With a strong pipeline of low-cost biosimilars targeting multiple therapeutic areas, Biocure is well-positioned to capitalise on these lucrative opportunities. The growth opportunities will be higher in emerging markets in the medium term where biosimilars are still nascent.
7) **CAR-T is revolutionary**. Given that approved CAR-T therapies will help revolutionise the treatment of certain cancer types, the development of a more cost efficient CAR-T therapy by firms such as Biocure is expected to expand the addressable market considerably. The global CAR-T therapy market is projected to grow significantly over the next decade to become a multi-billion dollar opportunity.
8) **Biocure has a solid leadership team**, with a number of PhDs on its board boasting deep expertise in the life sciences arena. Dr. Sang-Mok Lee, the CEO and President, is the driving force behind some of Biocure's biosimilar products.
9) **Biocure is dual listing on the Frankfurt Stock Exchange.** This will not only broaden its investor base, but also add to its market reputation and support its global expansion plans.
10) **We believe Biocure is undervalued** at its current market value. Our valuation using the risk-adjusted DCF methodology yields C$0.49 per share base case and C$0.93 per share bull case. In our view, re-rating will be driven by the progress of pipeline products as they advance further into the clinic.

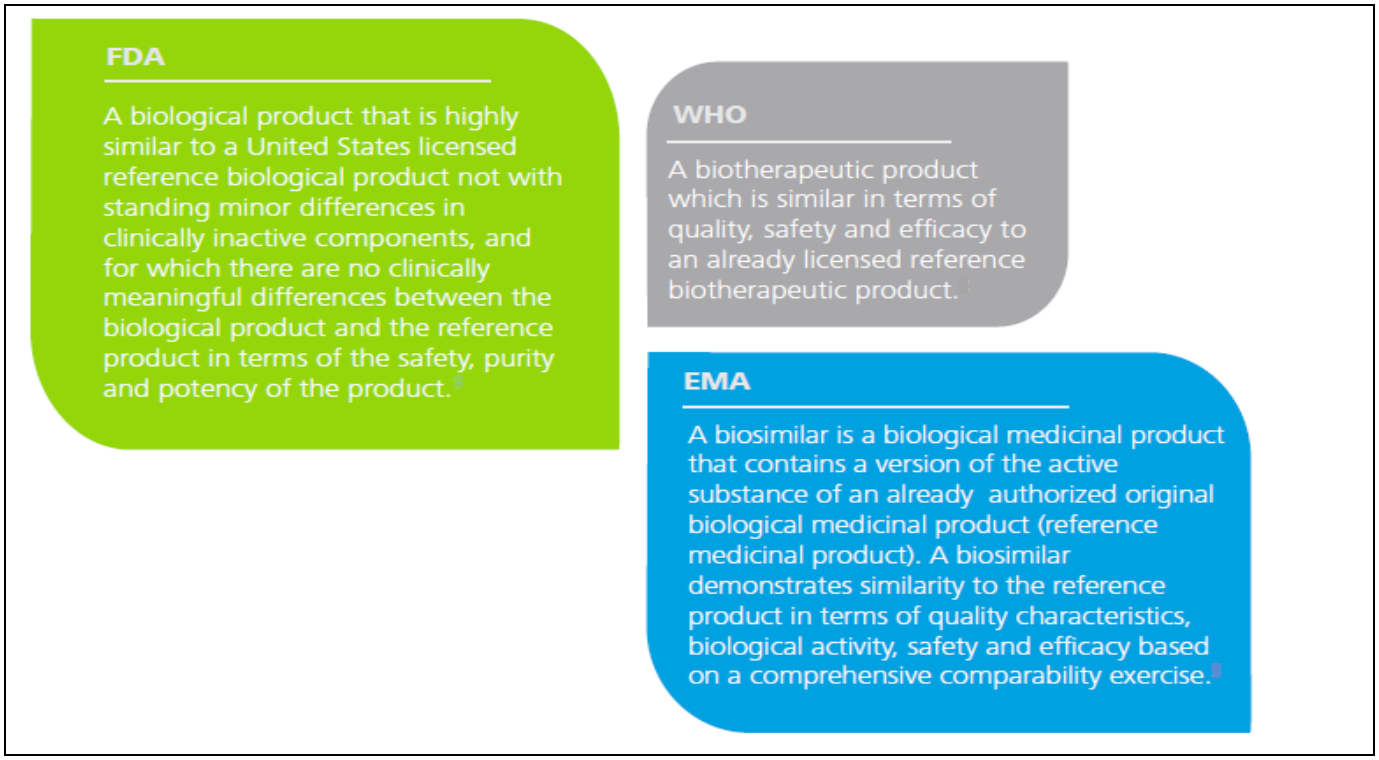
Biocure — Leveraging its bio-engineering expertise

In March 2017, the Canada-based Gravis Energy Corp signed a reverse merger agreement with BiocurePharm Corp, a South Korean privately held entity established in 2005. The deal was executed in November 2017, creating Biocure Technology Inc. Since then, this entity has been trading on the Canadian Securities Exchange. As a merged entity, Biocure Technology has completely shifted its focus towards the development of biosimilars.

Biosimilars are based on large and complex molecules from living organisms and can be considered low-cost, generic versions of biologics

What are biosimilars? Biosimilars are products that are similar but not identical to reference/originator biologic products. Simply put, a biosimilar is a generic version of a biological drug. While biosimilars are defined differently by global health agencies, including the FDA, WHO and EMA (Figure 1), these are typically large-weight and complex molecules that are produced in living cells through genetic engineering. The underlying philosophy behind biosimilars is to make key life-saving drugs affordable to a large section of the population. Thus, the price competitiveness of biosimilars against the original reference products is generally quite high.

Figure 1: 'Biosimilars' definitions by global health agencies



Source: Deloitte – 'Winning with biosimilars: Opportunities in global markets'

Biocure has been built on bio-engineering expertise. A key strength of several emerging biotech companies in South Korea is the ability to produce biological molecules at a low cost. Over the years, the biotech industry in South Korea has been witnessing rapid growth primarily driven by the supportive measures of the domestic government. The government has been investing heavily in local biopharmaceutical companies and providing them required capital and regulatory assistance. Notably, Biocure's in-house skill in bio-engineering has enabled low-cost biosimilars to be developed based on recombinant protein technology, cell-culture technology, protein purification

Biocure's in-house expertise in bio-engineering has enabled the development of low-cost biosimilars

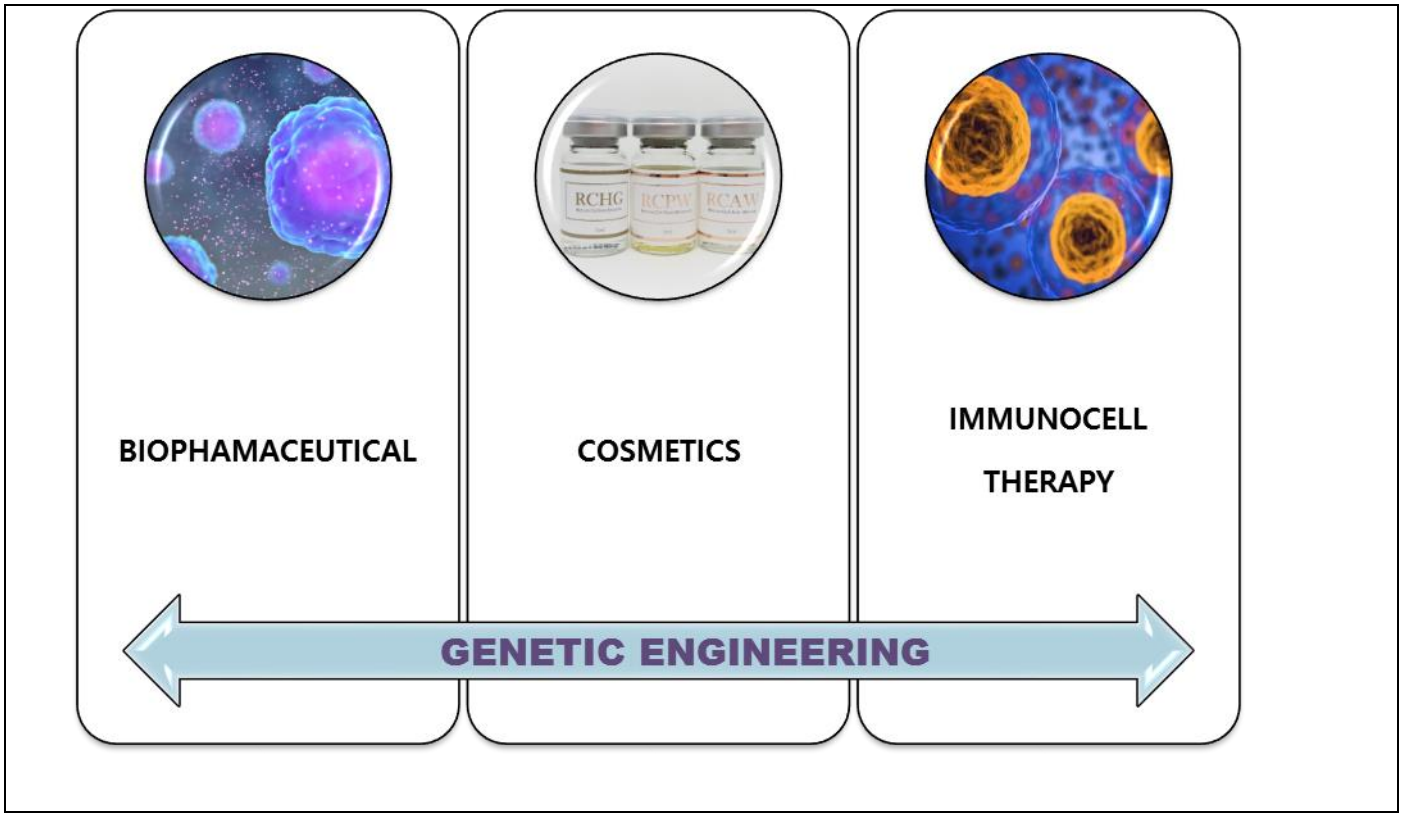
technology and bio-processing technology. This has enabled Biocure to develop biosimilars for biological drugs that were blockbusters during their period of market exclusivity. There are three biosimilars currently in development as alternatives to Betaseron (for Multiple Sclerosis), Lucentis (for Age-related Macular Degeneration) and Neulasta (for neutrophenia in cancer patients).

The product portfolio also comprises a CAR-T cell product being developed for cancer

Besides biosimilars, the company's product portfolio (Figure 2) has a CAR-T cell product for cancer treatment. CAR-T cell therapy is a relatively new treatment approach that utilises the body's own immune system to fight cancer. Biocure's CAR-T cell product has generated solid preclinical data and is currently undergoing clinical trials.

Biocure has access to a third-party GMP-compliant facility in Korea on a long-term lease/fee basis, and this will reduce upfront capital requirements as well as support its export activities in the future.

Figure 2: Product portfolio



Source: Company

Biocure's competitive advantage in biosimilars

***Biocure's competitive advantage is that it can make biologicals using* E coli**

Biocure knows how to make biosimilar drugs less expensively than its competitors. Unlike small molecule drugs, which are made using simple chemical reactions, large molecule drugs or 'biologicals' are made using living organisms as 'factories' to make the protein. Traditionally the cellular 'factory' of choice has been mammalian cells, and in particular a cell line called 'CHO'. Biocure's competitive advantage is that it can make biologicals using the bacterium *Escherichia coli* (*E. coli)* instead. This makes Biocure's cost of production much lower.

Biological drugs are made using cellular 'factories'. Biological drugs are basically proteins. To make a biological drug, scientists first need the DNA sequence for the protein. They then insert that sequence into a living cell—usually a yeast[3], bacterial, or mammalian cell, although even plant or insect cell lines have been used — in a process called 'transformation'. The resulting 'recombinant' DNA[4] instructs the transformed cell to produce the protein molecules. Those cells are then cultivated at a large-scale, in huge fermenters similar to those that make wine or beer, after which the protein can be isolated from the cells, purified, and formulated as the active ingredient in a biologic drug. The processes that allow the manufacture of biological drugs, called 'genetic engineering', were worked out in the 1970s[5], with the first genetically engineered drug to gain FDA approval being human recombinant insulin, in 1982.

Some cells can be made in bacterial cells, such as *E. coli*, others are better in mammalian cells. The pioneers of biological protein production back in the 1970s and 1980s used a bacterium called *E. coli* as their expression system. That was because *E. coli* culture grows very quickly and is easy to maintain, while the cells are easy to transform. However bacterial systems are tricky when it comes to expression of target proteins, because the bacterium used needs to facilitate proper translation of protein structure where that protein has been properly folded.

***E. coli* based production of biologicals is ideal,** because of the cost. With CHO as with other mammalian expression systems there is high material and production costs, not to mention high upfront investments. Protein yield from CHO cells tends to be low[6], that that yield comes in a long production cycle. We believe that *E. coli,* since it does not labour under these cost disadvantages, could cut costs by as much as 80% so long as the protein is properly expressed[7].

Biocure's scientists have developed *E. coli*-based expression systems for complex biologicals. Over the years since Biocure's founding in 2005 Dr Sang-Mok Lee and his colleagues have worked to develop high yield *E. coli*-based expression systems to produce biosimilars. There are three basic aspects to the Biocure know-how:

- **Novel strains of *E. coli*:** Biocure's team has developed techniques to genetically modify *E. coli* so that it can express target product as Active Pharmaceutical Ingredient[8].
- **Purification techniques**: Biocure's team know how proteins can be purified from *E coli* as drug substance for drug product. Purification of

[3] Most notably *Saccharomyces cerevisiae* and *Pichia pastoris*.
[4] So called because the DNA has been cut from somewhere else and recombined into its new host.
[5] Proc Natl Acad Sci U S A. 1973 Nov;70(11):3240-4.
[6] For example, for monoclonal antibodies, a yield of grams per litre per day in the single digits.
[7] As a rough guide to cost differentials, see *The Challenge of Building Better Biologic Drugs* by Feliza Mirasol, Pharmaceutical Technology, 2/8/2018.
[8] For an example of this kind of work from another group see Nat Commun. 2015 Aug 27;6:8072.

protein from *E. coli* is more difficult than from mammalian cell because there are a lot of host cell-derived heterogenous proteins.

- **Quality Control techniques**: Biocure's team is very experienced in biopharmaceutical manufacturing Quality Control and Quality Assurance, using the appropriate regulatory guidance.

Biocure is now going after biosimilar markets where it can make a difference, either as the first or second biosimilar in a market, or where it can pursue new indications for the protein with its biosimilar. The *E. coli*-based production process, combined with South Korea's lower cost base[9], suggests a strong competitive advantage for Biocure as it goes after emerging markets where cost has traditionally been an issue in terms of patient access to biologicals.

Strong product portfolio targeting multiple treatments

Biocure is in the preclinical development stage of three biosimilar products in South Korea targeting diverse therapeutic areas. It is also developing a CAR-T cell therapy for leukaemia. The details of these products are as follows:

Interferon beta-1b will be used for treating relapsing forms of Multiple Sclerosis

Interferon-β: Interferon-beta is a naturally occurring protein that controls the body's antiviral responses. Interferon beta-1b, to be used for treating relapsing forms of Multiple Sclerosis, is expected to be the first product to be commercialised out of Biocure's product portfolio and the preclinical trials are taking place this year. Interferon beta-1b is expected to be one of the few biosimilar products for Multiple Sclerosis in a multi-billion-dollar market. Notably, the total global market size of Multiple Sclerosis is projected to be ~US$24.8bn by 2024[10]. The originator of Interferon-beta was Schering AG, now part of Bayer, and the relevant patent expired in 2010. Biocure is developing a generic version of Schering's/Bayer's Multiple Sclerosis drug Betaseron[11], which was a US$0.9bn drug in 2010[12].

Ranibizumab: Ranibizumab will be used for treating macular degeneration. It will be also used to treat a type of ophthalmic disease known as macular edema. It is an anti-angiogenic administration that has been approved to treat the 'wet' type of Age-related Macular Degeneration (wAMD), a common form of vision loss in older people. Lucentis, the originator product developed by Genentech (a Roche subsidiary), lost its US market exclusivity in 2020 and will lose its European market exclusivity in 2022. While Roche sells Lucentis in the US, Novartis sells it in the rest of the world. Global sales of Lucentis stood at US$4.3bn at its peak in 2014[13]. wAMD is the representative disease for aging societies. It is noteworthy that the number of patients who need Ranibizumab is increasing rapidly. In Korea, the number of patients who need the drug has lately been rising at close to 40% p.a., the highest growth rate in the world[14].

Filgrastim: Filgrastim will be used to treat neutropenia, a lack of certain white blood cells caused by cancer, bone marrow transplant, chemotherapy, and other conditions. The original product developer was Amgen, and Neulasta enjoyed worldwide sales of US$4.5bn before the end of US market exclusivity in 2018. Given funding constraints, the company is evaluating an opportune

[9] GDP per capita of ~US$32,000 versus US$65,000 in the United States.
[10] Source: https://www.thepharmaletter.com/article/multiple-sclerosis-therapeutics-market-to-be-worth-24-8-billionby-2024.
[11] https://www.betaseron.com.
[12] Source: Bayer 2010 Annual Report, page 60.
[13] https://www.evaluate.com/vantage/articles/news/novartis-sees-past-lucentiss-decline.
[14] Source: Statistic Bureau, MIC; Ministry of Health, Labour and Welfare, United Nations.

moment to commence preclinical and clinical testing in Korea first, because Filgratim is used widely for cancer treatment in that country. Biocure will try to collaborate with local parties in other countries.

Biocure is targeting to launch CAR-T for ALL in South Korea by end 2022

CAR-T cell therapy: Chimeric Antigen Receptor modified T cell immunotherapy, typically known as CAR-T cell therapy, is one of the most competitive and advanced treatments for ALL yet to be developed. It works by extracting T cells from the patient's blood and then genetically engineering them to produce Chimeric Antigen Receptors on their surface. Thereafter, the patient receives the CAR-T cell therapy in an infusion, which can target and destroy cancer cells. With solid preclinical data and continuing clinical trials this year, the innovative cell therapy is due for market launch by the end of 2023. Notably, during the clinical work conducted at the Beijing University Hospital in China, Biocure established a cure rate of 94.6% involving 63 leukaemia patients[15]. While CAR-T cell therapy is highly effective, the cost of treatment, ~US$450,000 a year, is too high. Owing to its bio-engineering expertise, Biocure expects to lower the production cost to provide treatment at a lower cost to terminal leukaemia patients. The company plans to run a Phase 1 study in Korea once the Investigational New Drug (IND) application, submitted in December 2020, is approved by South Korea's Ministry of Food and Drug Safety. Biocure is targeting first commercialisation of a CAR-T product in South Korea.

Recombinant Human Growth Factors: Since 2015 Biocure has developed technology for the production of five human recombinant growth factors, useful in various cosmetic applications. Biocure is mulling a spin-off of this product line to maximise its business efficiency and focus on CAR-T cell therapy and other biosimilars.

CAR-T cell therapy — Beginning of a revolution in cancer immunotherapy

Adoptive cell transfer (ACT) is an immunotherapy technique that involves collecting and employing a patient's own immune cells to treat cancer. There are different types of ACTs that involve the use of various immune cells, such as tumour-infiltrating lymphocytes (TILs), T cell receptors (TCRs), and chimeric antigen receptors (CARs). CAR-T cell therapy is one of the most clinically advanced therapies among the various ACT approaches[16].

How the path-breaking therapy works

Post infusion, CAR-T cells recognise a specific antigen on cancer cells and destroy them

CAR-T cell therapy selectively directs a cell-mediated immune response against cancer cells, thereby providing extended periods of disease remission, making it a very promising cancer treatment. The CAR involved in CAR-T cell treatment is composed differently depending on the target and CAR-T cell generation. The antigens targeted are usually surface antigens with an epitope that is specific to cancer cells. The key steps involved in this therapy (Figure 3) are as follows:

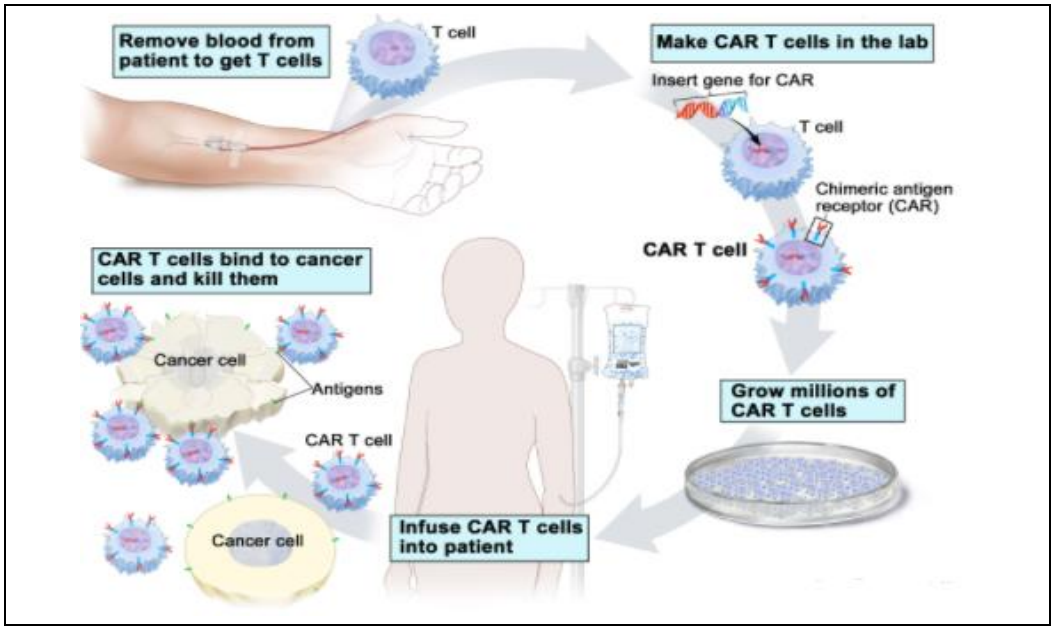
1) **Collection of T cells from the patient.** T cells are obtained through a technique that involves drawing blood from the body and separating one or more blood components, such as plasma, platelets, or white blood cells. Thereafter, the remaining blood is returned to the patient's body.
2) **Reengineering T cells in the laboratory.** T cells are then genetically engineered in a laboratory by introducing DNA that will help in the

[15] See Biocure's 10 September 2020 press release headlined 'BiocurePharm, Korea Provides Corporate Update'.
[16] See CAR-T Cells: Engineering Patients' Immune Cells to Treat Their Cancers, National Cancer Institute, 30 July 2019.

production of CARs on the cell surface. These reengineered cells are now known as CAR-T cells.

3) **Multiplication of reengineered CAR-T cells.** The reengineered CAR-T cells are multiplied in the laboratory and the frozen cells are then transferred to the hospital or trial site where the patient is being treated.
4) **Infusion of CAR-T cells into the patient's body.** In the hospital, the patient is given a brief course of chemotherapy before the infusion of CAR-T cells into the body. Thereafter, the CAR-T cells are expected to recognise and attack cells that have the targeted antigen on their surface.

Figure 3: CAR-T cell therapy mechanism



Source: National Cancer Institute

The key merits of this therapy are as follows:

- **High reactivity and treatment**: CAR-T cell therapies have higher reactivity with cancer than existing treatments.
- **High specificity**: CAR-T cell therapies are specifically engineered to identify and kill tumour cells
- **Long-term benefits:** CAR-T cell therapies have the potential to enhance immune memory against cancer cells[17].

Biocure – Forerunner of CAR-T cell therapy in Korea

Biocure is moving quickly with its BCP401 CAR-T cell therapy for ALL in Korea. Biocure expects to commence Phase I clinical trials for BCP401 in late 2021, post obtaining approvals from South Korea's Ministry of Food and Drug Safety.

[17] See *CAR-T Cell Therapies Market (3rd Edition),* Root Analysis Business Research & Consulting, March 2021.

After BCP401, Biocure plans to deepen its CAR-T product pipeline (Figure 4). It is currently working on the development of a second CAR-T product, which is expected to treat CLL.

Figure 4: Biocure's CAR-T pipeline

Program	Indication (Target)	Approach & Status	Discovery	Pre-clinical	Phase I	Phase II	Exit
BCP401	Leukemia	• CAR-T therapy targeting CD19 antigen • Preclinical efficacy / toxicity test completed, together with establishment of manufacturing and other processes to submit its IND application in December 2020 • Phase I of 9-12 patients to evaluate the safety and tolerability of BCP401, followed by Phase II of ~30 patients		★	2021	2022	Conditional market approval after Phase II in 2022
BCP402	Lung Cancer, Breast Cancer and Pancreatic Cancer	• ROR1 is an antigen specific to CLL cancer cell and expression in normal cell is very low (making it suitable for CLL diagnostic or CAR-T treatment) • Established JV 'Oncocart' with Koln University Hospital Clinical in Germany to progress CAR-T therapy targeting ROR1 antigen	★		2023	2024	Out-license to big pharma after Phase II
BCP403	Solid tumor	• Therapy to regulate expression of suppressor receptor of tumor cells with potential to develop relevant antibodies and receptors	★				

Source: Company

During clinical trials in China, BCP401 demonstrated a 94.6% complete remission rate

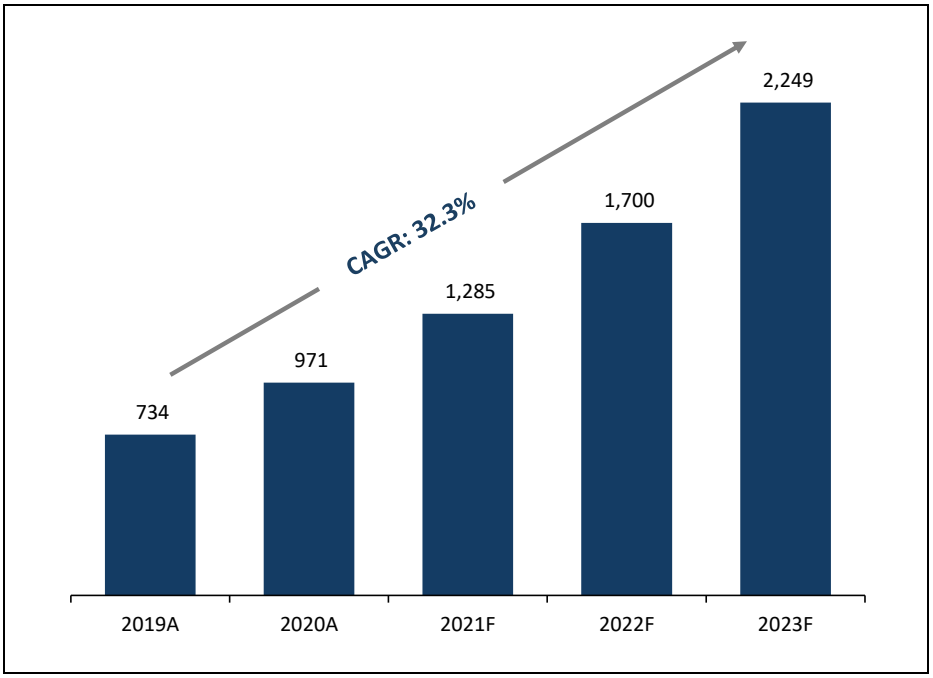
Substantial market potential for BCP401. Biocure is targeting commercialisation of its CAR-T product, BCP401, in South Korea by the end of 2022. The company demonstrated encouraging results during preclinical trials in 2018, where the data established that its CAR-T cell therapy in the treatment of ALL was non-toxic and had good efficacy. These trial results depicted a complete remission of the cancerous cells in 7–28 days from the injection of reengineered CAR-T cells into mice. Further, during the clinical trial conducted in China, complete remission rate was very high, at 94.6%

Bicocure is expected to generate significant revenue post the launch of BCP401 in the market. The Korean market presents a multi-billion dollar business opportunity and there is expansion potential in Asia and Europe through partnerships and licensing deals.

CAR-T cell therapy market to expand significantly

In 2019, the global CAR-T treatment market was valued at ~US$734m. The market is expected to grow at a CAGR of 32.3% and reach ~US$2.2bn by 2023 (Figure 5). This market is projected to further grow to ~US$8.3bn by 2028 according to estimates by Coherent Market Insights.

Figure 5: Global CART-T cell therapy market size (US$m)



Source: Research and Markets – 'CAR-T Therapy Market Report'

Importantly, a rising cancer burden and the high failure and mortality rate linked to the use of conventional treatment options remain the key drivers of the CAR-T therapy market. More than 750 CAR-T therapies are under development in the clinical (62%) and preclinical (38%) stages across the globe. Moreover, ~220 research-focused deals for this therapy were struck during 2011–2020.

At present, some of the leading players in the global CAR-T cell therapy market are Bellicum Pharmaceuticals, Bristol-Myers Squibb, Cellectis, Eureka Therapeutics, Gilead Sciences, Immune Therapeutics, Novartis and Sorrento Therapeutics.

Upon commercialisation of its BCP401 product, Biocure will be part of a huge addressable market, which will likely be worth over US$8bn by the next decade. While the currently approved CAR-T therapies have helped revolutionise cancer treatment, the development of a more cost-efficient CAR-T therapy by firms such as Biocure is expected to open up this market further. Key CAR-T therapies currently approved by the FDA are as follows:

Novartis' Kymriah was the first CAR-T therapy product approved by the FDA in August 2017

- **Kymriah:** Novartis' Kymriah was the first CAR-T therapy product approved by the FDA in August 2017 for refractory or relapsed B cell precursor ALL in children and young adults. The study that led to the approval of Kymriah demonstrated an overall remission rate of 81%[18] within three months. Kymriah registered sales of US$474m for Novartis in 2020.
- **Yescarta and Tecartus:** Yescarta, developed by Kite Pharma, gained FDA approval in October 2017. The clinical study depicted a 54% complete remission rate in patients with refractory or relapsed large B-cell lymphoma, who had failed two previous lines of cancer treatment. Yescarta posted sales of US$563m in 2020. Notably, Gilead acquired Kite Pharma for US$11.9bn in August 2017 to make its foray into the cell

[18] N Engl J Med. 2018 Feb 1;378(5):439-448.

therapy space. Gilead has another CAR-T therapy product, Tecartus[19], which received FDA approval for relapsed or refractory mantle cell lymphoma in July 2020. Tecartus recorded sales of US$44m in 2020.

– **Breyanzi:** Bristol-Myers Squibb received FDA approval for its CAR-T product, Breyanzi, in February 2021 for the treatment of diffuse large B-cell lymphoma (DLBCL). It is worthwhile to mention that when Celgene acquired Juno Therapeutics for US$9bn in January 2018, it predicted peak sales of US$3bn[20] for Breyanzi. Thereafter, in late 2019, Celgene was acquired by Bristol-Myers Squibb.

Upside for Biocure in low-cost CAR-T cell therapy

CAR-T cell therapy has launched the first launch of two products in 2017 and has been developed an effective treatment for haematological cancer such as pALL (paediatric Acute Lymphoblastic Leukaemia) and DLBCL (Diffuse Large B Cell Lymphoma). New indications are extending to other haematological cancer such as CLL (Chronic Lymphocytic Leukaemia), MCL (Mantle Cell Lymphoma), and FL (Follicular Lymphoma) as well as AML (Acute Myeloid Leukaemia) and MM (Multiple Myeloma).

Low-cost CAR-T cell therapy by Biocure will accelerate healthcare reimbursements, thereby increasing patient access to this novel treatment

Expensive CAR-T cancer treatments will face hurdles from the healthcare insurance reimbursement system. Industry experts estimate that CAR-T therapy costs ~US$1-1.5m in the US, including administration and hospitalisation costs. With this price tag, insurance approval for CAR-T will continue to be a long-drawn process, particularly in the US. The high expense associated with the therapy may make it impractical for large-scale adoption in the future, if other existing treatments offer better value as first-line options in cancer treatment. Low-cost CAR-T cell therapies by Biocure could help resolve the issue of healthcare reimbursements associated with CAR-T cell therapies.

Biocure plans to provide BCP401 at a 30–40% lower price point than existing FDA-approved products

Biocure can enhance the accessibility of CAR-T with its cost-efficient product. While Kymriah and Yescarta CAR-T treatments have been commercially available since 2017, they remain inaccessible to many patients owing to their high cost. For instance, a single treatment with Kymriah costs about US$475,000 (Figure 6) and likewise, Yescarta comes with a price tag of US$373,000 per patient.

Notably, Biocure aims to offer Asian and European markets a more cost-efficient CAR-T cell therapy. It plans to supply BCP401 at a price that will be 30–40% lower compared with existing FDA-approved products. Therefore, Biocure's ability to lower its cost of CAR-T therapies will help it gain access to a huge population of cancer patients across the globe.

[19] Generic name brexucabtagene autoleucel, see tecartus.com.
[20] See the Celgene press release dated 22 January 2018 and headlined 'Celgene Corporation to acquire Juno Therapeutics'.

Figure 6: Different CAR-T therapies

Therapy	Target	Manufacturer	Stage	Indication	Pricing (US$)
Kymriah (tisagenlecleucel)	CD19	Novartis	FDA approved	ALL	$475,000, per 1 dose
Yescarta (axicabtageneciloleucel)	CD19	Gilead / KITE	FDA approved	Non-Hodgkin lymphoma	$373,000 per 1 dose
JCAR017 (lisocabtagenemarealeucel)	CD19	BMS / Juno	Submission	Leukemia, lymphoma, NHL	
BB2121 (idecabtageneciclucel)	BMCA	Celgene	Phase II	Multiple myeloma	
AUTO-1	CD19	Autolus	Phase I/II	Leukemia, lymphoma	
JCAR104	CD19	Juno	Phase I	NHL	
UCART19	CD19	Cellectis/ Servier/ Allogene	Phase I	Leukemia, lymphoma	
BCP401	**CD19**	**BiocurePharm**	**Submission to IND**	**ALL**	

Source: Company

Biosimilars market to continue expanding at a rapid pace

In 2020 something like 240 biosimilar candidates were under development across multiple diseases. The FDA and EMA have approved several biosimilars for the treatment of diseases such as diabetes, Crohn's disease, Rheumatoid Arthritis and cancer[21]. As of December 2020, the FDA had approved 29 biosimilars corresponding to nine different reference products (RPs)[22], and by February 2021, the EMA had approved 69 biosimilars[23].

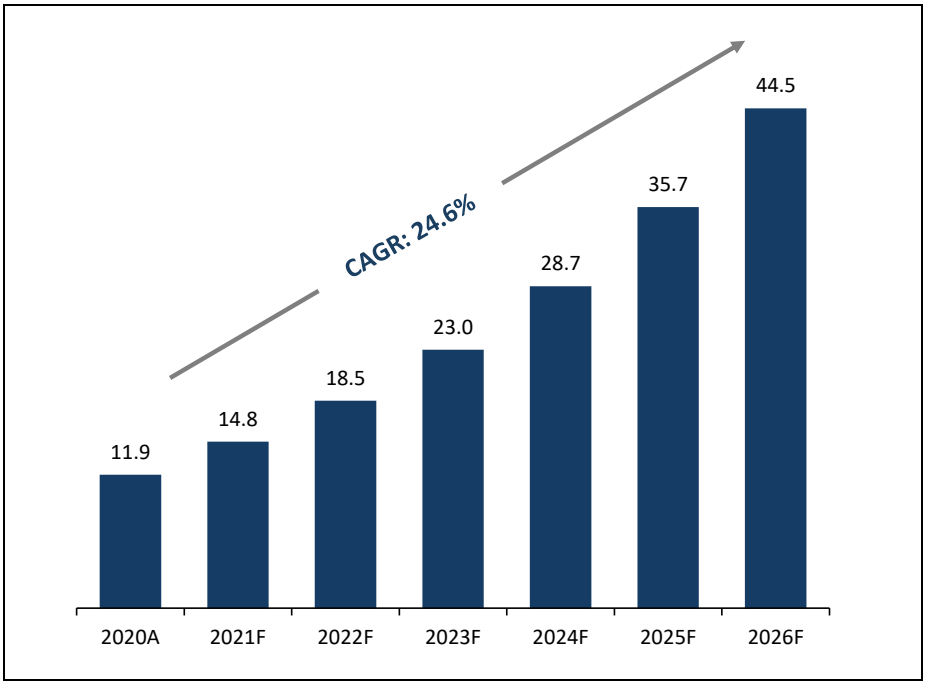
The history of biosimilars began in Europe back in 2006 with the approval of Omnitrope (Somatropin), used in the treatment of growth disorders in children and growth hormone deficiency in adults. In the US, it was the Biologics Price Competition and Innovation Act (BPCI Act) of 2009 that provided a strong regulatory pathway and fillip to biosimilars. The availability and use of biosimilar medications are expected to save US$100bn in drug expenditures over the next five years, due to high uptake of biosimilars within their first year of market launch. Bevacizumab, Trastuzumab and Rituximab, the three most recently announced biosimilars in 2019, have seen high market uptake within the first year of their launch, with a Defined Daily Dose share of 42%, 38% and 20%, respectively. By the end of 2021, these biosimilars are expected to have a market share of ~60%, which is significantly higher than the previous uptake of biosimilars[24].

In 2020, the global biosimilars market was valued at US$11.9bn, and this is expected to reach ~US$45bn by 2026, registering a CAGR of 24.6% (Figure 7). Biosimilars have made treatment of many life-threatening conditions, such as cancer, diabetes as and chronic inflammatory disorders, affordable. There are several blockbuster biological drugs that are set for patent expiration in the coming decade, making biosimilars an attractive market for pharmaceutical players to expand into[25]. A few biosimilar developers have even started evaluating treatments for COVID-19. For instance, Celltrion Healthcare's Infliximab biosimilar, Remsima, is in Phase II trials and is

[21] Drugs. 2020; 80(2).
[22] See *Biosimilars 2020 Year in a Review* by Fish & Richardson, 5 February 2021.
[23] See B*iosimilars approved in Europe*, Generics and Biosimilars Initiative, 12 February 2021.
[24] See IQVIA's institute report dated 29 September 2020 and headlined '*Biosimilars in the United States 2020-2024*'.
[25] See Glo*bal Biosimilars Market 2020-2025*, Research and Markets, 14 June 2021.

expected to control cytokine release syndrome (CRS) associated with COVID-19[26].

Figure 7: Global biosimilars market (US$bn)



Source: Reports and Data – 'Biosimilars Market Size, Trend and Growth'

While COVID-19 has opened up a potential opportunity for biosimilars, the pandemic has also had a negative impact on this industry. Due to the pandemic, the FDA's approval of non-COVID treatments has reduced and this is slowing down the process of product approval for biosimilars.

In our view, the addressable markets for the key biosimilars in Biocure's pipeline are huge and will provide multi-billion dollar opportunities to the company. These opportunities are described below.

Biocure's biosimilars can address multi-billion dollar markets

The Interferon-β drugs market, which was estimated at US$3.7bn in 2020, is expected to be valued at US$4.7bn in 2027. The global Interferon-β medicines market will grow in response to the rising prevalence of Multiple Sclerosis. According to data provided by the Multiple Sclerosis Trust (MST), the disease had affected 2.5 million people worldwide by 2020[27]. In 2016, the global Multiple Sclerosis medication market was valued at US$16.3bn, and this is expected to grow to US$25–27bn by 2025[28].

Increased prevalence of chronic diseases such as cancer will fuel growth of the Pegfilgrastim biosimilars market. Pegfilgrastim is a PEGylated form of the recombinant human granulocyte colony-stimulating factor (G-CSF) analogue, filgrastim. These medications are used during cancer treatment to lower the risk of infection in individuals who are receiving immunosuppressive treatments such as chemotherapy. The global pegfilgrastim biosimilars market is expected to grow from US$876m in 2019 to US$1.1bn in 2023 at a

[26] See *Biosimilar Developers and the Battle Against COVID-19* by Skylar Jeremias, AJMC – The Center for Biosimilars, 2 September 2020.
[27] See *Interferon Beta Drugs Market Analysis*, Coherent Market Insights, October 2020.
[28] V.M. Biosimilar Drugs for Multiple Sclerosis: An Unmet International Need or a Regulatory Risk?; Neurol Ther; 2019; 8; 177–184.

CAGR of 6.3%[29]. Mylan's Fulphila, Coherus's Udenyca and Sandoz's Ziextenzo — the three biosimilars of Neulasta – controlled 30% of the pegfilgrastim market in July 2020. Neulasta enjoyed US$4.5bn in global sales before the end of US market exclusivity in 2018[30].

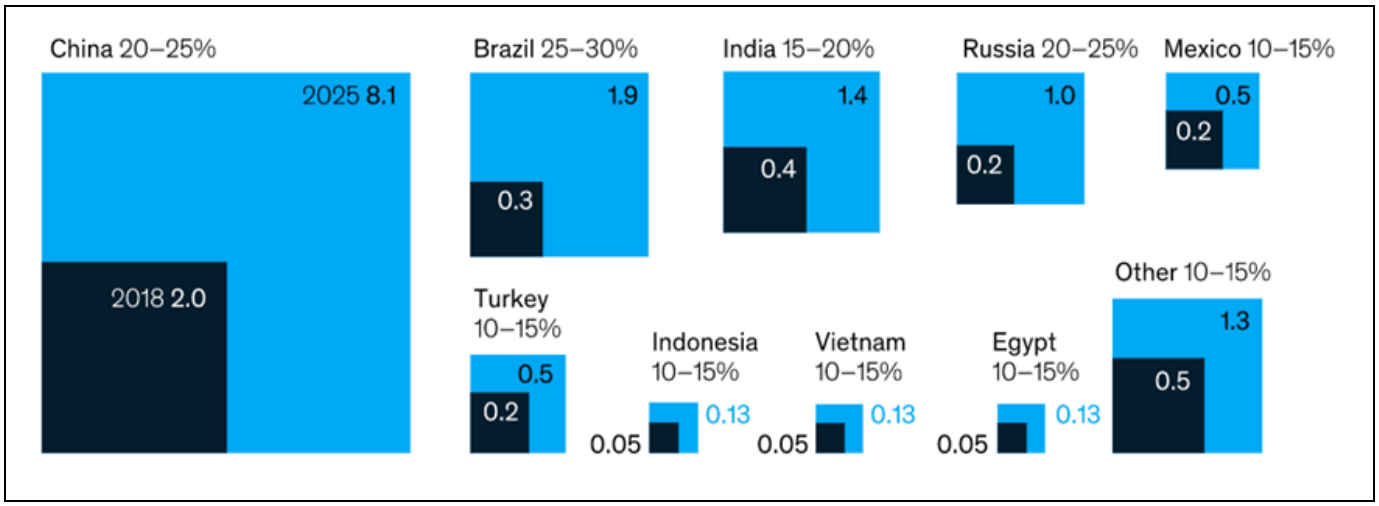
Ranibizumab originator product (Lucentis) loses market exclusivity in US: Ranibizumab, a monoclonal antibody, is used to treat Age-related Macular Degeneration, macular oedema, degenerative myopia and diabetes complications. Lucentis, the originator product marketed by Roche, used in the treatment of 'wet' Age-related Macular Degeneration, was approved by the FDA in June 2006 and by the EMA in January 2007. Lucentis lost its US market exclusivity in 2020 and will lose its European market exclusivity by 2022[31]. Prior to losing its exclusive status, Lucentis was a US$3.7bn drug for Roche in 2018[32].

High demand for biosimilars in emerging markets

Emerging markets such as China, India, Brazil and Mexico offer high growth opportunities for biosimilars

Currently, North America has ~30% share in the global biosimilars market, but it is the Asia Pacific market that is anticipated to grow at the fastest rate in the next five years. The presence of multiple large-scale companies in North America involved in the research and development of competitive biosimilars has had a significant role to play in the high market share of the region. However, future growth will be fuelled by the Asia Pacific region (Figure 8), driven by low patient access to biologics, greater need to make treatments affordable and the growing involvement of large pharmaceutical players in the region.

Figure 8: Projected biosimilars market in emerging economies (US$bn, annual % increase during 2018–2025)



Source: McKinsey– 'What's next for biosimilars in emerging markets?'

Emerging markets have been a nursery for biologic alternatives, which include copies of biologics that have not been subjected to a specific biosimilar comparability approach. In India, there are more than 70 such products on the market, while in China, there are more than 40. The quality of biosimilars

[29] See *Global Pegfilgrastim Biosimilars Market,* The Business Research Company, December 2020.
[30] See *The Booming Biosimilars Market of 2020,* Drug Channels, 6 October 2020.
[31] See *Biosimilars of ranibizumab*, Generics and Biosimilar Initiative, 4 December 2020.
[32] See *Novartis gets FDA boost in crowded eye drug market* by John Miller, Thomson Reuters, 8 October 2019.

is expected to improve with maturity of regulatory frameworks, making them more adaptable to multiple geographical markets.

Multinational companies, such as Boehringer Ingelheim, Lonza and Amgen, are seeking to expand and focus their efforts on emerging economies, where biologic treatment rates are still low. In China, several therapeutic areas show wide gaps in the proportion of patients treated with biologics when compared with the US. For instance, in China, as of 2020, biologics were used to treat 20–25% of newly diagnosed breast cancer patients, compared with more than 70% in the US. Less than 10% of colorectal cancer patients were treated with biologics in China as opposed to 55% in the US. In Brazil and Mexico, up to 40% of the patients with tumours failed to receive any treatment via biologics in 2020. These countries offer a critical opportunity to help patients afford treatment through biosimilars and gain access to high-quality care [33]. Regulatory pathways for biosimilars have been defined for most of the emerging markets but are still under continuous change in China and Russia[34].

Recombinant non-glycosylated proteins is the leading product segment for global biosimilars

Based on product type, the biosimilars market is bifurcated into recombinant non-glycosylated proteins, recombinant glycosylated proteins, and recombinant peptides (Figure 9). In 2019, recombinant non-glycosylated proteins accounted for a sizable portion of the biosimilars market (~62% market share), and this segment is anticipated to grow at a 26.1% CAGR through 2025.

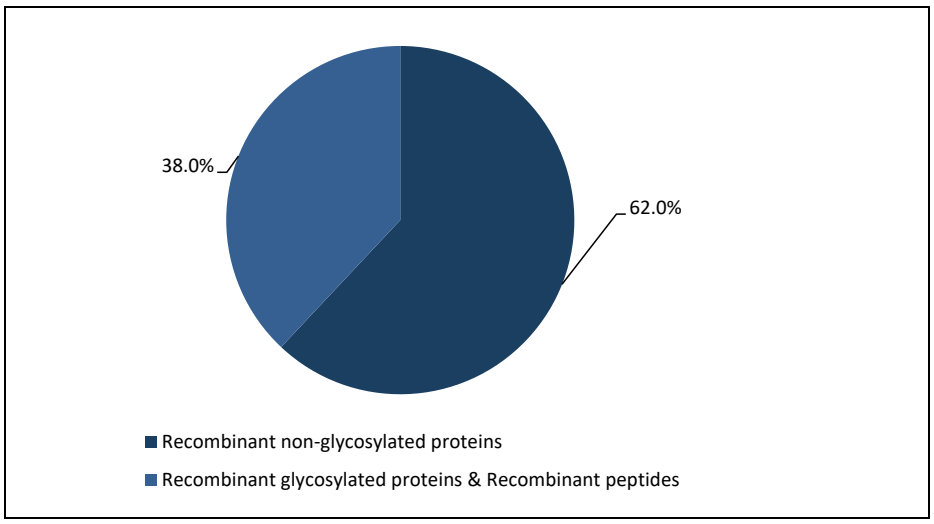
Recombinant non-glycosylated proteins will lead the biosimilars market, with ~62% market share

The recombinant non-glycosylated proteins segment is further divided into human growth hormone (HGH), granulocyte colony-stimulating factor (filgrastim), insulin and interferons. The demand for recombinant non-glycosylated protein biosimilars is driven by an increase in the incidences of chronic diseases, diabetes and growth hormone deficiency-related disorders[35].

The recombinant glycosylated proteins segment is further subdivided into erythropoietin (EPO), monoclonal antibodies (mAbs) and follitropin. In the recombinant glycosylated proteins segment, monoclonal antibodies are a major revenue generator. mAbs are widely employed in the treatment of cancer, diabetes and autoimmune illnesses. With the use of genetic engineering, pharmaceutical businesses are expanding their efficacy in hybridoma-based technologies to generate improved mAbs.

[33] Source: McKinsey– 'What's next for biosimilars in emerging markets?', 2019.
[34] See *Biosimilars Market*, Transparency Market Report, 8 January 2020.
[35] See *Biosimilars Market Research Report,* Market Research Future, February 2021.

Figure 9: Biosimilars market share by product type (2019)



Source: Reports and Data – 'Biosimilars Market Size, Trend and Growth'

Loss of market exclusivity for key biologics

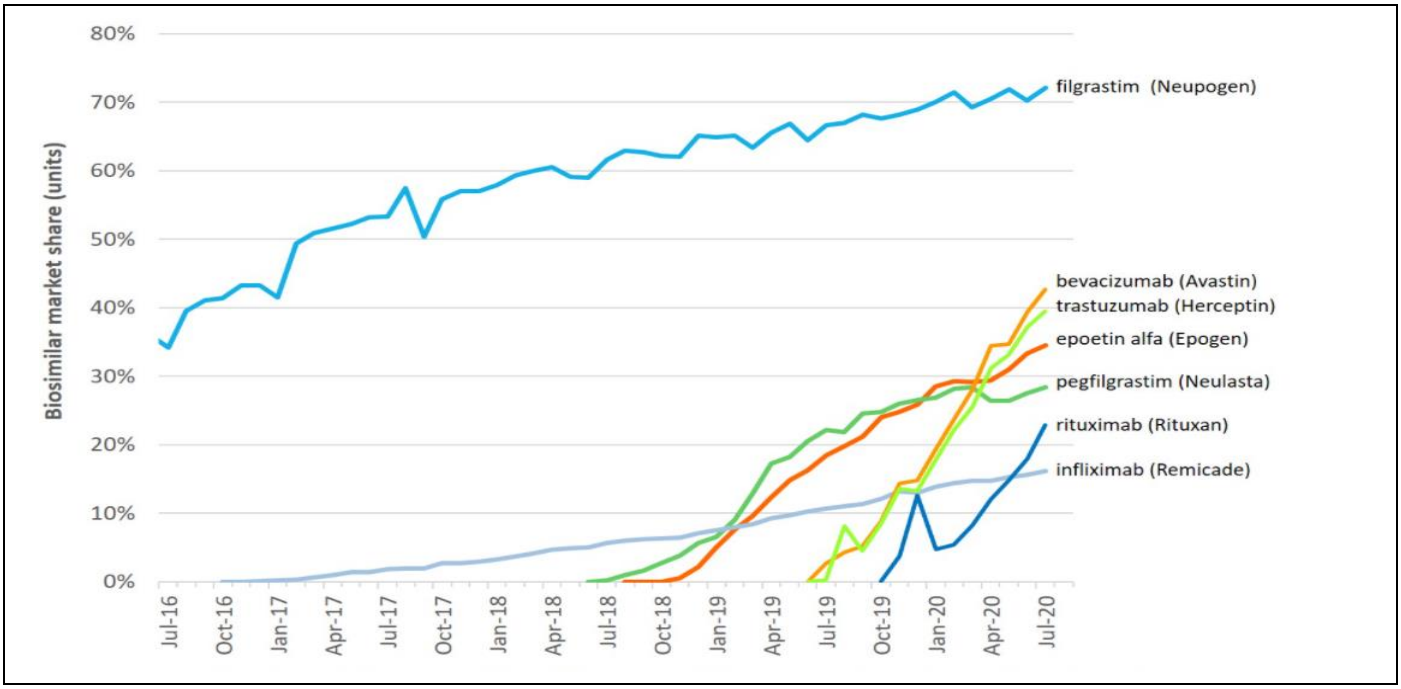
Biosimilars are viable low-cost treatment alternatives for high-cost branded biologics

Biosimilars' lower cost compared with RPs is stimulating market competition, which can help keep healthcare budgets in check and improve patient access to biologics therapy. In the US, the use of biosimilars is expected to bring down the spend on biologics by $US54bn between 2017 and 2026[36]. In Q2 2020, cost savings from use of biosimilars in the US healthcare system amounted to ~US$5.6bn, with annualised savings of ~US$6.5bn [37]. Competition has already decreased the average list price of biologics, resulting in increased patient access to biologics in the European Economic Area.

Many innovative biologics, such as Herceptin (five variants) and Remicade (four variants), are now competing with biosimilar equivalents. In the past five years, the unit market share of the biosimilar versions of seven reference provider-administered biologics has shown a significant upward trend (Figure 10).

[36] See *Biosimilars Cost Savings in the United States – Initial Experience and Future Potential,* Rand Corporation, 2017.
[37] See Amgen's report dated 21 October 2021 and headlined '*Where Biosimilars are headed in the US'.*

Figure 10: Up-trend in the market share of provider-administered biosimilars, 2016–2020



Source: Drug Channels – 'The Booming Biosimilar Market of 2020'

Ten major biologics set to lose patent protection in the next four years. Ten important biologics, including Humira, Avastin and Stelara, will lose their market exclusivity in the next four years (Figure 11). In 2019, these biologics collectively generated US$45bn in revenue, and their patent expirations will open up a huge market for other biopharma players in the industry[38].

Figure 11: Key biologics losing patent protection in next four years

Biologic	Molecule	Manufacturer	2019 Sales (USD, Bn)	Patent Expiration
Humira	Adalimumab	Abbvie	19.2	2023
Avastin	Bevacizumab	Roche	7.76	2022
Stelara	Ustekinumab	Janssen	6.36	2024, 2023
Soliris	Eculizumab	Alexion	3.95	2020, 2021
Simponi	Golimumab	Janssen	2.19	2024, 2024
Cimzia	Certolizumab pegol	UCB	2.01	2021, 2024
Lucentis	Ranbizumumab	Novartis	2.01	2022, 2020
Benlysta	Belimumab	GSK	1.41	2021, 2023
Yervoy	Ipilimumab	BMS	0.39	2021, 2023
Nulojix	Belatacept	BMS	0.15	2021, 2023

Source: Consultancy.eu – 'Europe's biosimilars market set for a major transformation'

[38] See *Europe's biosimilars market set for a major transformation*, Consultance.eu, 15 April 2021.

Smaller firms are driving biosimilar development, while large corporations are mostly responsible for marketing. Six multinational pharmaceutical companies are currently developing 13% of all biosimilar drugs under development[39]. The other 87% is being developed by 41 smaller companies with varied levels of biologic or biosimilar experience. In our view, this trend bodes well for companies such as Biocure that are focussed on development and many not have deep pockets for marketing, which is better undertaken by the larger players.

Favourable regulatory environment in the UK

A favourable regulatory environment and reductions in data requirements for market approval will drive growth in the UK

In the UK, a group of regulators from the Medicines and Healthcare Products Regulatory Agency (MHRA) contended that comparative biosimilar efficacy trials are unnecessary to demonstrate that drug candidates are equivalent to RPs. The group claimed that, except in extreme cases, analytical testing and a pharmacokinetic trial are sufficient to demonstrate biosimilarity[40].

Based on this contention, the UK MHRA has issued draft guidance for a reduction in such data requirements. The guidance states that a comparative efficacy trial would not be needed in most cases; however, such a determination must be supported by strong evidence and will be made only after consideration of all other elements of an application for biosimilar approval. The draft guidance came into effect from January 2021 and grants the MHRA complete authority over evaluation and approval of all medicinal products for use in the UK[41].

We believe this is a highly favourable development for biosimilar companies such as Biocure, as there is a high possibility that similar practices may be adopted by other European countries in the near future, thus providing regulatory relaxation for biosimilar developers.

Valuing Biocure

Using a risk-adjusted DCF, we value Biocure at C$49m base case and C$93m bull case. Our key assumptions are listed below:

- Our valuation reflects an aggregate payoff in Biocure's lead asset BCP401. We model only the Korea market for leukaemia, which according to the company, amounts to ~US$2bn per annum. We assume a 50-60% market penetration to incorporate BCP401's attractive value proposition which include superior overall survival rate compared to existing FDA-approved CAR-T therapies. We also assume Biocure will out-license its product to a potential large pharma company upon the release of positive results from its Phase 2 clinical trials, expected sometime in 2022. Based on our top-down inputs, we estimate ~C$1.2-1.6bn in peak sales per annum to be earned by Biocure's potential partner. With an assumed royalty rate of 10-11%, this will cut through to ~C$124-172m in peak annual royalty sales for Biocure.
- A 30-35% probability of clinical success given preclinical data has already demonstrated good efficacy and safety profile. Also note the ~94% remission rate demonstrated in patients enrolled in a clinical trial in China between 2017 and 2018.

[39] See IQVIA's institute report dated 29 September 2020 and headlined '*Biosimilars in the United States 2020-2024*'.
[40] See *UK Regulators Contend Biosimilar Efficacy Trials Are Redundant*, AJMC – The Centre for Biosimilars, 19 September 2020.
[41] See *UK Regulators Seek Response on Waiving Comparative Efficacy Testing,* AJMC – The Centre for Biosimilars, 8 October 2020.

- A 14.6% discount rate[42] is assumed to reflect the heightened risk of a clinical-stage drug development company.
- A 15-year commercial life, with initial sales to commence in 2023, sequentially ramping up towards its full penetration by 2027.
- Continued R&D and SG&A throughout the life of the product with each expense constituting ~10% and ~30% of royalty sales, respectively.
- A 25% corporate tax rate is assumed. As Biocure has accumulated significant tax losses over the years, we estimate the company will pay its first tax in 2025.
- We assume the company to raise another C$6m to take it through to the end of its clinical trial for BCP401.

Biocure's deep pipeline of CAR-T treatment programmes and its biosimilars enable significant optionality. We note Biocure currently has a number of pipeline assets in the discovery/preclinical stages targeting various indications such as lung cancer, breast cancer and pancreatic cancer. Given their early stage of development, we think it is too speculative to ascribe values to those assets. However, we do think that these assets possess substantial option value as they provide Biocure with the optionality to pursue multiple avenues of commercial opportunities should its BCP401 fail to yield positive clinical results. Overall, we believe our valuation range is further supported by the option value available in Biocure's pipeline assets.

Re-rating Biocure

In our view, re-rating of the Biocure stock will be driven by the achievement of the company's key near and medium-term milestones, including the following:

- Approval of CAR-T product – The company is targeting commercialisation of its CAR-T product in South Korea. It aims to conduct a Phase I study in Korea once the IND application is approved by South Korea's Ministry of Food and Drug Safety. It will be positive for the company if the management is able to stick to its timelines for Phase I.
- Publication of clinical data related to the CAR-T product – Encouraging readings/results from the clinical testing of Biocure's CAR-T product will help validate the prospects of this technology.
- Increased sales of competing CAR-T products – We believe the surge in sales of competing CAR-T products could be in favour of the company, as its acceptance in the pharmaceutical industry will grow in tandem.
- Completion of development work on biosimilars – Biocure is still in the preclinical stages for its three key biosimilar products, including Interferon beta-1b, Ranibizumab and Filgrastim. We believe any positive news on advancement towards clinical trials of its biosimilars will bode well for the company.

[42] 14.6% discount rate would represent a risk-free rate of 2%, a market risk premium 9%, and a beta of 1.4.

Comparable companies

We have considered public peers for Biocure under two categories—biosimilars and CAR-T cell therapy. In order to shortlist comparable companies, we have looked at entities in the above-mentioned categories operating in developed countries with market capitalisation below US$500m (Figure 12). A majority of the shortlisted firms are based in the US and South Korea and have a strong product pipeline. The average market capitalisation of the comparable companies at ~US$240m[43] is quite high compared with Biocure's current capitalisation, and we think this denotes upside potential to be achieved by the company as its pipeline products enter clinical stages.

Figure 12: Comparable public companies in biosimilars and CAR-T categories

Company	Domicile/Founded	Description	Market Cap (US$m)	Biosimilars Pipeline
Xbrane Biopharma (OM: XBRANE)	Sweden/2008	A biotechnology company that develops, manufactures and sells biosimilars.	361	– **Xlucane:** It will be used for the treatment of age-related macular degeneration, diabetic-related macular edema and retinal vein occlusion (in Phase III stage). – **Xcimzane:** It will be used for rheumatoid arthritis, psoriasis and Crohn's disease (in preclinical stage). – **Xdivane:** It will be used for melanoma, lung cancer, renal cell carcinoma, head and throat cancer (in preclinical stage).
Prestige BioPharma (KOSE: A950210)	Singapore/2015	A biopharmaceutical firm that mainly engages in the development of new and similar antibody drugs for solid tumours, pancreatic cancer and arthritis.	335	– **HD201:** It is a Trastuzumab biosimilar for breast and gastric cancer and currently under Phase III development. – **HD204:** It is a Bevacizumab biosimilar for solid tumours (in Phase III stage). – **PBP1502:** It is an Adalimumab biosimilar for arthritis (in preclinical stage). – **PBP1510:** It is a first-in-class antibody indication for pancreatic cancer in preclinical stage.

[43] As at mid-July 2021.

SunBio (XKON: A067370)	South Korea/1997	A biotech company that develops biosimilars, biopharmaceutical products and medical devices based on its proprietary technologies of pegylation. It also offers MucoPEG, a medical device for treatment of dry mouth syndrome, along with SynoGEL, a viscosupplement for arthritic knees.	318	– **PEGfilgrastim:** It has been marketed in the EU (under the trade name Pelgraz) and Canada (under the trade name Lapelga) since 2018. It is targeting oncology support to help the body replenish white blood cells post chemotherapy. – **PEG-EPO** and **PEG-uricase** biosimilars are in the preclinical stage. While PEG-EPO will be used for the treatment of anaemia owing to chronic kidney disease, PEG-uricase will be used for the treatment of refractory gout.
PanGen Biotech (KOSDAQ: A222110)	South Korea/2010	A specialised biologics company that develops biosimilar products, including EPO, recombinant factor VIII and G-CSF. It also provides Chinese Hamster Ovary (CHO) cell lines for proteins and monoclonal antibodies.	94	– **EPO:** Phase III trial completed. – **Factor VIII:** It will be used for the treatment of Hemophilia A. – **G-CSF:** It is to be used for the treatment of Neutropenia. – **Interferon-β:** It will be used for the treatment of Multiple Sclerosis.
Company	**Domicile/Founded**	**Description**	**Market Cap (US$m)**	**CAR-T Pipeline**
Autolus Therapeutics (NasdaqGS: AUTL)	UK/2014	A clinical-stage biopharmaceutical company that develops T cell therapies for the treatment of cancer.	475	– **AUTO1:** It is a CD19-targeting programmed T cell investigational therapy for the treatment of adult ALL. – **AUTO3:** It is a first dual-targeting, bicistronic (with two chimeric antigen receptors within one vector), programmed T cell investigational therapy for the treatment of relapsed or refractory diffuse large B-cell lymphoma.

Mustang Bio (NasdaqGM: MBIO)	US/2015	A company focussed on developing next-generation therapies for patients with cancer and rare genetic diseases.	279	– **MB-106:** It is a third generation fully human CD20-targeted CAR-T cell therapy for the treatment of Non-Hodgkin's lymphoma and CLL. – **MB-105:** It is a CAR-T cell therapy for the treatment of prostate and pancreatic cancer. – **MB-101:** It is the first CAR-T to demonstrate durable remission in solid tumour setting
Anixa Biosciences (NasdaqCM: ANIX)	US/1982	A biotechnology company developing a number of programmes addressing cancer and infectious diseases.	114	– The company's therapeutics programmes include the development of a chimeric endocrine receptor T cell technology focussing on the treatment of ovarian cancer.
Chimeric Therapeutics (ASX:CHM)	Australia/2020	A biotechnology firm that develops and commercialises chimeric antigen receptor T cell therapy drugs for solid tumours in Australia.	87	– **CTLX-CAR-T:** Post completion of preclinical research in September 2020, the company commenced dosing of patients with glioblastoma (brain cancer) as part of Phase I clinical trials at the City of Hope Cancer Centre in Los Angeles.
Celyad Oncology (ENXTBR: CYAD)	Belgium/2007	A clinical-stage biotechnology company focussed on the discovery and development of CAR-T cell therapies for cancer.	79	– **CYAD-101:** The leading allogeneic candidate is a NKG2D receptor-based CAR-T for the treatment of refractory metastatic colorectal cancer. – **CYAD-211:** It is developing the short hairpin RNA (shRNA)-based allogeneic CAR-T candidate for relapsed or refractory multiple myeloma.

Source: S&P Capital IQ, Pitt Street Research

Leadership team with rich experience

Biocure has an experienced leadership team with extensive specialisation in the life sciences domain. The current board members are listed below (Figure 13):

Figure 13: Biocure's board members

Name and Designation	Profile	Affiliations (current and past)
Sang-Mok Lee CEO and President, Director	– Dr. Lee has been the President and CEO of the company since its inception in 2005. – Is a PhD in Microbiology from Busan National University, South Korea, and is currently an adjunct professor in Microbiology at Chungnam National University, South Korea.	Committee member of KOFST (the Korean Federation of Science and Technology Societies)
Konstantin Lichtenwald CFO, Director	– Has more than a decade of experience in the field of finance and accounting, including corporate compliance, initial public offers and reverse takeover services. – Holds a Bachelor of Business Administration degree from Pforzheim University, along with the professional designations of CPA, CGA and ACCA.	Member of the Association of Chartered Certified Accountants of UK, and member of Chartered Professional Accountants of BC and Canada
Collin (Sang-Goo) Kim Director	– Had a 16-year tenure at Hanwha Corp, a Korean business conglomerate, where he was associated with the international trading business for various industrial products. – Holds a Bachelor of Business Administration degree from Korea University, Seoul.	Columbia Capital, ArcPacific Resources Corp.
Berkan Unal Director	– Has ~10 years of experience in the biopharmaceutical industry – Currently works as Business Development Director for the American gene and peptide synthesis company, GenScript[44] Biotech. – Studied Bioprocess Engineering and Medical Biotechnology at Berlin Technical University of Applied Sciences, Hamburg University of Technology and Imperial College London.	Several biotech companies in Switzerland and Germany
Danny Joh Director	– Has a vast experience of 20 years in biopharmaceutical firms, spanning early-to-late-stage product development in various platforms, including biologics, small molecules, and gene therapy. – Is a PhD in Biochemistry from Texas A&M University and has an MBA degree from Rice University.	Chiron, Sangamo, Biomarin, Genentech

Source: Company

[44] Piscataway, NJ, HKSE: 1548, genscript.com.

Risks related to Biocure

Risks specific to Biocure. We see five major risks for Biocure as a company and as a listed stock:

- **Timing risk.** There is the risk that BCP401 and the biosimilar products may take longer than expected to move through the clinic.
- **Regulatory risk**. There is the risk that regulators may decline to approve Biocure's products, even if Biocure considers the data submitted to be adequate.
- **Commercial risk**. There is the risk that Biocure may fail to find commercial partners for its products.
- **Uptake risk**. There is the risk that Biocure's products are still too expensive in the healthcare markets in which it wants to participate.
- **Funding risk**. There is the risk of future capital raisings proving dilutive to existing shareholders.

Risks related to pre-revenue Life Science companies in general.

The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.

Since most biotechnology and medical device companies listed on stocks exchanges in Canada and around the world fit this description, the 'term' speculative can reasonably be applied to the entire sector.

The fact that the intellectual property base of most biotechnology and medical device lies in science not generally regarded as accessible to the layman adds further to the riskiness with which the sector ought to be regarded.

Caveat emptor. Investors are advised to be cognisant of the abovementioned specific and general risks before buying any the stock of any biotechnology and medical device stock mentioned on this report, including Biocure.

Appendix I – Glossary

Acute Lymphoblastic Leukaemia (ALL): A cancer of the lymphoid line of blood cells characterized by the development of large numbers of immature lymphocyte

Acute Myeloid Leukaemia (AML): A blood cancer characterised by proliferation and accumulation of myeloid blasts in the bone marrow that are blocked at various stages of differentiation. The disease is called acute because patients develop abnormal numbers of these cells very quickly.

Adoptive T cell therapy: Cancer treatment in which a patient's own T cells are engineered to increase their cancer-fighting properties, and then returned to the patient.

Bevacizumab: Bevacizumab is a type of anti-angiogenesis agent, and a type of monoclonal antibody used to treat certain types of cervical cancer, colorectal cancer, non-small cell lung cancer, renal cell carcinoma (a type of kidney cancer) and glioblastoma (a type of brain cancer).

Biologics: A biologic drug (biologics) is a product that is produced from living organisms or contains components of living organisms. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies.

Biosimilars: A biosimilar is a biologic medical product highly similar to another already approved biological medicine (the 'reference medicine' or 'originator medicine').

Blockbuster: A pharmaceutical drug with more than US$1bn in annual sales.

Chimeric antigen receptor T cells (CAR-T cells): Chimeric antigen receptor T cells (also known as CAR-T cells) are T cells that have been genetically engineered to produce an artificial T cell receptor for use in immunotherapy.

Chinese Hamster Ovary (CHO) cell lines: The CHO cells are an epithelial-like cell line that are highly amenable to transfection and have emerged as the gold standard for the manufacturing of approved therapeutic proteins.

Chronic Lymphocytic Leukaemia (CLL): CLL is a typically slow-growing cancer that begins in lymphocytes in the bone marrow and extends into the blood. CLL is the most common form of leukaemia in adults.

Cytokine Release Syndrome (CRS): CRS is a systemic inflammatory response that can be triggered by a variety of factors such as infections and certain drugs.

Erythropoietin (EPO): EPO is a hormone produced by the kidney that promotes the formation of red blood cells by the bone marrow.

Follitropin: Follitropin also called as Follicle stimulating hormone (FSH) is a hormone made in the pituitary gland. In females, it acts on the ovaries to make the follicles and eggs grow. In males, it acts on the testes to make sperm.

Granulocyte colony-stimulating factor (G-CSF): Also known as colony-stimulating factor 3 (CSF 3), it is a glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream.

Human Growth Hormone (HGH): HGH is a peptide hormone that stimulates growth, cell reproduction and cell regeneration in humans.

Infliximab: It is a type of monoclonal antibody that blocks the action of a cytokine called tumour necrosis factor alpha. It is being studied in the

treatment and prevention of weight loss and loss of appetite in patients with advanced cancer.

Interferons: Interferons are a group of signalling proteins made and released by host cells in response to the presence of several viruses. In a typical scenario, a virus-infected cell will release interferons causing nearby cells to heighten their anti-viral defences.

Interferon-β: Interferon-β is a cytokine in the interferon family used to treat Multiple Sclerosis.

Investigational New Drug (IND) – A request filed with the drug regulator for authorisation to conduct human trials of a new drug or biological product.

Monoclonal antibodies (mAbs): A type of protein made in the laboratory that can bind to substances in the body, including cancer cells. A monoclonal antibody is made so that it binds to only one substance.

Non-Hodgkin's lymphoma (NHL): It is a cancer of the lymphatic system. It occurs when tumours develop from the lymphocytes. A lymphocyte is a type of white blood cell.

Pegfilgrastim: A drug that is a form of filgrastim and is used to prevent infection in adults and children with neutropenia (lower-than-normal number of white blood cells) caused by some types of chemotherapy. Pegfilgrastim helps the bone marrow make more white blood cells and is able to stay in the body longer than filgrastim.

Pharmacokinetics: It is a branch of pharmacology dedicated to determine the activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localised in the tissues and excreted.

Ranibizumab: Ranibizumab is a monoclonal antibody fragment (Fab) created from the same parent mouse antibody as bevacizumab. It is an anti-angiogenic that has been approved to treat the "wet" type of age-related macular degeneration, diabetic retinopathy and macular oedema.

Reference Products (RPs): A reference product is an already approved biological product against which a proposed biosimilar product is compared.

Remission: It means that the signs and symptoms of the cancer are reduced. Remission can be partial or complete. In a complete remission, all signs and symptoms of cancer disappear.

Rituximab: Rituximab is a monoclonal antibody used alone or with other drugs to treat adults with certain types of B-cell Non-Hodgkin’s lymphoma or CLL.

T cell receptor (TCR): A group of proteins found on T cells (a type of immune cell that recognises and binds to foreign substances). T cell receptors bind to certain antigens (proteins) found on abnormal cells, cancer cells, cells from other organisms and cells infected with a virus or another microorganism.

Trastuzumab: It is a monoclonal antibody used alone or with other drugs to treat certain types of breast cancer, stomach cancer and gastroesophageal junction cancer.

Tumour-infiltrating lymphocytes (TILs): A type of immune cell that has moved from the blood into a tumour. Tumour-infiltrating lymphocytes can recognise and kill cancer cells.

Appendix II – Capital Structure

Class	In millions	% of fully diluted	Note
Ordinary fully paid shares	99.9	92.5%	
Options	6.3	5.9%	Wtd. avg. exercise price of ~C$0.28
Warrants	1.8	1.7%	
Fully diluted shares	**108.0**		

Source: Company

Appendix III – Major Shareholders

Biocure has one major shareholder – Sang-Mok Lee (CEO and President) – who owns 27.4% stake in the company.

Appendix IV – Analyst Qualifications

Stuart Roberts, lead analyst on this report, has been an equities analyst since 2002.

- Stuart obtained a Master of Applied Finance and Investment from the Securities Institute of Australia in 2002. Previously, from the Securities Institute of Australia, he obtained a Certificate of Financial Markets (1994) and a Graduate Diploma in Finance and Investment (1999).
- Stuart joined Southern Cross Equities as an equities analyst in April 2001. From February 2002 to July 2013, his research speciality at Southern Cross Equities and its acquirer, Bell Potter Securities, was Healthcare and Biotechnology. During this time, he covered a variety of established healthcare companies, such as CSL, Cochlear and Resmed, as well as numerous emerging companies. Stuart was a Healthcare and Biotechnology analyst at Baillieu Holst from October 2013 to January 2015.
- After 15 months over 2015–2016 doing Investor Relations for two ASX-listed cancer drug developers, Stuart founded NDF Research in May 2016 to provide issuer-sponsored equity research on ASX-listed Life Sciences companies.
- In July 2016, with Marc Kennis, Stuart co-founded Pitt Street Research Pty Ltd, which provides issuer-sponsored research on ASX-listed companies across the entire market, including Life Sciences companies.
- Since 2018, Stuart has led Pitt Street Research's Resources Sector franchise, spearheading research on both mining and energy companies.

Cheng Ge is an equities research analyst at Pitt Street Research.

- Cheng obtained a B.Com in Finance and an LLB from the University of New South Wales in 2013, and has passed all three levels of the CFA Program.
- Before joining Pitt Street Research, he worked for several financial services firms in Sydney, where his focus was on financial advice.
- He joined Pitt Street Research in January 2020.

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