ALIGN
RESEARCH

Hemogenyx Pharmaceuticals

1st March 2018

Potential game changer to re-set blood cancer patients offers the possibility of exponential upside

Hemogenyx Pharmaceuticals (HEMO) is a preclinical-stage biopharmaceutical company focused on the development of its novel treatments which aim to transform the bone marrow transplantation procedure (BMT). A BMT is a potential life-saver for late-stage patients with blood diseases such as leukemia and lymphoma.

Two product candidates could revolutionise bone marrow transplants

BMTs (a specialised type of cell therapy) are a last resort for blood cancer patients for whom traditional chemotherapy treatments have failed. But preparation of patients ('conditioning') and the bone marrow transplant itself can be harmful and have low rates of efficacy, respectively. HEMO's novel products, for both the Conditioning and Cell Therapy steps look to address and mitigate the limitations and dangers involved to change the way such transplants are carried out and to ultimately prolong survival. **Proof of principle for both products has been achieved, with defined preclinical milestones set for the next c.14 months.**

Preclinical, immuno-oncology deals highlight upside potential

Big pharma are increasingly looking to early stage candidates to fill their development pipelines, with immuno-oncology being a recent area of heightened interest. **Recent in-licensing deals in the sector have seen upfront payments in the hundreds of millions of US dollars, with acquisitions and IPOs valued at over half a billion US dollars**.

Shares look highly attractive on a risk/reward basis

Hemogenyx is capitalised at just under £15 million & looks to us to be one of the lowest valued biopharma development plays on the whole of the market with an EV of less than £13 million. Our very conservative DCF based analysis of the Conditioning Product alone suggests an initial target price of 18.15p, implying 332% upside. **We therefore initiate coverage of Hemogenyx with a Conviction Buy stance.**

Table: Financial overview – Hemogenyx LLC

Year to end Dec	2014A	2015A	2016A
Revenues ($)	-	10,095	-
Pre-Tax ($)	-	(266,739)	(635,757)
EPS ($)	-	(0.02)	(0.05)

Source: Company admission document

This investment may not be suitable for your personal circumstances. If you are in any doubt as to its suitability you should seek professional advice. This note does not constitute advice and your capital is at risk. This is a marketing communication and cannot be considered independent research.

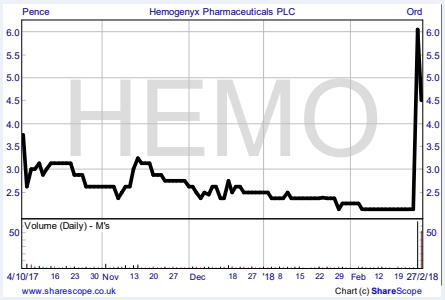
CONVICTION BUY – Price Target 18.15p

HEMOGENYX PHARMACEUTICALS

Key data

EPIC	HEMO
Share price	4.2p
52 week high/low	6.05p/2.125p
Listing	LSE Main Market
Shares in issue	356,042,854
Market Cap	£14.95m
Sector	Biopharma

Share price chart



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IMPORTANT: Hemogenyx is a research client of Align Research. Align Research owns shares in Hemogenyx. For full disclaimer & risk warning information please refer to the last page of this document.

Corporate Background

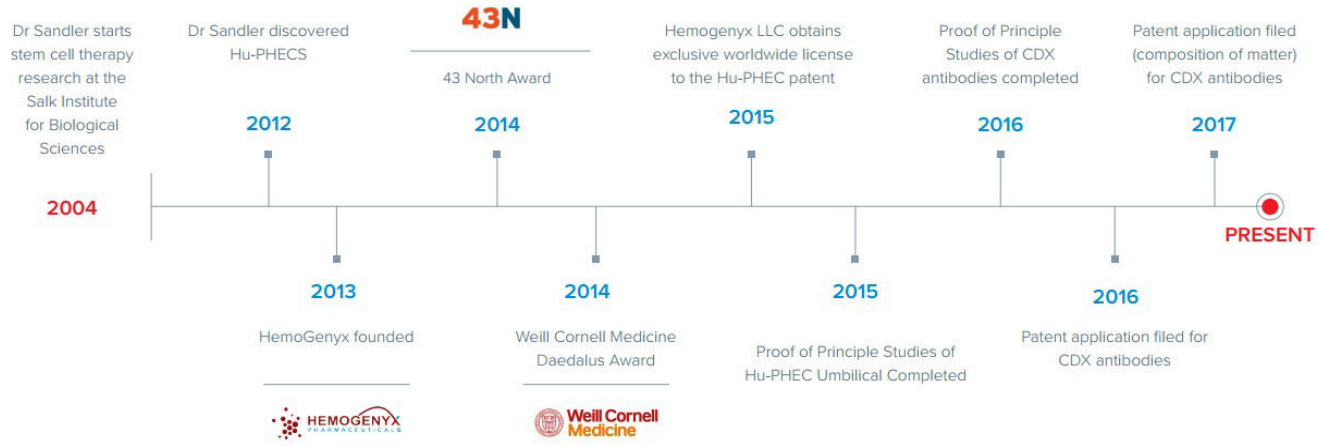
Hemogenyx Pharmaceuticals (HEMO) is a preclinical-stage biopharmaceutical company focused on the discovery, development and commercialisation of novel therapies and treatments relating to bone marrow/hematopoietic (blood-forming) stem cell (BM/HSC) transplants for blood diseases, including leukemia, lymphoma and bone marrow failure. The company's therapies are designed to provide new treatments in bone marrow/stem cell transplants, improving their success and safety. The business is headquartered in London, with wholly owned U.S. operating subsidiary, Hemogenyx LLC, operating from a state-of-the-art research facility in Brooklyn, New York.

Hemogenyx LLC was co-founded by Dr. Vladislav Sandler and Alexis M. Sandler in late 2013 to develop the company's **Hu-PHEC product candidate** (which Dr. Sandler discovered while working at Cornell University) and later, the **CDX bi-specific antibody product candidate**. In November 2014 the business was one of 11 winning finalists in the inaugural 43North business competition, and received a $250,000 investment from Empire State Development, the economic development arm of New York State, in exchange for a 5% equity stake in the business.

In 2015 Hemogenyx LLC established a research laboratory at the New York State Center of Excellence in Bioinformatics and Life Sciences in Buffalo, New York. Collaboration with scientists from Roswell Park Cancer Institute allowed the company to obtain access to the Institute's facilities and instrumentation, which proved to be invaluable for successfully completing proof of principle studies of Hu-PHEC. **Later that year, Hemogenyx received the FDA's Orphan Drug Designation ("ODD") for Hu-PHEC to treat aplastic anaemia**.

Further, in February 2016 the company received an investment of $1 million from private equity firm Bonsai Capital and subsequently established an advanced research laboratory at the Downstate Biotechnology Incubator in Brooklyn, New York. The laboratory has the equipment necessary to conduct advanced research and development and for the successful completion of preclinical studies.

Hemogenyx joined the standard listing segment of the Official List of the LSE on 5th October 2017 following the reverse takeover of Silver Falcon Plc. The terms of the deal saw Hemogenyx Pharmaceuticals acquired for £8 million in consideration for 228,571,428 new ordinary shares at a price of 3.5p each. Along with the acquisition, £2 million (£1.685 million net) was raised through the issue of 57,142,857 new ordinary Shares in a placing and subscription at a price of 3.5p. Added to existing funds and contracted revenue from research collaboration work, this gave the company total cash of c. £3.1 million & which is currently being applied to further development of its two candidates.



Hemogenyx corporate timeline. Source: Company

Market Background

According to figures from the American Cancer Society's Cancer Facts & Figures 2018 report (CFF 2018), the blood cancers leukemia, lymphoma and myeloma are expected to cause the deaths of 58,100 people in the US in 2018, down slightly from an estimated 58,300 in 2017. **For 2018, that equates to c.9.5% of all deaths from cancer in the year based on estimated total deaths of 609,640.** What's more, an estimated 1,290,773 people in the US are estimated to be either living with, or are in remission from one of the three diseases, with another 174,250 expected to be diagnosed in 2018, up from 172,910 in 2017.

The CFF 2018 report suggests that from 2005 to 2014 the overall leukemia incidence rate increased by 1.6% per annum, incidence rates for lymphoma were stable over the period, with no figures given for myeloma. While 5 year survival rates have improved significantly over the past 40 years, with a 64% survival rate for leukemia and 51% rate for myeloma between 2007-13, these remain below the 69% 5 year survival rate seen for all cancers.

BM/HSC Transplantations

After exhausting all conventional treatment options such as chemotherapy, radiation therapy and immunotherapy, a **bone marrow/Hematopoietic Stem Cell (BM/HSC) transplant** is typically the only remaining choice for blood cancer patients. However, as discussed in more detail below, this form of treatment can have low rates of efficacy and be harmful to patients. **Hemogenyx seeks to fundamentally change how bone marrow transplantation is performed and allow more people who need transplants to be able to obtain them by eliminating the need for a donor and improving their efficacy.**

A BM/HSC (bone marrow/Hematopoietic Stem Cell) transplant is the process of replacing diseased or damaged bone marrow or bone marrow stem cells with healthy tissue. The transplant sees a patient receive stem cells, derived from either their own (autologous) or a donor's (allogeneic) bone marrow. These replace their own stem cells that have been destroyed by disease or by cancer treatments such as radiotherapy. HSCs are cells capable of self-renewal and differentiation into specialised blood cells found in bone marrow in adults which continue to reproduce or self-renew throughout life. **The desired clinical effect of the transplantation is that the transplanted cells will be accepted by the patient and regenerate the entire blood system, facilitating their recovery from certain types of blood cancers and blood disorders.**

BM/HSC transplantations are used for life-threatening diseases including leukemia, lymphoma, aplastic anaemia and multiple myeloma. However, due to high risks associated with the procedure it is only reserved as an option for patients who have received unsuccessful traditional cancer treatments. Risks come at all stages of the BM/HSC transplantation process.

Conditioning – the first stage, conditioning a patient for transplantation, sees a regime of radiation and chemotherapy to eliminate diseased HSC from the patient's bone marrow to prepare them for the healthy HSC transplant. This has traditionally been achieved by administering maximally tolerated doses of chemotherapeutic agents, with or without radiation. Regimes currently in use, albeit 'reduced intensity' ones, are still highly toxic and have severe side effects that can be life threatening due to their "off-target" activity - where drugs attack healthy cells as well as diseased cells. Side effects can include high mortality and morbidity rates, radiation damage to the heart or lungs, problems with the thyroid or other hormone-making glands, problems with fertility, damage to bones or problems with bone growth, and development of another cancer years later.

BM/HSC Transplantation – the second stage sees the transplantation of healthy BM/HSC into the conditioned patient and their engraftment (when the cells start to grow and make healthy blood cells). According to data from the Center for International Blood and Marrow Transplant Research, up to 50% of BM/HSC transplants fail due to rejection by the body, procedural complications or a relapse of the disease. This is further exacerbated by an acute shortage of BM/HSC donors – up to 60% of patients who require a transplant from an unrelated donor are unable to find a match.

Hemogenyx's two product candidates aim to address and mitigate the limitations and dangers involved in these two parts of the transplantation procedure, which are where a substantial proportion of problems currently arise.

Pipeline

Hemogenyx Pharmaceuticals' operating subsidiary Hemogenyx LLC is currently focusing on the development of two distinct but complementary products, both of which it believes hold the potential to revolutionise the way BM/HSC transplants are being performed, mitigating the dangers and limitations associated with the current standard of care.

The Conditioning Product

CDX bi-specific antibodies for conditioning patients undergoing BM/HSC transplantations

To avoid the use of harmful and dangerous chemotherapeutic agents and radiotherapy for conditioning patients undergoing BM/HSC transplantations (discussed above), Hemogenyx is developing an immunotherapy method, using CDX bi-specific antibodies, to selectively eliminate unwanted hematopoietic stem cells/hematopoietic progenitors (HSC/HP) in patients. **CDX antibodies belong to a class of bi-specific antibodies that redirect a patient's own immune cells to eliminate unwanted HSC.**

The antibodies function by binding the targeted unwanted cells to the patient's own immune cells, which function to kill the target unwanted cells. This step clears sufficient 'niche' space (specialized environment) in the bone marrow for the transplant of HSC. This allows transplanted cells to engraft in the recipient and (in certain cases) may help to eradicate the source of malignancy. **As a result, CDX bi-specific antibodies can potentially provide a more selective and targeted approach to conditioning patients, avoiding the damaging effects of chemotherapy and radiotherapy.**

To date, Hemogenyx has achieved proof of principle for the use of CDX antibodies. It has functionally validated CDX bi-specific antibodies *in vitro* and *in vivo* in humanized mouse models, demonstrating that the CDX antibody-targeted conditioning regime is efficient and well tolerated, providing a good environment for subsequent stem cell transplantation.

When fully tested and in use, the company anticipates that the CDX antibodies will be an "off-the-shelf" product available and applicable for conditioning patients for all BM/HSC transplantations that require conditioning, including those using conventional BMT procedure and wanting to replace the current harsh conditioning regime.

Providing further clinical and commercial potential, Hemogenyx is also investigating whether the candidate will be effective as a targeted treatment for certain types of leukemia. On 26th February 2018 the company announced that first data results have shown that **CDX bi-specific antibodies are capable of attacking and eliminating the blood cancer Acute Myelogenous Leukemia (AML) *in vitro*.** Using these new humanised mice the company is confident it should be able to demonstrate that CDX bi-specific antibodies are effective in the treatment of AML, a disease which accounts for roughly 1.8% of cancer deaths in the US, with c.20,000 new cases diagnosed in the US and 18,000 cases in Europe every year.

Intellectual property

Hemogenyx filed a provisional patent application relating to the CDX bi-specific antibodies in the US on 4th April 2016. The invention summarised is a method of eliminating hematopoietic stem cells/hematopoietic progenitors (HSC/HP) in a patient using bi-specific antibodies specifically binding to a protein predominantly expressed on the surface of HSC/HP and to a protein uniquely expressed on a surface of immune cells. The bound bi-specific antibodies redirect immune cells to eliminate HSC/HP. The invention relates to the required conditioning of a patient prior to a BM/HSC transplant.

Further, on 4th April 2017, a PCT (Patent Cooperation Treaty) application was filed by Hemogenyx which includes additional claims that extend the CDX Patent set out in the provisional patent application to protect specific sequences of several high quality clones discovered and validated by Hemogenyx. The claim extension transforms the original "method" provisional patent application into a "composition of matter" PCT application.

Following the news of 26th February 2018, the company announced it has filed a provisional patent application relating to the development of a new type of humanised mice with a chimeric mouse-human blood system that can be used to advance product development, as well as for other disease modelling and drug development.

Development Plans

The CDX bi-specific antibody conditioning product is Hemogenyx's lead candidate. At the time of admission to the LSE the company set out its development plans for the candidate for the following 18 months (up to around early Q2 2019), with it intending to further progress the pre-clinical development programme, with a view to moving into phase 1 clinical trials. In the coming months Hemogenyx expects to complete a pre-Investigative New Drug (IND) consultation program with the FDA, a precursor to beginning the Phase 1 clinical trials in humans.

Additionally, the company intends to apply to the FDA to obtain Orphan Drug Designation (ODD) for the product in relation to patient conditioning for pre-BM/HSC transplantation in a number of different blood cancers and disorders. The company believes that it will be capable of receiving ODD status for its products in connection with BM/HSC transplantations as this procedure is performed in less than 200,000 people in the US (see page 10), an upper limit for the ODD classification. Other objectives include completing preclinical evaluation and the required IND-enabling studies, filing an IND application with the FDA and final preparations for moving into Phase 1 clinical trials.

Overall, it is expected that by the end of the 18 month timeframe set out at Admission, all work preparatory to human trials will be completed in relation to the CDX conditioning product candidate and that, subject to the raising of additional funds, the product will then be able to commence Phase 1 trials.

Conditioning Product development plans
Completion of pre-IND consultation programme
Preclinical evaluation of additional clones of CDX antibodies
Completion of IND-enabling studies
Submission of IND application to FDA
Application for Orphan Drug Designation
Final preparations in readiness for start of Phase 1 trials

Table: Conditioning product targeted development milestones. Source: Company admission document.

Cell Therapy Product

Hu-PHEC for the generation of cancer-free, patient-matched blood stem cells

To solve the problems and limitations associated with the transplantation stage of BM/HSC transplantations, Hemogenyx uses **Human Postnatal Hemogenic Endothelial Cells (Hu-PHEC)**, cells that are capable of generating cancer-free HSC for use in BM/HSC transplantations.

The product candidate derives from Dr. Sandler's discovery, while working at Cornell University, that the cells that give rise to blood forming stem cells (HSC) continue to exist in postnatal mammals, including humans. It was previously believed that they existed only up to birth. Dr. Sandler also developed the method of their isolation and use. **As a result of his work, Dr. Sandler was awarded the inaugural Daedalus Fund Award for Innovation at Cornell, allowing him to pursue the Hu-PHEC cell-related research and treatments which Hemogenyx is undertaking.**

Hu-PHEC are a naturally occurring cell type found in postnatal mammalian tissues, which can be easily isolated before treatment and do not require heavy manipulation before use. Hu-PHEC are considered "healthy" because they do not have accumulated blood cancer-related mutations and/or chromosomal rearrangements, making them a perfect candidate for autologous BM/HSC transplantations. **As the cells are cancer free they can improve the efficacy of the therapy, with the potential to effectively "re-set" a patient's regenerated blood system to a cancer free state.** They can also be isolated from a related or unrelated matching donor for allogeneic transplantation.

Preclinical proof of principle has been achieved for the use of Hu-PHEC for hematopoietic system regeneration, with studies in animal models indicating that the newly discovered class of blood stem cells are capable of safe and efficient restoration of the human hematopoietic system. **If current work is successful Hemogenyx believes that Hu-PHECs should be applicable to all BM/HSC transplantation candidates, eliminating the difficult task of identifying donors and managing the complexity and issues for clinicians and patients with allogeneic BM/HSC transplants.**

Exclusive licence

Cornell University applied for patent protection of the method of PHEC isolation and their use for hematopoietic system regeneration in November 2014. Hemogenyx LLC subsequently obtained an exclusive worldwide licence to the pending patent in early 2015 giving the rights to sub-licence, to make, use and sell the Hu-PHECs throughout the world until expiry of the patent rights. Consideration for the licence was an issue fee of $347,500 ($325,000 of which was paid in the form of a loan from Cornell at 5% per annum), licence maintenance fees, milestone payments, an earned royalty, a percentage of sub-licence fees, plus a royalty on sub-licence fees, and a minimum annual royalty.

Hemogenyx currently has three Hu-PHEC products under development:

Hu-PHEC Umbilical – this uses Hu-PHECs derived from the umbilical cord and placenta of new born babies (subject to parental consent). The product will be targeted for mostly allogeneic transplantations where currently cord blood is used as the source of HSC. Hemogenyx believes that it can solve the problem of insufficient numbers of HSC in a single cord blood unit by using Hu-PHEC Umbilical in combination with HSC obtained from the cord blood of the same donor.

This approach will likely greatly increase the number of transplantable cells obtained from the same donor, eliminating the need for additional cord blood units or donors. It will be applicable both to allogeneic and autologous transplants but will initially mainly be used in relation to donor transplants. **To date the functional engraftment of human umbilical cord Hu-PHEC has been demonstrated in (immunocompromised) mouse models.**

In one of its key achievements to date, Hemogenyx LLC has been granted FDA Orphan Drug Designation (ODD) for the use of Hu-PHEC Umbilical to treat aplastic anaemia, or bone marrow failure. This is a rare disorder in which the bone marrow fails to create enough blood cells. The ODD provides a number of benefits which help to accelerate the development of the drug, including financial incentives, assistance in clinical research study design and a period of marketing exclusivity if regulatory approval is ultimately received. Hemogenyx applied for ODD in this regard as the results should support its use in expanding the application of Hu-PHEC treatment for more complex and frequently diagnosed blood diseases, such as lymphomas and leukemia.

Hu-PHEC Liver - derived from the adult livers of those patients who are considered candidates for BM/HSC transplantation. These cells have the advantage that, unlike regular BM/HSC cells, they are significantly less affected by the mutations or chromosome rearrangements often causing blood malignancies. Hu-PHEC Liver will be targeted to replace virtually all traditional autologous BMT/HSC transplantations and to a large degree eliminate allogeneic transplantations. **The Directors believe that Hu-PHEC Liver and Hu-PHEC Liver Expanded (see below) will greatly increase the ability to obtain "healthy" HSC from a patient's own body and therefore will largely eliminate the need to seek cells from a donor**.

Developments to date include Hu-PHEC being successfully isolated and transplanted from mouse livers and functional engraftment of Mouse-PHEC (M-PHEC) demonstrated in mouse models. While yet to achieve proof-of-principle, autologous liver Hu-PHECs also have the potential to be used as vehicles for gene therapy for the treatment of a large range of inherited, metabolic, immune and infectious diseases, thus opening up further significant potential clinical and commercial markets.

Hu-PHEC Expanded - is intended for use in any BM/HSC transplantation where the number of transplantable cells is insufficient for a successful procedure and where genetic correction of disease causing mutations or chromosome rearrangements is necessary prior to transplantation. To date, initial data has been obtained and collated on the method of expansion of Hu-PHEC cells to allow a larger quantity of cells to be created for transplantation.

Hemogenyx believes that expanded Hu-PHEC should provide an unlimited source of "healthy" HSC for both autologous and allogeneic BM/HSC transplantations. **The product candidate is therefore potentially capable of bringing about a revolution in the treatment of blood diseases, greatly increasing the chances of successful and long-lasting treatment and substantially increasing the number of patients affected by blood diseases to whom BM/HSC transplantation can offer a clinical cure.**

Potential benefits

Overall, the directors believe that the Hu-PHEC cell therapy products have two main benefits. Firstly, the potential to improve the efficacy of autologous BM/HSC transplants since Hu-PHEC do not have accumulated mutations or chromosome rearrangements, so that the success rate for patients receiving autologous transplants will significantly increase due to a lower rate of relapse. Secondly, they could largely eliminate the need for allogeneic transplants and BM/HSC donors because these cells are a 100% match to the patient and thus result in significantly better outcomes than an allogeneic transplant.

Development Plans

The current plans for Hu-PHEC are based on the Hu-PHEC Umbilical product candidate, with Hemogenyx focusing on preparation for a Pre-IND Consultation Program with the FDA. The company aims to concentrate on pre-clinical toxicology studies, probably the most important work needed prior to opening an IND application for clinical trials. It will also continue development of the other Hu-PHEC cell preparations, applying for ODD status for use of Hu-PHEC in a number of other blood diseases (in addition to the one already achieved for aplastic anemia).

Around 18 months from the admission date the company expects that, for certain Hu-PHEC products, key preclinical milestones should have been completed and that subsequent activities preparatory to clinical trials should be able to commence.

Cell Therapy Product development plans
Preclinical toxicological studies for Hu-PHEC Umbilical
Pre-IND consultation with FDA in relation to Hu-PHEC Umbilical
Continuing research and development for methods of expansion of Hu-PHEC

Table: Cell Therapy Product targeted development milestones. Source: Company admission document.

Partnerships

In October 2017, as part of its preclinical development program, Hemogenyx appointed LakePharma, Inc., the largest US-based biologics contract research organization, as its service provider for the development and manufacturing of its CDX bi-specific antibodies. LakePharma was chosen after a thorough evaluation process, with Hemogenyx attracted to the speed, quality and sophistication of LakePharma's services. LakePharma has already been providing antibody engineering and bioproduction services to Hemogenyx for several years and helped the company to create the underlying IP for its CDX technology.

Further, on 20th November 2017 the company announced it has entered into a collaboration with the University of Oxford to test new means of accelerating and improving the process by which transplanted blood stem cells grow and make healthy blood cells. Under the agreement Hemogenyx will use the experience of University of Oxford researchers in administering certain biologics to stem cells to attempt to accelerate and improve the engraftment (the process by which blood stem cells integrate into the bone marrow and make healthy blood) of hematopoietic stem and progenitor cells in animal models. **If successful, this approach has the potential to dramatically improve the efficiency and safety of bone marrow transplants.**

At Oxford, Hemogenyx also will test whether this approach facilitates the conversion of Hu-PHEC into fully functional, transplantable blood stem cells. Leading the Oxford team is Professor Jagdeep Nanchahal, a surgeon scientist focussing on defining the molecular mechanisms of common diseases and translating his findings through to early phase clinical trials. After completing fellowships in microsurgery and hand surgery in the USA and Australia he was appointed as a senior lecturer at Imperial College. His research is now focussed on promoting tissue regeneration by targeting endogenous stem cells and reducing fibrosis.

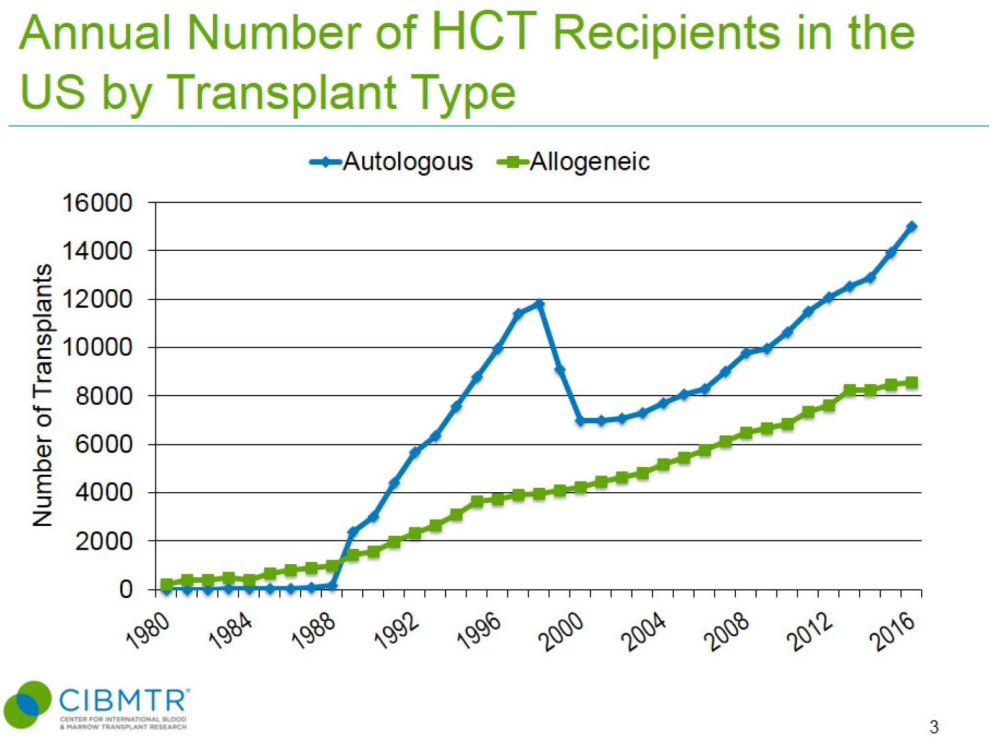
Market Opportunity

The number of BM/HSC transplantations for the treatment of blood cancers has grown significantly in recent years. According to a report from Future Market Insights entitled *Bone Marrow Transplant Market: Global Industry Analysis and Opportunity Assessment 2016-2026*, more than 75,000 bone marrow transplants were performed globally in 2015 and the count is expected to increase by approximately 25% by the end of 2020.

A 2014 report from Milliman Inc. (*U.S. organ and tissue transplant cost estimates and discussion*) suggested there were 21,169 transplants performed in the US in 2014, with 8,709 allogeneic transplants and 12,460 autologous transplants.

More recent data from the Centre for International Blood and Marrow Transplant Research (CIBMTR) states there were over 23,000 transplants performed in the US in 2016. As the table below from CIBMTR shows, the estimated annual number of allogeneic transplants recipients surpassed 8,000 a year in 2013, rising to 8,539 in 2016. The number of autologous transplants is growing at a faster rate mainly from transplants performed for plasma cell and lymphoproliferative disorders extending to older patients.

The market is currently larger in Europe where in 2014 an estimated 40,829 BM/HSC transplantations were performed, 57% being autologous and 43% allogeneic.



Source: D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2017. Available at: http://www.cibmtr.org

Addressable market value

Hemogenyx's initial focus will be on the US market, although Europe and other large markets represent a significant opportunity in the longer term. **A recent report from Transparency Market Research estimates the global market for hematopoietic stem cell transplantation to increase at a CAGR of 12.8% from 2017 to 2025, rising from a value of $13.06 billion in 2016 to $37.61 billion by the end of 2025.**

To give an idea of the total market size in the US, using the 2014 figures from Milliman, the average full cost (from start to finish, including pre/post-transplant care and drug therapy costs) of an allogeneic HSC transplant was $930,600, with autologous transplants costing $378,000. **Multiplied by the estimated transplant numbers, this gives a total estimated market size for the year of c.$12.8 billion.** Further, based on pricing information from the CIBMTR and other sources, the average cost of allogeneic BM/HSC transplants in the US was shown to have been $200,000 per patient in 2014.

More relevant for Hemogenyx, with Milliman estimating average prices for CDX conditioning of $50,000 for Europe and $80,000 for the US, the implied markets in these two geographies using the 2014 patient numbers is **c.$1.7 billion in the US and c.$2 billion in Europe.**

Relevant for Hu-PHEC Umbilical, Milliman estimates the average cost of transplant procurement for allogeneic HSC transplants in the US is $55,700, for a total market size of **c.$485 million.** With around 20,0000 patients seeking transplants annually, according to the Health Resources Services Administration (HRSA), there are currently c.11,000 patients unserved, bringing the potential addressable market to approximately **$1.1 billion** in the US alone.

In the case of Hu-PHEC Liver, Milliman estimates the cost of autologous transplant procurement to be $10,700. However, as suggested in an Expert's Report (by Aruwon consultancy and included in the Admission document), if clinical studies with Hu-PHECs indicate a significantly reduced risk of relapse this would justify a pricing premium. Assuming the procurement price rises to the same level as allogeneic this would imply a total market in the US of at least **$694 million.**

While the current addressable markets are large, a major attraction of the Hemogenyx investment case is that the company believes its products, as they become available, could dramatically increase the overall market size. This is due to them being designed to enable blood disease sufferers who are currently considered unsuitable for BM/HSC transplants to receive them. For example, patients considered unable to receive or survive the severe chemotherapy and radiotherapy currently required in patient conditioning would add to the market size due to being able to receive Hemogenyx's safer CDX conditioning product.

The cell therapy product candidates are also expected to expand the market size as they will reduce the number of patients unable to receive a transplant due to the difficulties in finding an appropriate donor. In the US alone, it is estimated that in 2012 some 10,000 patients failed to receive treatment for that reason. **Using the estimated average cost of $200,000 per transplant, this represents an expansion opportunity of $2 billion in the US alone.**

Financials

The accounts of operating subsidiary Hemogenyx LLC to date reflect costs associated with setting up the company and the preclinical development work completed. For the year to 31st December 2016 no revenues were made with a net loss of $635,757 being posted. Major expenses for the period included $216,525 on staff costs, $129,852 on contractors and $112,281 on consumable supplies and equipment. The balance sheet showed net assets of $479,004 at the period end, with cash standing at $113,905. Total borrowings stood at $372,500, mainly reflecting the Cornell University loan, with the cashflow statement showing the receipt of the $1 million equity investment from Bonsai Capital during the year.

Under the terms of the licence agreement with Cornell University the loan provided to fund the initial licence fee was repayable upon a change of control of Hemogenyx LLC, an event which happened upon the October listing in London. On the day of listing it was announced that Cornell had elected to receive payment of the $372,350 owed half in new shares (which were issued at 3.5p each) and half in cash which was payable within 30 days.

Cash position sufficient to meet key milestones

Following the £2 million placing on admission to the Main Market Hemogenyx received net proceeds of c.£1.685 million after associated costs of c.£315,000. **Added to cash within Silver Falcon and to Hemogenyx LLC's existing funds gave total net cash resources of c.£3.1 million**. Hemogenyx also makes modest amounts of income via collaborating with third-parties and allowing them to use its proprietary animal models for the evaluation of the immunogenicity of biologics (products made from living organisms or which contain components of living organisms) being developed for clinical use. As a by-product, Hemogenyx will also be able to utilise the results of such research in respect of its own product candidates.

Fortuitously for investors, the company believes that its current cash resources should be sufficient to enable it to undertake all work preparatory to human trials in relation to the CDX conditioning product candidate and to have met a number of key milestones on the way to clinical trials in relation to the cell therapy product candidate.

At admission, the majority of the funds - £1.89 million - were allocated for completion of preclinical studies for the CDX bi-specific antibody product candidate and further preclinical development of its Hu-PHEC cell therapy product candidates. Additional working capital amounts to £743,000 and £117,000 for contingency. Another £350,000 was earmarked for expansion and maintenance of the intellectual property suite, including additional patent applications and repayment of the Cornell loan. While the company originally expected that Cornell would elect to have the entire sum paid to it in cash following admission, as discussed above, half was paid in shares, thus reducing expected cash outflow.

Prior to admission the company also entered into a Lock-in Warrant Instrument with certain qualifying shareholders. This entitles them to one Lock-in Warrant for every two ordinary shares held, with each warrant entitling the holder to buy one ordinary share at an exercise price of 4p. This is subject to the condition of not having dealt in the shares they held as at the admission date up until the 60th day following admission. **A maximum 62,021,429 Lock-in Warrants can be issued, which, if fully exercised (within two years of the admission date), could bring in an additional £2.48 million for the company.**

Recent Trading

At its AGM in December 2017 Hemogenyx provided a strategic update on its developments, stating that laboratory activities are progressing well and to plan, with capacity expanded and a modest scientific recruitment program complete. The company believes it is well-advanced on the planned development steps announced on admission and is looking forward to the next 12 months, *"with great confidence and high expectations."*

Activities continue to focus on working with LakePharma and Oxford University to progress CDX and Hu-PHEC. To date, work with LakePharma is said to be progressing successfully toward the immediate goal of a pre-IND meeting with the FDA and subsequent submission of an IND application to the FDA.

At the University of Oxford, work is ongoing to examine the action of certain biological molecules on stimulating transplanted blood stem cells to transition - faster and more effectively - from a dormant to activated state to produce healthy blood cells. Hemogenyx anticipates that the resulting increase in the number of activated blood stem cells will result in the accelerated engraftment of hematopoietic stem cells when transplanted in a BMT and could lead to additional uses of Hu-PHEC.

Hemogenyx also announced that it has expanded its material transfer agreement with a major US research university, under which it has secured a reliable high-quality supply of human tissues for the development of both CDX and Hu-PHEC. **The company is evaluating additional collaborations with a range of potential academic and corporate partners and will provide updates in due course.**

Director share purchases

On 5th February 2018 Dr. Vladislav Sandler purchased 26,800 ordinary shares in the company at a price of 2.37p each to take his holding to 40,478,010 shares, or 11.37% ownership of the company. Additionally, Non-Executive Adrian Beeston purchased 200,000 shares on 9th February 2018, taking his holding to 6,331,969.

Management

Chief Executive Officer – Dr. Vladislav Sandler

Dr. Vladislav Sandler is the Co-Founder and CEO of Hemogenyx and a research Assistant Professor at the State University of New York (SUNY) Downstate. Dr. Sandler is a widely-published stem cell scientist with decades of experience in scientific research. In particular, Dr. Sandler has extensive experience developing novel methods of direct reprogramming of somatic cells into functional and engraftable hematopoietic stem cells, as well as developing novel sources of pluri- and multi-potent cells.

Dr. Sandler has conducted his research in Israel, Canada and the United States, including at the Children's Hospital at Harvard Medical School, the Salk Institute for Biological Sciences, Harvard University and Albert Einstein College of Medicine. He also led a team of scientists at Advanced Cell Technologies, Inc. and was most recently on the faculty of Weill Cornell Medical College. While at Cornell, Dr. Sandler made the significant discovery that the cells that give rise to blood stem cells during mammalian development continue to exist after birth, and he developed the method of isolation of these cells from humans. As a result of this important work, Dr. Sandler was awarded the inaugural Daedalus Fund Award for Innovation at Cornell. He went on to found Hemogenyx in order to further pursue this significant scientific discovery and his dedication to the translation of science into clinical practice.

Dr. Sandler has published numerous peer-reviewed papers, and has received a number of awards and fellowships for his scientific research. Dr. Sandler received his PhD from the University of British Columbia. He is a member of the International Society for Stem Cell Research.

Chairman – Dr. Robin Campbell

Robin Campbell, PhD has more than 30 years' experience working in the pharmaceutical industry with large companies (Shell Research, Beecham International (now GSK)), start-ups (Porton International, PafraBio) and in investment banking primarily in life sciences investment research (including Credit Suisse, Jefferies).

Currently his specialty is searching out investable opportunities in the broader life sciences sector, and helping smaller companies raise growth capital. Robin has helped list a number of companies onto AIM and other international exchanges, advised companies on secondary fundraisings, private equity raises, M&A and has a broad reach into institutional and retail investor networks.

As a pharmaceutical and biotech analyst, his experience extends back more than twenty years with a range of firms including Credit Suisse First Boston, Hoare Govett and Jefferies International and more recently he has acted in a consultancy role in relation to a range of life sciences IPOs, AIM introductions and M&A activity.

He has a degree in Microbiology from King's College London and a Ph.D. in Immunobiology from Liverpool University. Dr. Campbell currently advises a number of private and listed businesses in respect to strategic and financial market opportunities.

Chief Operating Officer- Lawrence Pemble

Lawrence Pemble has over the past six years developed experience in establishing, financing and developing new businesses. He has led financing rounds, M&A activities, worked for public companies and has held executive roles, up to and including CEO, for start-up and private equity backed ventures, both in private and public capacities.

He has worked extensively in the Private Equity industry, where he has held executive positions in life science and technology focused companies, most recently a Director of Blackcomb Technologies Limited, a Canadian private equity firm focused on military electronics and in Bonsai Capital Limited, a life sciences focused Private Equity company where he is currently a Director. Prior to this, he held a number of managerial and development positions in resources companies, in the gold and oil and gas sectors.

Finance Director – the Finance Director position is currently vacant following the resignation of former Silver Falcon CFO Timothy Le Druillenec in November. Hemogenyx is currently in process of putting in place appropriate arrangements for the future financial management of the company.

Non-Executive Director - Alexis M. Sandler

Alexis M. Sandler is the co-founder of Hemogenyx, for which she has served as the Chief Operating Officer. An attorney with fifteen years of experience in intellectual property and copyright, Ms. Sandler handles day-to-day legal and operational matters for the company.

Ms. Sandler began her legal practice in Los Angeles at Hogan & Hartson LLP (now Hogan Lovells), specializing in media and intellectual property law. She then worked for several years at Katten Muchin Rosenman LLP representing studios, production companies, television networks, technology companies and other major media companies in all aspects of entertainment, media and intellectual property law. For three years, Ms. Sandler worked as the Director of Business and Legal Affairs for a division of the Fox Entertainment Group, where she advised the company on important intellectual property, corporate and other legal and business matters. Ms. Sandler went on to become the General Counsel at a Smithsonian affiliate museum in New York City, and is currently the Associate General Counsel at The Museum of Modern Art and the Secretary of the Board of Directors of its affiliate institution, MoMA PS1. Ms. Sandler received her AB from Harvard University, her JD from the UCLA School of Law and her MA from New York University. She is a member of the State Bar of New York and the State Bar of California.

Non-Executive Director - Peter Redmond

Peter Redmond is a corporate financier with some 30 years' experience in corporate finance and venture capital. He has acted on and assisted a wide range of companies to attain a listing over many years, on the Unlisted Securities Market, the Full List and AIM, whether by IPO or in many cases via reversals, across a wide range of sectors, ranging from technology through financial services to natural resources and biotech, in recent years often as a director and shareholder of the companies concerned. He has been active over many years in corporate rescues and reconstructions on AIM and in reverse transactions into a range of investing companies. He was a founder director of Cleeve Capital plc (now Satellite Solutions plc) and Mithril Capital plc (now BeHeard plc), both of which were admitted to the Standard List of the London Stock Exchange, and took a leading role in the reconstruction and refinancing of AIM-quoted Kennedy Investments and 3Legs Resources plc. He is a director of AIM-quoted Pires Investments plc.

Non-Executive Director - Adrian Beeston

Adrian Beeston specializes in the financing and structuring of small to medium size businesses, and the flotation of these companies on the American Stock Exchange, AIM Exchange and TSX Venture Exchange. Prior to this, Adrian was at Altium Capital, a major pan-European corporate finance house, where he focused primarily on the raising of private equity.

Major and Director Shareholdings

Shareholder	Number	%
Alexis Sandler*	75,090,685	21.09
Dr. Vladislav Sandler*	40,478,010	11.37
Craig Auringer	31,407,913	8.82
Flascherberg Capital Anstalt	27,996,487	7.86
Ron Valk	17,131,193	4.81
Plum Capital	11,692,863	3.28
43 North LLC	11,371,429	3.19
Adrian Beeston*	6,331,969	1.78
Peter Redmond*	5,040,714	1.41
Robin Campbell*	1,142,857	0.32

*Source: Company. * = Director*

Key Risks

General biotechnology industry risks

Hemogenyx faces all of the typical risks involved in the research and development of new drugs, including high costs of product development, long lead times to market, potentially unsuccessful results from clinical trials, a strict regulatory environment and a reliance on third parties.

Preclinical stage of development

While Hemogenyx's two product candidates have delivered encouraging results so far, being at a preclinical stage there is no guarantee that positive results can be repeated in clinical trials and that expected timeframes can be met. The development of clinical products for new medical treatments is inherently uncertain, with high failure rates in clinical studies for both early and late-stage development products. Products can frequently run into unforeseen issues of safety and efficacy upon entering clinical trials in human subjects.

Funding risk

Hemogenyx has funded its operations via a series of equity fundraisings and the Cornell loan discussed above. Minimal revenues have been earned to date and it will be at least several years before revenues are earned from its product candidates, if at all. While the company has raised capital to support its preclinical development activities, assuming that the candidates advance beyond the pre-clinical stage, further capital will need to be raised to fund clinical trial activities from Phase 1 and beyond.

Competition risk

Human immunotherapy is a rapidly evolving area so it is possible that developments by competitors will make Hemogenyx's technologies obsolete. While there are a number of prospective developments at various stages in respect of both products none of those known by the Directors attempt to fully deal with the major problems encountered in BM/HSC conditioning and transplantations. While both Hemogenyx's product candidates will compete with existing forms of treatment they are being developed in order to have improved efficacy and safety.

Reliance on key individuals

Hemogenyx is reliant upon a number of key individuals to progress its development plans, in particular founder Dr. Vladislav Sandler. To mitigate the risk the company has contractual arrangements which include non-compete restrictions in place with such persons to lessen the risk of them ceasing to be involved with the company. The board are also supported by an experienced scientific advisory team.

Valuation & Assessment

To highlight the broad potential value contained within Hemogenyx we have carried out a discount cash flow (DCF) analysis based on a number of conservative assumptions as follows:

- Revenues are earned from the Conditioning Product only, in the US and European markets.

- The number of transplants in both markets (using the 2014 Milliman report figures as a base) are assumed to grow by 3% annually.

- The estimated cost of conditioning in the US and Europe ($80,000 and $50,000 respectively) rises by 2% per annum.

- Market value equals number of transplants multiplied by cost per treatment.

- Orphan Drug Designation is received in the US in 2019. In both markets, first revenues are earned in 2025, with sales peaking with a 10% market share in 2029.

- Net cash position of zero as at Q2 2019 as all current cash is spent on meeting the expected development milestones as per the admission document.

Method

To derive our valuation we calculate forecast peak revenues for the Conditioning Product of $783.2 million in 2029 in the US and Europe combined. We then discount them back at a rate of 12% per annum to the start of Q2 2019 – the period when all work preparatory for human trials is expected to be completed in relation to the Conditioning Product candidate in readiness for Phase I trials.

The discounted figure of $231.3 million is then adjusted for the industry accepted probability of success. We thus use a figure of 5.1%, as per the estimated overall likelihood of approval (LOA) from Phase I to approval for oncology candidates calculated in the 2016 report *Clinical Development Success Rates 2006-2015* from bio.org. This adjusted discounted revenue figure of $11.8 million is then multiplied by the Enterprise Value/Revenue multiple of the US listed Biotechnology Industry, which is currently 7.619 (*Source: https://ycharts.com/*). **This equates to a value of $89.9 million, or £64.62 million at the current £/$ exchange rate of 1.39107, equivalent to 18.15p per share.**

We consider this approach to be extremely conservative for a number of reasons. Firstly, we note that **this valuation only considers revenues earned from the Conditioning Product in the US and Europe**, so does not consider other markets. Furthermore, we do not account for a potential increase in the market size coming from patients who were previously unable to receive the chemotherapy and radiotherapy currently required in patient conditioning but who could use the Conditioning Product due to its higher safety. **Our valuation, at this stage, ascribes no value to the Hu-PHEC product candidates.**

Factor	Value
Peak Annual Revenues ($)	783,155,613
Revenues Discounted to Q2 2019 at 12% ($)	231,334,998
Multiplied by probability of success ($)	11,798,085
Multiplied by industry EV/Sales ratio ($)	89,889,609
Divided by £/$ (£)	64,619,041
Price per share (p)	**18.15**

Key model outputs. Source: Align Research

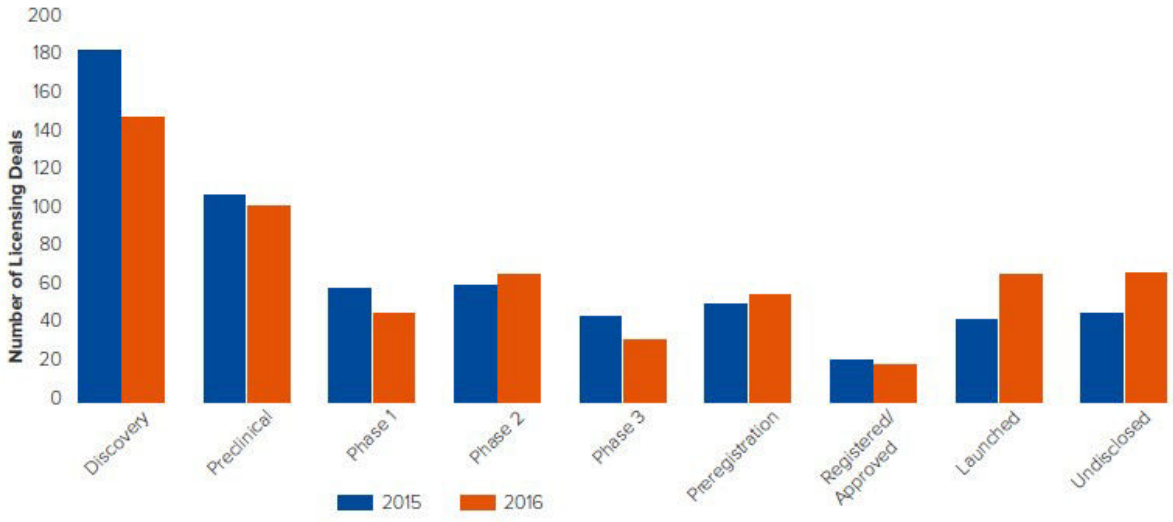
Recent deals

Another meaningful way of reflecting the potential near-term value is by looking at recent corporate transactions within the preclinical immuno-oncology sector, particularly in-licensing deals and acquisitions.

In company presentations management have commented that they are talking to potential industry collaborators and that they expect to announce agreements before entering into the planned Phase 1 clinical trials. **We believe that Hemogenyx is well positioned to attract attention from larger industry players given the promising nature of its candidates, along with the company being in the industry "sweet spots" of both preclinical development and oncology.**

While preclinical candidates present higher risk, recent industry trends have seen big pharma increasingly agree in-licensing deals at early development stages as they look to fill their pipelines with promising long-term assets and have more influence over their development. The most recent annual report from QuintilesIMS, the *IMS Pharma Deals: Review of 2016*, highlights that the majority of therapeutic licensing deals in 2016 were signed in the discovery and preclinical stages of development (see table below). More recent data from Life Science Nation's Licensing Deals platform finds that in 2017 41.1% of in-licensing deals were done at the preclinical stage.

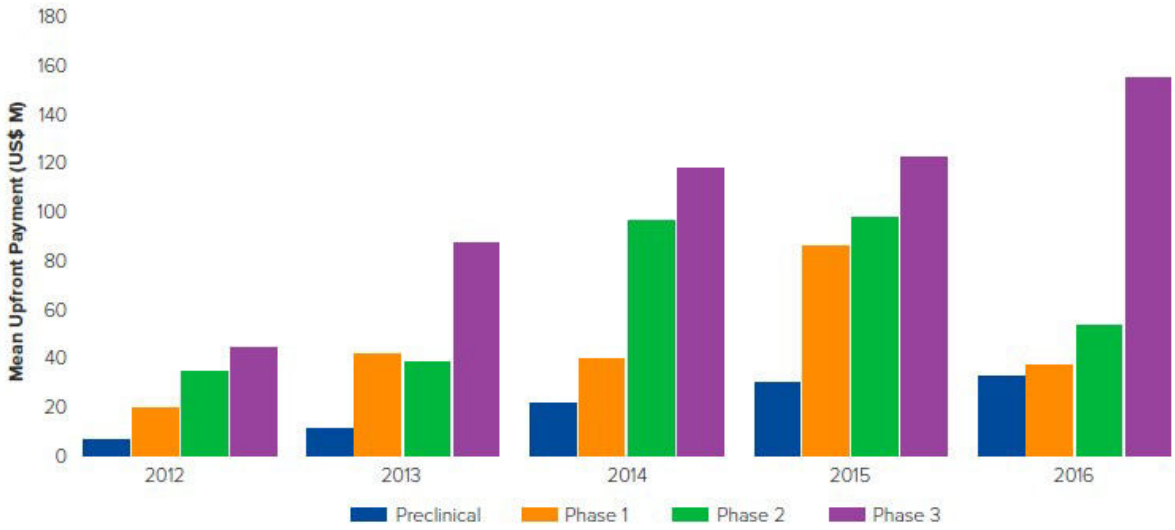
Figure 9: Therapeutic licensing deals by development stage, 2015 vs. 2016



Source: IMS PharmaDeals

Also encouraging for Hemogenyx, given the increased interest in preclinical assets QuintilesIMS finds that mean upfront payments for preclinical licensing deals have grown rapidly from 2012 to 2016.

Figure 10: Mean upfront payment for licensing deals by development stage, 2012-2016



Source: IMS PharmaDeals

By sector, QuitilesIMS finds that oncology remained the leading therapeutic area for partnering deals in 2016 and the immuno-oncology field in particular saw significant investment in R&D alliances, with there being a, *"land grab for next-generation assets"* in the field. Highlighting the potential near-term value that could be realised by Hemogenyx, some recent preclinical stage deals in the immuno-oncology sector have run into the many hundreds of millions, several of which we discuss below.

AbbVie/argenx

In April 2016, global biopharmaceutical company **AbbVie (NYSE: ABBV)** and Euronext & Nasdaq listed **argenx (ARGX)** agreed a collaboration to develop and commercialise ARGX-115, argenx's preclinical-stage human antibody program targeting the novel immuno-oncology target GARP, a protein believed to contribute to immuno-suppressive effects of T-cells.

Under the deal argenx received an upfront payment of **$40 million** from AbbVie for the exclusive option to license ARGX-115, with the company eligible to receive two near-term preclinical milestones of $10 million each. The first of these was triggered in April 2017. In addition, argenx is also eligible to receive additional development, regulatory and commercial payments up to **$625 million** upon achievement of pre-determined milestones as well as tiered, up to double-digit royalties on net sales upon commercialisation.

Merck/IOmet Pharma

In January 2016, NYSE listed **Merck (MRK)** acquired IOmet Pharma Ltd, a privately held UK-based drug discovery company focused on the development of innovative medicines for the treatment of cancer, with a particular emphasis on the fields of cancer immunotherapy and cancer metabolism. The acquisition provided Merck with IOmet's preclinical pipeline of IDO (indoleamine-2,3-dioxygenase 1), TDO (tryptophan-2,3-dioxygenase), and dual-acting IDO/TDO inhibitors. The upfront purchase price was **$150 million**, with future additional milestone payments of up to **$250 million** contingent upon certain clinical and regulatory milestones being achieved.

Celgene/EngMab

In September 2016, Nasdaq listed **Celgene (CELG)** acquired Switzerland-based, privately-held biotechnology company **EngMab AG** for **$625.3 million** plus contingent development, regulatory and commercial milestones. EngMab's lead molecule is EM901, a T-cell bi-specific antibody targeting B-cell maturation antigen (BCMA) in patients with multiple myeloma. The acquisition also included an additional undisclosed program. The company plans to file an Investigational New Drug (IND) application for EM901 in late 2017.

Celgene/Jounce Therapeutics

In one more notable deal, in July 2016 Celgene agreed a global strategic collaboration with **Jounce Therapeutics (JNCE)** to obtain options on Jounce's lead product JTX-2011, which at the time was preclinical but has since entered clinical development, and up to four undisclosed early-stage immuno-oncology programmes. JTX-2011 is a monoclonal antibody that binds to and activates ICOS, the Inducible T cell CO-Stimulator, a protein on the surface of certain T cells that is believed to stimulate an immune response against a patient's cancer.

Jounce received an upfront payment of **$225 million** and **a $36 million** equity investment from Celgene. In addition, aggregate payments for development, regulatory and commercial milestones could potentially be **$2.3 billion** in total across all programs reaching commercialisation. Jounce went on to list on the Nasdaq in January 2017 in an IPO valuing the company at just under **$500 million.**

Conclusion

Shares in Hemogenyx initially slipped from the admission fundraising price of 3.5p to a low of 2.125p but rose significantly at the end of February on the back of the news that its CDX bi-specific antibodies are capable of attacking and eliminating Acute Myelogenous Leukemia *in vitro*. At the current price of 4.2p the company is capitalised at £14.95 million, which, adjusting for our estimation of net cash, implies an enterprise value (EV) of around £13 million.

Whilst we accept that the company is arguably the earliest stage biopharma company listed in London it is also one of the lowest valued biopharma development plays on the whole of the market. Given the significant potential of its product candidates, and the possibility of a material licensing deal or acquisition, we see significant potential value here on a risk/reward basis.

Over the coming months we expect that news on the completion of the development milestones will act as a catalyst for the share price and trigger a meaningful re-rating. An announcement regarding completion of the pre-IND consultation programme for the conditioning product could be one of the more near-term drivers, as could further updates from Oxford University and additional preclinical development work.

Overall, while the stock does patently have a high risk profile and many uncertainties, we do however see the potential for Hemogenyx shares to deliver exponential upside in the medium to long-term pending successful development of its candidates and the announcement of any deals signed with industry partners.

We set our initial target price at 18.15p as per our valuation above, implying some 332% upside from the current 4.2p. The present low valuation, combined with the upside potential, provides investors with a healthy risk appetite with the opportunity to take a position at the nascent stage of the company's development curve and leads us to initiate coverage with a Conviction Buy stance.

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Hemogenyx is a research client of Align Research. Align Research owns shares in Hemogenyx. Full details of our Company & Personal Account Dealing Policy can be found on our website http://www.alignresearch.co.uk/legal/

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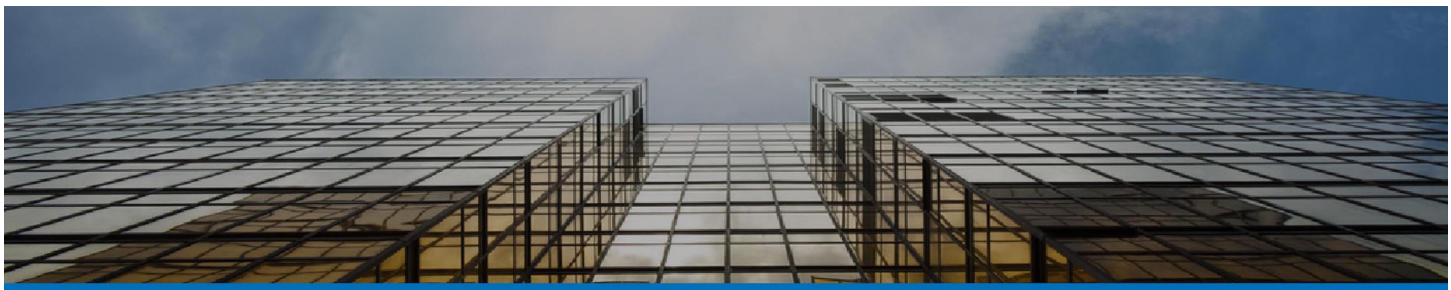

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