ARROWHEAD
BUSINESS AND INVESTMENT DECISIONS

Diligence and Valuation Report

Arrowhead Code:	69-02-04
Coverage initiated:	29 April 2012
This document:	23 June 2014
Fair share value bracket – DCF	€2.93– €3.90
Share price 20 June 2014:	€2.66[i]

Analyst Team

Snehal Mahajan
+1 (212) 619-6889
snehal.mahajan@arrowheadbid.com

NYSE Alternext

Company:	HYBRIGENICS SA
Ticker:	EPA: ALHYG
Headquarters:	Paris, France
CEO:	Dr. Rémi Delansorne, D.V.M, Ph.D.
CFO:	Mr. Guillaume Floch
Senior Director, Head of Clinical R&D	Dr. Jean-François Dufour-Lamartinie
Website:	www.hybrigenics.com www.hybrigenics-services.com

Market Data

52-Week Range:	€0.52– €3.98[ii]
Average Daily Volume (3M Avg):	521,103[iii]
Market Cap (20 June 2014) :	€68.9 MM

Financial Forecast (in EUR) (FY Ending – Dec.)

	'14E	'15E	'16E	'17E	'18E	'19E	'20E
High NI (MM)	(7.78)	11.74	12.63	4.14	2.13	12.09	8.30
High EPS	(0.30)	0.45	0.49	0.16	0.08	0.47	0.32
Low NI (MM)	(8.03)	9.68	7.68	2.82	0.66	7.71	5.17
Low EPS	(0.31)	0.37	0.30	0.11	0.03	0.30	0.20

Company Overview: Hybrigenics SA is a France-based biotechnology and pharmaceutical company that specializes in Research and Development (R&D) of new pharmaceutical drugs to cater to medical needs mainly in the field of oncology. Incorporated in 1997, Hybrigenics is a publicly held company listed on the Alternext (NYSE-Euronext) in Paris, and has been included in Euronext's composition of French "CAC® PME" index on April 1, 2014.

The Company's main research and development program is based on Inecalcitol, a synthetic chemical derivative of Calcitriol, which is a naturally active form of vitamin D. The Company's R&D pipeline includes the development of oral Inecalcitol for Prostate Cancer - Phase II, Chronic Lymphocytic Leukemia (CLL) - Phase II, and Chronic Myeloid Leukemia (CML) in combination with Imatinib. In addition, Hybrigenics' research program also investigates the action of enzymes called Deubiquitinating Enzymes (DUBs) in the recycling of oncoproteins and the utility of proprietary patented DUB inhibitors against various cancer indications. Through its subsidiary, Hybrigenics Services, the Company markets specialized scientific services in all areas of life sciences to researchers involved in identifying, validating and inhibiting protein interactions in animal, plant or microbiological cells. In 2011, Hybrigenics collaborated with Servier Laboratories to explore the role of Ubiquitin-Specific Proteases (USPs) in the degradation of oncoproteins and the use of proprietary USP inhibitors against various cancer types.

Arrowhead is updating coverage on Hybrigenics SA with a fair value bracket of €2.93 in the low bracket and €3.90 in the high bracket scenario using the Discounted Cash Flow (DCF) Valuation Method.

Key Highlights: (1) Hybrigenics' clinical programs are based on 'Inecalcitol', for which the Company has received world exclusivity with respect to all therapeutic indications. The Company has recently acquired patents in the U.S. and Europe for the use of high doses of Inecalcitol; **(2)** Inecalcitol is recognized as a key ingredient in developing drugs for treating diseases such as Prostate Cancer and CLL; **(3)** Inecalcitol for CLL has been designated with Orphan drug status in Europe and the U.S.; **(4)** In Phase II of CLL, positive results were observed; among the 17 patients being treated with a 2 mg daily oral dose of Inecalcitol for over 6 months, the Total Lymph Count (TLC) stabilized for at least 6 months in 10 patients and decreased by -90% in one of them after 10 months of treatment; **(5)** Hybrigenics has been awarded world exclusivity of 'Yeast Two-hybrid (Y2H) Screening' technology valid up to 2022, a specialized scientific service to identify and validate protein interactions in animal, plant or microbiological cells; **(6)** In addition to CLL, Acute and Chronic Myeloid Leukemias were identified as additional orphan therapeutic indications for Inecalcitol; **(7)** With the acquisition of Dualsystems Biotech's Y2H activities and Imaxio's genomic activities, Hybrigenics Services has demonstrated the steps initiated towards inorganic business expansion; **(8)** Hybrigenics tied up with Servier Laboratories to explore the role of Ubiquitin-Specific Proteases (USPs) in the degradation of oncoproteins and received its first milestone validating the Company's R&D expertise.

Key Risks: Key risks include cash flow uncertainty; risk of loss on invested capital; risk associated with the success of pipeline, drug approval and commercialization of drugs; and inadequate experience in global development.

Valuation and Assumptions[iv]: Given the due diligence and valuation estimates, Arrowhead believes that Hybrigenics' fair share value lies in the €2.93 to €3.90 bracket calculated using the DCF method. Based on the Risk Adjusted Net Present Value (rNPV) 'Peak Sales' method, the fair value lies in the €3.16 to €4.67 bracket. The rNPV for the drug R&D programs for oral Inecalcitol for Prostate Cancer and CLL is €45MM and €88MM respectively.

Table of Contents

1. Summary and Outlook

We are updating coverage on Hybrigenics SA, headquartered in Paris, France, involved in research and development of innovative drugs to cater to unmet medical needs in areas such as oncology and dermatology. The Company's fair value is €2.93 in the low bracket scenario and €3.90 in the high bracket scenario (DCF Valuation Method). Based on the NPV 'Peak Sales' method, the fair value lies in the €3.16 to €4.67 bracket. The rNPV for the drug R&D programs for oral Inecalcitol for Prostate Cancer and CLL is €45MM and €88MM, respectively.

Key Highlights:

(1) Hybrigenics' clinical programs are based on 'Inecalcitol', for which the Company has received world exclusivity with respect to all therapeutic indications. The Company has recently acquired patents in the U.S. and Europe for the use of high doses of Inecalcitol.

(2) Inecalcitol is recognized as a key ingredient in developing drugs for treating diseases such as Prostate Cancer and CLL.

(3) Hybrigenics key drug, Inecalcitol for CLL, has been designated with Orphan drug status in Europe and the U.S., providing the Company with several benefits such as 10 years of marketing exclusivity, protocol assistance at discounted rates, and faster registration process in the country.

(4) In Phase II of CLL, positive results were observed; among the 17 patients being treated with a 2 mg daily oral dose of Inecalcitol for over 6 months, the TLC stabilized for at least 6 months in 10 patients and decreased by -90% in one of them after 10 months of treatment.

(5) Hybrigenics was awarded world exclusivity of 'Yeast Two-Hybrid Screening' technology valid up to 2022, which is a very specialized scientific service to identify and validate protein interactions in animal, plant or microbiological cells.

(6) In addition to CLL, Acute and Chronic Myeloid Leukemias were also identified as additional orphan therapeutic indications for Inecalcitol.

(7) With the acquisition of Dualsystems Biotech's Y2H activities and Inaxio's genomic activities, Hybrigenics Services demonstrates the steps initiated towards inorganic business expansion.

(8) The Company tied up with Servier Laboratories to explore the role of Ubiquitin-Specific Proteases (USPs) in the degradation of oncoproteins and received its first milestone which validated its R&D expertise.

Key risks: Key risks include cash flow uncertainty; risk of loss on invested capital; risk associated with the success of pipeline, drug approval and commercialization of drugs; and inadequate experience in global development.

Industry Overview: R&D is one of the most important aspects of the pharmaceutical industry wherein the innovation and discovery of new targets and drug compounds defines the success of the industry. However, the global pharmaceutical industry decreased its R&D expenditure due to unsatisfactory R&D productivity and lower returns. Decline in rate of innovation (lower number of drugs submitted for regulatory approval), a low success rate for drugs in late-stage development and a decline in sales from new drugs launched resulted in a decline in the industry valuation. Further, difficulty in developing new drugs that are better than the existing drugs caused the termination of 55 projects in phase III during the period 2008-2010.[v] As per World Preview report 2013 from market intelligence firm Evaluate Ltd, the global pharmaceutical industry is expected to increase its R&D (Drug Discovery and Development) expenditure to $149B by 2018 at a compounded annual growth rate (CAGR) of 1.4% from 2012 despite the recent decline. According to the report, the pharmaceutical industry is also expected to gradually recover from the adverse effects of the patent cliff in the U.S., with sales forecasted to reach $895B by 2018. Primary drivers of recovery in the R&D expenditure would be led by improved investor confidence, as the adverse effects of the patent cliff in the U.S. subside and an expected surge in drug approvals would aid R&D productivity.[vi]

French Industry Overview: France has a very high per capita consumption of drugs. Patients have to pay relatively very little for their medicines because a large proportion of the medical costs are borne by statutory and supplementary health insurance, which is held by almost 90% of the population.[vii] Given the focus on fiscal consolidation, the French government had implemented many cost containment measures in 2010 and 2011. Savings through price cuts for generic medicines and reimbursement listing would mean lesser healthcare spending by the country. However, the French generics market is expected to grow rapidly due to government incentives and the loss of patent protection for several high-volume products. Although, several patents are expected to expire in the coming years, patented medicines would still represent about two-thirds of the market (€18.1B) by 2015.[viii]

France is one of Europe's largest producers of drugs with over 210 production sites. This has attracted a lot of investment in France. Some of the key drivers for the industry are the adoption of high-value innovative treatments driven by an aging population, physician preference for prescribing branded drugs and patient brand loyalty. Recently, the French Health Industries Strategic Advisory Board has proposed a change in the complex tax structure in the pharmaceutical industry to attract investments.

2. Business Overview [ix]

Incorporated in 1997, Hybrigenics SA is a French biotechnology and pharmaceutical company which discovers and develops novel drugs that are targeted to address the unmet medical needs in the areas of oncology, and dermatology. The Company's internal R&D segment 'Pharma' has developed an advanced program based on Inecalcitol, a vitamin D analogue active which can be orally administered. Inecalcitol is mainly administered as a first-line treatment for metastatic castrate-resistant/hormone-refractory Prostate cancer in combination with Sanofi-Aventis' Taxotere®, which is the current gold-standard chemotherapeutic treatment for this indication. The Company is also developing Inecalcitol for treating Chronic Lymphocytic Leukaemia (CLL) by oral administration.

In 2011, the Company collaborated with Necker Institute in Paris to conduct basic research and design a clinical trial on CLL using Inecalcitol. In 2012, this trial was accepted by the French National Agency for Drug Safety and subsequently, the enrolment process for phase II clinical trial of Inecalcitol in CLL was commenced. The trial was funded by a private placement of €3.3MM in two tranches of €1.45MM and €1.85MM at a price €1.01 per share. These funds were mainly used to scale up the chemical production of Inecalcitol and also for conducting CLL trials. In 2014, Inecalcitol was designated with Orphan drug status for the treatment of CLL in Europe and the U.S. In February 2014, the Company completed the enrolment process for the phase II clinical trial, and the final trial results are expected to be reported soon. In addition to Inecalcitiol for CLL, several researchers lately conducted a study on Inecalcitol's efficacy on the growth of human Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML) progenitors and stem cell. Their study indicated that the use of Inecalcitol in AML and CML may possibly be the new additional orphan therapeutic indications. In order to start clinical trial on these new diseases, the Company raised total funds of €6.1MM through private placement and Capital raise under "TEPA" (Capital raise under the French tax deduction mechanism) law.

Hybrigenics' research program also includes a tie-up with Servier Laboratories to explore the role of USPs in the degradation of oncoproteins and how proprietary USP inhibitors can be used against various cancer types. In January 2014, with respect to this ongoing research collaboration, the Company received its first milestone payment of €0.33MM demonstrating the Company's expertise in exploring the role of USPs during the drug discovery process.

The 'Services' division provides recurring revenue through fee-based services and has around 1,000 customers including Pfizer, L'Oréal, GSK, Harvard, John Hopkins, Vanderbilt, Columbia, etc. Hybrigenics has a fully owned subsidiary, Hybrigenics Services SAS (since 2010), which provides ISO 9001-certified 'Yeast Two-Hybrid' (Y2H) screening platform used for identification, validation and inhibition of protein interactions for researchers in all areas of life sciences. They also provide bioinformatics tools, an extensive database, a compound library and a small molecule screening platform. In September 2012, Hybrigenics Services renewed its 3-year research services agreement worth US$2.4MM with American Life Sciences. As per the agreement, the yearly commitment has been increased from US$0.70MM to US$0.79MM. In October 2013, the Company acquired the genomics division of Imaxico in order to tap the booming market of genomics services in Europe. Further, with respect to this acquisition, the Company received €1.3MM through private placement from Pradeyrol Development to finance the future growth of the genomics services.

Hybrigenics' R&D pipeline includes the development of oral Inecalcitol in the treatment of Prostate Cancer (Phase II) and CLL (Phase II). The Company independently performs discovery through early clinical development and proposes to enter into licensing agreements or collaborations with leading pharmaceutical companies for further development and commercialization of these drugs. Hybrigenics has acquired several patents related to Inecalcitol and USPs as summarized below:

Table 1: Patents Summary

Sr. No.	Patent	Date of patent receipt	Patent Expiry Year	Patent Granting Authority	Comments
1	Therapeutic uses of high doses of Inecalcitol (doses higher than one milligram per day)	Filing in 2009: already granted in Europe	2029	European Patent Office	According to Patent Cooperation Treaty (PCT), the same patent application is still under process in countries such as Australia, Brazil,

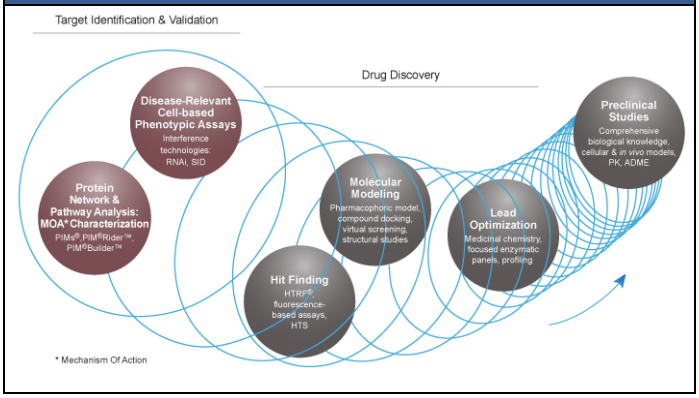
2	Therapeutic uses of high doses of Inecalcitol (doses higher than one milligram per day)	Filing in 2009: granted in the United States	2029 (Granted extra 308 days, indicating the patent to remain in force until March 22, 2031)	US Patent and Trademark Office	Canada, China, South Korea, India, Israel, Japan, Mexico, New-Zealand, Ukraine, Russia, and Singapore.
3	"14-epimerization" step in the synthesis of Inecalcitol	Filing in 2010: already granted in Europe	2030	European Patent Office	These patent applications are still under examination by the United States Patent and Trademark Office and by the World Intellectual Property Organization under the (PCT) procedure, to get worldwide protection in the following countries: Australia, Brazil, Canada, China, South Korea, United States, India, Israel, Japan, Mexico, New-Zealand, Ukraine, Russia, and Singapore.
4	Innovative formulations of Inecalcitol: tablets, new generation of soft gelatin capsules and drinking solutions	Filing in 2010: already granted in Europe for tablets and new generation of soft gelatine capsules	2031	European Patent Office	
5	Five patent families in total on USP inhibitors	Filed between 2005 and 2011	Depends on the family	European Patent Office	Some patents have already been granted in Europe and/or the U.S.; so far none have been rejected

2.1 Products/Services and Technology

2.1.1 Drug discovery

Hybrigenics runs drug discovery programs primarily in oncology, starting from target identification and validation to proof of principle in animal models of human diseases, including screening of small molecules, lead optimization and preclinical evaluation of drug candidates. These programs are or will be partnered with larger pharmaceutical or biotechnology companies at various stages of research or development. In addition to pursuing its own internal drug discovery programs, Hybrigenics collaborates with pharmaceutical and biotechnology companies for joint research and product development. The 'Pharma' division currently constitutes about 21.8% of the revenue of the group in 2013.

Chart 1: Drug Discovery and Development Process



Inecalcitol: Presently, Hybrigenics is undertaking development of Inecalcitol, a vitamin D analogue, against Prostate cancer and CLL. Inecalcitol is currently in Phase II development for the given diseases, after which, a Phase III registration trial to compare the efficacy of existing treatment of prostate cancer on overall survival with or without Inecalcitol will be completed.

Ubiquitin Specific Proteases (USP): Hybrigenics undertakes investigation of USPs for the discovery and development of new cancer therapeutics. The Company has discovered innovative small molecule inhibitors of USPs showing potent anti-tumour activity in vivo. The Company has built a platform in the molecular cell biology, enzymology and pharmacology of USPs, and a patent portfolio covering advanced screening assays and original small molecule inhibitors.

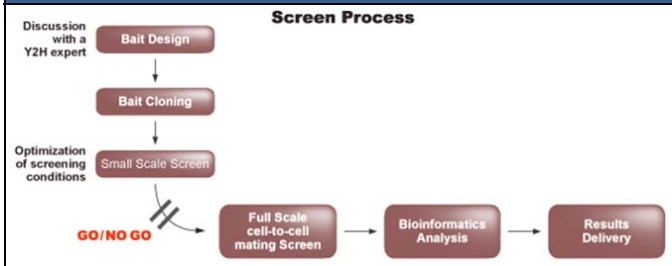
2.1.2 'Yeast Two-Hybrid' system (Protein Interaction Studies):

The 'Services' division is dedicated to the understanding of proteins' functions in cells through the elucidation and modulation of protein interaction networks in given cell types, tissues or organisms using a license from Pasteur Institute to run the "ULTImate Y2H" screens.
The 'Services' division currently constitutes about 78.2% of the revenue of the group in 2013.

The Company offers customized fee based service in all life sciences for:

- Discovering novel protein interactions in given cell types
- Validating existing interactions in cells
- Inhibiting protein interactions with small chemical or natural compounds

Chart 2: Y2H Screening Process



The services are provided to each customer by a team of a sales engineer, a protein interaction expert, a chemist and a bioinformaticist throughout the duration of the project and are facilitated by Y2H screening platform, bioinformatics tools, extensive database, and a compound library.

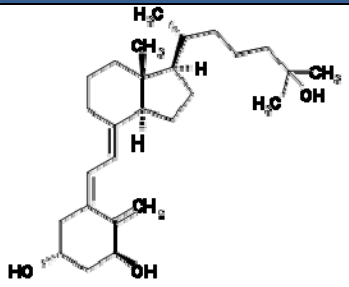
The Company has recently introduced new services to identify interactions between small molecules and protein targets. Using the Y2H model, small molecules can be used as "bait" against the cDNA or genomics libraries involving millions of "prey" protein fragments helping in identifying target proteins with which the tested molecule interacts.

2.2 Technology

2.2.1 Inecalcitol, a Vitamin D3 Analogue

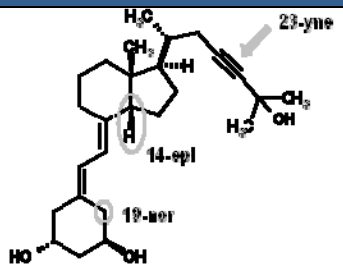
Inecalcitol is a synthetic chemical derivative of Calcitriol, the naturally active metabolite of vitamin D. Inecalcitol has been optimized to be more potent than Calcitriol and to play an active role in slowing down the growth of cancerous cells as well as hyper-proliferating normal cells, such as cells from skin affected by Psoriasis, or from benign (non-cancerous) hypertrophic prostate. Vitamin D is known to play a vital role in regulating calcium absorption from the gut, storage in mineral form in the bones, and excretion by the kidney making it highly effective to prevent Rickets in infants. Both vitamin D and Calcitriol can cause Hypercalcemia at high or frequently repeated doses. In addition, Hypercalcemia is known to cause kidney toxicity by accumulation of calcium-containing micro-crystals as well as heart and muscle dysfunction by impairing contractions. However, Inecalcitol has been optimized in such a way that it reduces the chances of Hypercalcemia as well as reduces toxicity as compared to Calcitriol thus making it a unique drug candidate for therapeutic use against cancer.

Chart 3: Calcitriol Chemical Structure



- Natural Vitamin D3 Metabolite
- Toxicity-limiting Hypercalcemia activity, even through the skin

Chart 4: Inecalcitol Chemical Structure



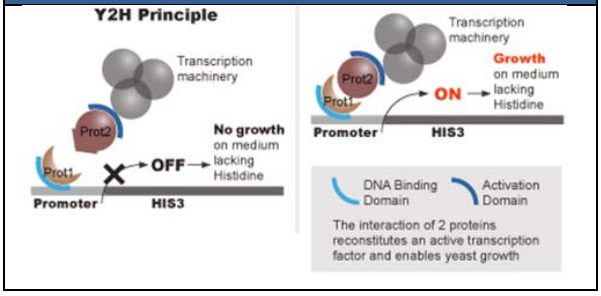
- Analogue of Calcitriol
- 10 times more potent on cell lines and 100 times less toxic than Calcitriol

2.2.2 Ubiquitin-Specific Protease (USP) Program

Proteases play a key role in a number of pathological processes and several protease inhibitors are already available as drugs (ACE, HIV-1 proteases inhibitors). USPs are de-ubiquitinating enzymes which remove ubiquitin from specific protein substrates and allow protein salvage from proteasome degradation, regulation of protein localization or activation. This pathway that regulates cellular protein turnover is implicated in the pathogenesis of a number of human diseases, including cancer. The only approved ubiquitin-proteasome system related therapeutic, Velcade®, has demonstrated proof of concept for proteasome inhibition in cancer. It shows, however, multiple undesirable side effects due to its broad ranging effects on protein degradation. A promising alternative to targeting the proteasome is to interact at the upstream level of ubiquitin conjugation/deconjugation to generate therapeutics with increased specificity and selectivity. Among the upstream ubiquitin transfer system, USP constitute one of the most favourable target classes due to their protease function being amenable to small molecule drug discovery.

2.2.3 'Yeast Two-Hybrid' (Y2H) system

Chart 5: Y2H System



The 'Yeast Two-hybrid' system was discovered in 1989 by Stanley Fields and others for the detection of protein interactions. The system was invented to account for the reconstitution of a functional Transcription Factor (TF) using plasmid expressing tools in genetically modified yeast cells. The technology is based on the physical binding of protein X with protein Y and reducing the proximity between DNA Binding Domain (DBD) of a transcriptional activator and its Activation Domain (AD) counterpart. The reconstitution of a functional TF activates the production of an auxotrophy marker (His3 commonly) which in turn allows His - yeast cells to grow on a selective medium lacking Histidine. Besides detection of protein interactions, versions have been developed to propose cDNA and genomic library screenings with researchers seeking such protein interactions in a given cell type, tissue or organism.

2.3 Overview of Drug Candidates

Hybrigenics is involved in discovering and developing Inecalcitol for various diseases. Presently, Prostate Cancer and CLL have been identified as two indications for treatment by oral administration of Inecalcitol.

2.3.1 Prostate Cancer

Inecalcitol drug can be used to enhance the efficacy of reference treatments in two stages of the disease. Firstly, it can be administered in combination with anti-hormonals (LH-RH agonists and anti-androgens) for the hormone-dependent stage and secondly with Taxane-based Chemotherapy (Taxotere® and Jevtana®, Sanofi) for the hormone-refractory stage. The drug is expected to be launched in 2022 in the U.S, European Union, and Japan, and is estimated to be priced at €40 per day at the time of launch; the drug will have patent protection up to 2032.

Presently, the Company is planning to conduct Phase IIb clinical trials. During the Phase IIa clinical trial results for Inecalcitol which were announced in September 2010, a total of 54 patients were enrolled to test 9 dose levels from 40 microgram up to 8 milligram per day for 18 weeks. From the study, the maximum tolerated dose along with Taxotere® chemotherapy was established as 4 mg per day for 18 weeks. It was observed that 85% patients with measurable prostate specific antigen (PSA) responded to the combination treatment with >30% decline in PSA within 3 months (Refer table 2). The response rate observed with Taxotere® alone was about 65%. Since there was no direct comparison of Taxotere® with or without Inecalcitol in the Phase IIa study and the difference between the two response rates is only interpreted as a strong presumption of efficacy, but not as a definitive proof, the main objective of the Phase IIb study will be to bring this clinical "proof-of-concept". (The marked depression of the levels of parathyroid hormone (involved in the physiological regulation of calcium levels) with a dosage of 4 mg per day of Inecalcitol was an additional observation in the phase II study.)

2.3.2 Chronic Lymphocytic Leukemia (CLL)

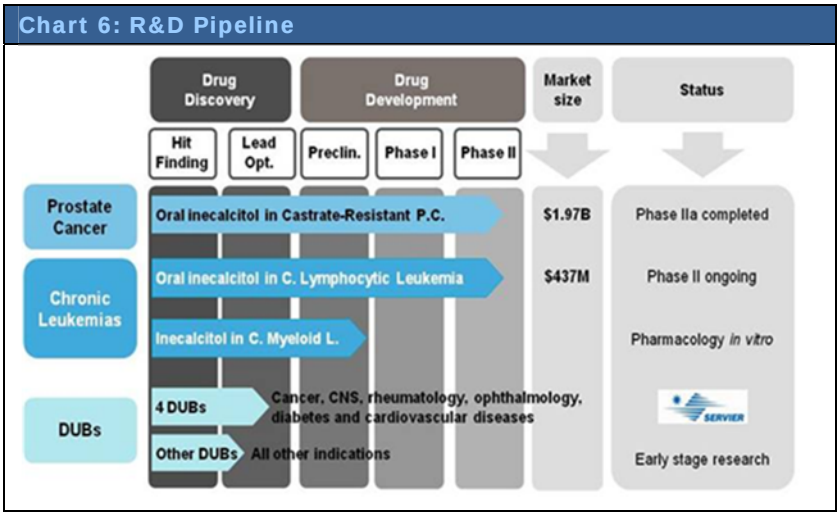
Inecalcitol for CLL is recommended to be administered daily in a dosage of 2 mg per day with the average treatment duration being 6 months and/or until progression of the disease. In March 2012, the Company announced the authorization grant by French National Drug Safety Agency for Phase II clinical trial of oral Inecalcitol under an Investigational Medicinal Product Dossier (IMPD) procedure. In September 2012, the Company announced that they have started phase 2 clinical trials of oral Inecalcitol in patients with CLL. The funding for these trials is secured

through a €3.3MM PIPE in March 2012. The open-label clinical study is expected to enrol 50 CLL patients across 6 centres in France and be coordinated by Professor Hermine, Head of Clinical Haematology at Necker Hospital in Paris, with the endorsement and active participation of the French Cooperative Group on CLL. The first thirteen patients have received their treatment. The reasoning for investigating Inecalcitol in CLL stems from a recent clinical observation that a patient, whose CLL cells over-expressed VDR, responded positively to a treatment with high oral doses of natural vitamin D every two weeks. A control patient whose CLL cells expressed low levels of VDR remained unresponsive to the same high doses of vitamin D. The frequency of natural vitamin D administrations is usually limited by the high risk of developing Hypercalcemia. The Company intends to test the effectiveness of Inecalcitol in patients with CLL cells over-expressing VDR as it can be administered every day at high doses without the risk of Hypercalcemia.

On February 04, 2014, the Company provided an update on the phase II clinical trial of Inecalcitol in CLL. The Company reported that the enrolment process in the phase II study was completed with 24 CLL patients as opposed to 50 patients that were previously decided to be enrolled for the study. Inferences made from the study were as follows: Out of 17 patients who were treated with oral Inecalcitol (2 mg per day) for more than six months the Blood Lymphocytes Counts (BLC) of 11 patients stopped increasing as soon as the treatment was started. Moreover, after 10 months of treatment, one out of 11 patients experienced a -90% decrease in BLC. In case of 10 patients, BLC remained stable for at least six months. BLC of six patients did not show any improvement at any point in time. Two patients were retracted from the study after a treatment period of four or five months, as they were required to undergo immuno-chemotherapy. There was no such occurrence reported, where patients had to be withdrawn from the study due to side effects such as hypercalcemia. Moreover, it is also important to note that in 2014, Inecalcitol, a key drug for the treatment of CLL was designated with Orphan drug status in Europe and the U.S.

2.4 R&D Pipeline

Chart 6: R&D Pipeline



2.5 Company Premiums

- **Patented Drugs and Unique Technology:** Hybrigenics' core competency lies within its drug discovery capabilities and its worldwide proprietary rights for the use of Inecalcitol. The Company is researching the use of oral Inecalcitol in the treatment for diseases such as Prostate Cancer and CLL (for which company has been awarded with Orphan drug status). In addition, the company is also planning to pursue the use of Inecalcitol for AML and CML which could represent additional orphan therapeutic indications. The Company has also received several patents related to therapeutic use of high doses, synthesis and innovative formulations of Inecalcitol. Additionally, they have received Composition of matter patents on the chemical inhibitors of Ubiquitin-Specific Proteases (USP's) and a license from Pasteur Institute to run the "ULTImate Y2H" screens.
- **Positive results for Inecalcitol clinical trials:** Hybrigenics has carried out successful trials for oral administration of its key drug, Inecalcitol which has given positive results for the hormone-refractory Prostate cancer when given in combination with Taxotere®. The results were as follows,
  - PSA decline >30% within 3 months : 85% of patients
  - PSA decline >50% within 3 months : 66% of patients
  - PSA decline >50% anytime : 76% of patients

Table 2: Drugs in combination with Taxotere®			
Drug	**Taxotere® Regimen**	**PSA decline > 30% within 3 months**	**PSA decline > 50% anytime**
Inecalcitol	3w	85%	76%
Custirsen	3w	n/a	58%
Thalidomide	w	n/a	53%
Taxotere® alone	3w	67%	45%
Dasatinib	3w	n/a	40%
Atrasentan	3w	35%	23%

The above table compares the performance of Inecalcitol in combination with Taxotere® against the performance of other drugs with Taxotere®. It is evident from the above table that the response rate observed with Taxotere® alone was about 67% for PSA decline >30%. However, when combined with Inecalcitol the response rate is the highest for castrate-resistant Prostate cancer i.e. 85% which is better than the other competitor drugs. It is also performing better in the PSA decline of more than 50% category with 76% response rate which again is the highest among the competitor drugs.

- **Inecalcitol Elected as an Orphan Drug for CLL in Europe and U.S.:** In 2014, American Food and Drug Authority and the European commission granted Orphan drug status to the Hybrigenics' key drug, Inecalcitol, for CLL. The Orphan drug status would avail the Company with several incentives such as
  - Customary 10 years of marketing exclusivity of Inecalcitol in the European pharmaceutical market from the date of approval
  - Protocol assistance, wherein the expert scientific advice that is required during the product development phase in terms of quality, clinical and non-clinical study is provided at discounted rates. This assistance procedure is anticipated to be of significant benefit to the Company as it would enable them to design the next phase III clinical study

  Additionally, the Orphan drug status for CLL will help the Company accelerate the drug registration process in Europe for the disease, which hardly has any required medical aid available in the market.

2.6 Company Risks

- **Cash Flow Uncertainty:** Presently, Hybrigenics does not have any drugs in the commercial stage. The Company's primary source of revenue is fees derived from services using 'Yeast Two-Hybrid' technology. However, these funds are not an adequate source of income to cover the costs of drug development as these agreements are short term in duration and small in value. Furthermore, the Company has not yet tied up with other companies for co-development of drugs, thereby creating additional uncertainty in the cash flows.
- **Risk of Loss on Invested Capital:** To date, the Company has already incurred large capital expenditure on CLL drug clinical trials. The study's positive result shall provide an evidence of the drug's potential in treating proliferative diseases, which further shall form a catalyst to attract a partner to develop Inecalcitol for CLL and other cancers. On the contrary, an unfavourable outcome would lead to a loss on invested capital as the company has made large investments on Inecalcitol R&D. This loss would ultimately hamper its business and financial conditions. However, the existence of the Company's services subsidiary offsets the risk of heavy investments in Inecalcitol, by investing steadily on expanding this division (through acquisitions and by launching the U.S. subsidiary) in all areas of life sciences. Thus, the presence of the services segment enables the Company to diversify its business model and reduces the risk of loss on invested capital.
- **Drug Discovery and Development Related Risks:** There is a risk associated with success of the pipeline/approval and commercialization of drugs. The discovery and/or development process may or may not yield the expected result. It is also subject to intense regulatory scrutiny.
- **Inadequate Experience in Global Development:** Inadequate experience in terms of global development is one of the biggest challenges faced by the Company. Its core competency spans across drug discovery and development only. However, due to inadequate experience in global development the Company plans to outsource the commercialization of these drugs to larger pharmaceutical companies who in turn will provide the initial funding as well as royalty on sales.

2.7 Corporate Strategy

- **Forming Strategic Partnerships:** For the 'Pharma' division, Hybrigenics follows the corporate strategy of building a patented pharmaceutical pipeline of drugs in the disease area of oncology. The Company plans to collaborate with larger global pharmaceutical firms for the purpose of funding, co-development and out-licensing. Through these collaborations, Hybrigenics will be able to build up its revenue base in the form of licensing fees including upfront and milestone payments as well as royalty on sales.

  The Company is currently planning to carry out Phase IIb clinical trial for Prostate Cancer drug and Phase II trial for CLL drug.

  In 2011, the Company formed a license and research collaboration agreement with Servier Laboratories, a privately-run French research-based Pharmaceutical company (turnover of €3.7B in 2010) in the field of deubiquitinating enzymes (DUBs). As per the agreement, Hybrigenics will identify and validate new targets among DUBs in these therapeutic areas and also screen potential therapeutic agents who are able to modulate four undisclosed targets, already chosen as exclusive DUBs of interest under the collaboration. On the other hand, Servier will provide the compounds to be screened as well as develop the selected compounds and commercialize the approved drugs. In the three years of collaboration, Hybrigenics will receive an upfront payment and milestone payments worth €4MM, which represents a research funding of €0.75MM per year since 2011 and also includes the upfront amount the Company received before initiating the research in 2011. Moreover, it is important to note that the Company received its first milestone payment of €0.33MM in January 2014. Further, depending on the achievement of predefined research, development and registration milestones, the Company is further eligible to receive payments amounting to €9.5MM or €11.5MM for each target, successfully leading to registration of a new drug, and to royalties on sales of companion diagnostic kits.

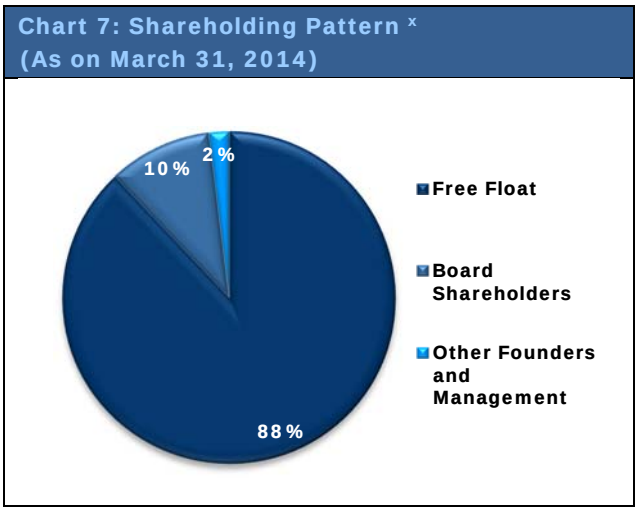
  Historically, it has been observed that the U.S. has been the key contributor to the Company's revenue, which accounts for 30% of the turnover of Hybrigenics Services. Therefore, in September 2013, the Company initiated a strategy to form a wholly-owned American subsidiary, Hybrigenics Corporation in the U.S., in order to augment the revenue contribution from this region, which has a huge biomedical R&D market. This incorporated subsidiary will represent the Company for R&D, regulatory and business development matters in the American terrain. Further, it would also help the Company in the commercialization of Hybrigenics Services' protein interactions fee-for-service activities.

See important disclosures on page 37 of this report

2.8 Shareholding Pattern

The total basic shares outstanding are 25.9 MM as on March 31, 2014 with a free float of 88%.

Chart 7: Shareholding Pattern [x]
(As on March 31, 2014)



2.9 Listing and Contact Details

Hybrigenics is listed on Alternext (NYSE-Euronext) in Paris (Ticker: ALHYG, Date of Listing – December 17, 2007)

Company Contacts

Address: 3-5 Impasse Reille, 75014 Paris - France
Contact No: +33 1 5810 3800;
Fax: +33 1 5810 3849
Email Id: contact@hybrigenics.com

Investor Contacts

1) Dr. Rémi Delansorne, CEO, Ph.D.
Contact No: +33 (0)1 58 10 38 00;
Email Id: investors@hybrigenics.com

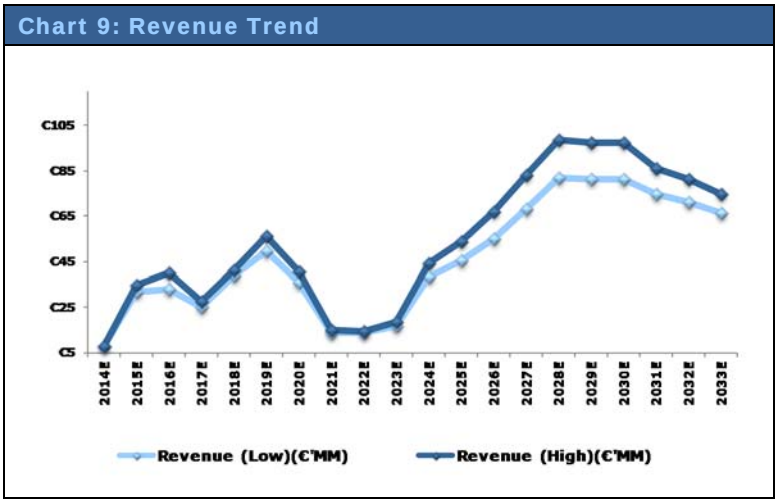
2) Julien Perez / Pierre Laurent, Financial Communication & Investors Relations – NewCap.
Contact No: +33 (0)1 44 71 94 94;
Email Id: hybrigenics@newcap.fr

3. Financial Analysis [xi]

3.1 Expected Future Trend (FY2014E - FY2033E)

3.1.1 Revenue and Operating Margin Trend

Chart 9: Revenue Trend

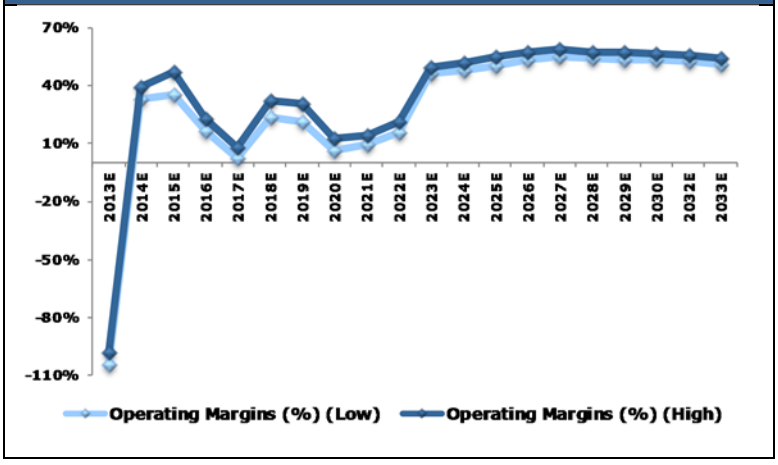


Arrowhead's future revenue estimates are based on revenue derived from two key drug programs to treat Prostate Cancer and CLL. While the CLL drug is expected to be launched in the market by FY2020, the Prostate Cancer drug is expected to be launched by FY2022. The Company plans to collaborate/out-license these drugs to large pharmaceutical companies for worldwide development and marketing. Arrowhead has assumed that by FY2014 and FY2016, the Hybrigenics management will successfully have built partnerships with large international Pharmaceutical companies for their two key drugs.

The initial growth in revenue is due to the upfront payments provided by the collaborating partner during the earlier years of partnership. However, the milestone payments for the Prostate Cancer drug program are expected to stop by 2021, thereby resulting in a sharp dip in the total revenue.

Post FY2022, the drugs meant for treating both CLL and Prostate Cancer are expected to start contributing to the turnover, which is reflected in the steep growth in revenue between FY2022 and FY2028. However, post FY2028, when the CLL drug reaches its peak, revenue is expected to slow down. Prostate Cancer drug is expected to reach peak revenue in FY2030 and slow down later.

Chart 10: Operating Margin Trend



The margins in the earlier years are estimated to be depressed due to the high cost of development associated with the drugs. Apart from development costs, margins are impacted by fixed costs and overhead costs. In the initial years, margins are expected to fluctuate based on the timings of the milestone payments provided by the collaborating partners. Margins are expected to improve from FY2022 onwards as both the drugs start contributing to the total revenue.

4. Key variable analysis [xii]

4.1 Market share captured in terms of number of patients tapped

Hybrigenics is currently developing drugs for treating Prostate Cancer and CLL. They are studying the administration of oral Inecalcitol for both Prostate Cancer and CLL. The Prostate Cancer drug program is currently in Phase II, while the CLL drug program is in Phase II. The Company plans to license out the rights of these drugs to large pharmaceutical companies for worldwide development and marketing. Therefore, it will have only three sources of revenue from these partnerships: upfront payments, milestone payments, and royalty revenue. The revenue estimates from these drugs are based on the estimated growth in the number of Prostate cancer and CLL patients in the key geographies (Company's target markets), i.e., U.S., Europe and Japan.

4.1.1 Market Share: Percentage of patients tapped – Prostate Cancer

Assuming that the oral Inecalcitol drug for Prostate Cancer will be launched in 2022, the market share captured by the Company post-launch is estimated to be as follows:

Table 3: Market share: Percentage of patients tapped – Prostate Cancer

%	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.04%	0.18%	0.62%	1.21%	1.49%	1.56%	1.59%	1.59%	1.61%	1.21%	1.00%	0.75%
High estimate	0.05%	0.18%	0.62%	1.22%	1.50%	1.57%	1.60%	1.60%	1.61%	1.22%	1.02%	0.75%

4.1.2 Market Share: Percentage of patients tapped – CLL

Assuming that the oral Inecalcitol drug for CLL will be launched in 2020, the market share captured by the Company post-launch is estimated to be as follows:

Table 4: Market share: Percentage of patients tapped – CLL

%	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Low estimate	0.13%	0.13%	0.15%	0.17%	0.60%	0.50%	0.55%	0.70%	0.82%	0.70%	0.60%	0.52%
High estimate	0.14%	0.14%	0.15%	0.18%	0.61%	0.52%	0.60%	0.75%	0.85%	0.72%	0.62%	0.50%

4.2 Revenue from Licensing Agreements (Deal Value)

Arrowhead has assumed that the Hybrigenics management will have successfully built partnerships with large international Pharmaceutical companies for Prostate Cancer in 2016 and CLL in 2014. The revenue from this partnership would be through upfront payments, milestone payments and royalty. The upfront payments, milestone payments and sales milestone payments are expected to come in the earlier years of partnership before the drugs become commercially available for sale.

- **Upfront payment** will be made at the commencement of partnerships
- **Milestone payments** will be made for phase II, phase III and final approvals. The deal value will decide the milestone payments or the future cash flow. Arrowhead believes that the deal value (or revenue received from the partner for drug development) would be higher or better in the high-bracket and lower in the low-bracket scenario
- **Royalty** will be paid on annual sales. The royalty payments are expected to arise once Hybrigenics' partners start generating revenue from sales

4.2.1 Revenue from Upfront and Milestone Payments – Prostate Cancer

According to Arrowhead estimates, the expected deal value for Prostate Cancer drug program lies between €115MM – €130MM. The upfront payments are expected to be in the range of €25MM in the low bracket and €30MM in the high bracket.

Table 5: Revenue from Upfront and Milestone Payments – Prostate Cancer

€ MM	2016E	2017E	2018E	2019E	2020E	2021E	Estimated Deal value (MM)
Low estimate	29	4	18	31	31	3	**€115**
High estimate	34	4	18	36	36	3	**€130**

4.2.2 Revenue from Upfront and Milestone Payments – CLL

According to Arrowhead estimates, the expected deal value for CLL drug program lies between €130MM – €140MM. The upfront payments are expected to be in the range of €25MM in the low bracket and €30MM in the high bracket.

Table 6: Revenue from Upfront and Milestone Payments – CLL

€ MM	2014E	2015E	2016E	2017E	2018E	2019E	Estimated Deal value (MM)
Low estimate	5	37	25	21	21	21	**€130**
High estimate	5	40	30	22	22	21	**€140**

4.3 Royalty Receipts

Royalty will be received on the annual revenue earned through sales. The forecasted total sales are based on Arrowhead's estimate for (a) the market share for each drug, and (b) growth in the number of patients in the key target markets. Royalty is estimated to be on an average 10% and 12% of the annual revenue in the low and high bracket scenarios respectively.

4.3.1 Royalty Receipts – Prostate Cancer

The royalty receipts are expected to commence in FY2022. Arrowhead expects the revenue to peak in 2030.

Table 7: Royalty Receipts – Prostate Cancer

€ MM	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.5	2.2	7.9	16.1	20.8	22.8	24.3	25.4	26.9	21.2	18.3	14.4
High estimate	0.7	2.6	9.5	19.5	25.1	27.5	29.3	30.7	32.3	25.6	22.4	17.2

4.3.2 Royalty Receipts – CLL

The royalty payments are expected to commence in FY2020. Arrowhead expects the revenue to peak in 2028.

Table 8: Royalty Receipts – CLL

€ MM	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Low estimate	2.6	3.0	4.0	5.0	20.8	19.7	24.6	35.6	47.3	45.7	44.3	43.2
High estimate	3.4	3.9	4.8	6.4	25.3	24.5	32.2	45.7	58.9	56.4	54.9	49.9

4.4 Success Rates

Arrowhead has assumed different probabilities of success based on the current development phase of the drugs. These probability figures indicate the possible success rates for the drug, that is, the likelihood of the drug compound reaching the target market. The success rate improves as the drug moves from one stage to the next. Arrowhead has multiplied the estimated cash flows with the probability rates to get probability weighted cash flows (risk adjusted). The different rates applied are summarized below:

4.4.1 Success Probability – Prostate Cancer

Table 9: Probability of Occurrence (Success) – Prostate Cancer

%	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	25%	50%	70%	75%	80%	85%	100%
High estimate	30%	55%	75%	80%	80%	85%	100%

4.4.2 Success Probability - CLL

Table 9: Probability of Occurrence (Success) – CLL							
%	2014E	2015E	2016E	2017E	2018E	2019E	2020E-2033E
Low estimate	30%	67%	72%	75%	85%	85%	100%
High estimate	35%	70%	75%	80%	87%	90%	100%

5. News [xiii]

- **Hybrigenics' Inecalcitol exhibits Synergy with Azacytidine in Preclinical Models of AML:** On June 20, 2014, Hybrigenics announced the results of the study covered by an international group of researchers on the synergy between Inecalcitol and Azacytidine in in-vitro and in-vivo preclinical models of AML. Azacytidine is a hypomethylating anticancer drug. As per the study, the combination of Inecalcitol and Azacytidine in in-vitro preclinical models has proved to inhibit the growth of human AML cell lines, to stimulate their differentiation into more mature and functional myeloid cell type or to induce their programmed cell death (apoptosis) more effectively than the addition of the individual activities of each compound alone. The in-vivo preclinical models were conducted on mice and have shown the same synergy as were exhibited by the in-vitro models. Azacytidine (Vidaza®, Celgene) and Decitabine (Dacogen®, Janssen-Cilag) are the preferred hypomethylating agents used for AML on senior (>65) and weak patients, who are not qualified to undergo standard induction Chemotherapy. As per the Company's Clinical R&D Head, combination of either of the above mentioned agents with Inecalcitol would be the clinical setting of choice to look for synergistic effects in a future phase II study in AML patients.
- **Hybrigenics' Inecalcitol for CLL awarded with Orphan Drug designation in the U.S.:** On May 20, 2014, Hybrigenics announced that Inecalcitol for the treatment of CLL has been awarded with Orphan drug designation by the American Food and Drug Administration of the U.S. Orphan designation would provide the Company with various development incentives of the Orphan Drug Act, including tax credits for qualified clinical testing. Additionally, a marketing application for CLL would not be subjected to a prescription drug user fee unless the application includes an indication other than the rare disease or condition for which the drug was designated.
- **Hybrigenics launched Helixio, a division established specifically for genomic services:** On April 03, 2014, Hybrigenics announced that the launch of Helixio, a new division dedicated to genomic services. A decision to start a new genomic division was prompted with the acquisition of Imaxio's genomics unit in October 2013, which gave the Company access to the latest technologies based on DNA or RNA microarrays ("Chips") as well as on sequencing. The Company's primary intention behind this activity is to expand genomic services by marketing it under the brand name Helixio®.
- **Hybrigenics included in Euronext CAC PME index:** On April 01, 2014, Hybrigenics announced that the Company has been included in the composition of French "CAC® PME" index launched by Euronext in March 2014. The CAC® PME index includes 40 French small and midcap companies listed in Paris that are representative of various business areas and show the highest market capitalization or liquidity. Hybrigenics was already a part of the Next Biotech Index which includes 27 values listed on various European markets of Euronext biotechnology.
- **Hybrigenics successfully raised €6.1MM to finance clinical phase II studies of Inecalcitol in AML and CML:** On March 26, 2014, Hybrigenics announced that they have successfully completed private placement and capital raise under the French Tax deduction mechanism according to the "TEPA" law for a total amount of about €6.1MM. With reference to these two transactions, the Company issued 2.5MM new shares at an average price of €2.41 per share. New shares issued represent 10.8% of the Company's capital before the capital raise and 9.8% of the capital after the capital raise. Through private placement, the Company raised €3.8MM by issuing 1.6MM shares at €2.35 per share. Through capital raised under "TEPA" law, the Company raised €2.3MM by issuing 0.9MM shares at €2.50 per share. As per the management, these funds will be utilized to finance two new phase II clinical studies of Inecalcitol in AML and CML.
- **Hybrigenics Inecalcitol effective in treating AML:** On March 05, 2014, Hybrigenics gave a presentation at the 12th International Congress on Targeted Anticancer Therapies in Washington, DC, USA, on the research study submitted by the international group of researchers from France, Belgium, UK, and Japan on the effectiveness of Inecalcitol in the in-vitro and in-vivo preclinical models of AML. According to their study, Inecalcitol is found to be thousand-fold more effective in-vitro as compared to the active metabolite of vitamin D in the following cases: 1) to inhibit the growth of human AML cell lines, 2) to stimulate their differentiation into more mature and functional myeloid cell type, or 3) to induce their programmed cell death (apoptosis). Researchers also conducted an experiment, wherein AML was injected in mice, in order to check the onset of disease, and it was found that treatment by Inecalcitol helped in averting the AML attack for a longer period.
- **Update on the Phase II clinical trial of Inecalcitol in CLL:** On February 04, 2014, Hybrigenics held a public seminar jointly organized by FlandersBio and Janssen Pharmaceutical in Hasselt, Belgium, in order to announce an update on the phase II clinical trial of Inecalcitol in CLL. The Company reported that enrolment in the phase II study was completed with 24 patients. Out of the 17 patients treated with oral Inecalcitol (2 mg per day) for more than six months, the BLC of 11 patients stopped increasing as soon as the treatment was started. Moreover, one out of 11 patients, after receiving the treatment for 10 months, experienced a -90% decrease in BLC. In case of

10 patients, BLC remained stable for at least six months. BLC of six patients did not show any improvement at any point of time. Two patients were withdrawn from the study after a treatment period of four or five months to receive immuno-chemotherapy. There was no such occurrence reported where, patients have to be withdrawn from the study due to side effects such as hypercalcemia. Further, the trial update also showed that 11 respondents (58%) and 8 non-respondents (42%) to Inecalcitol treatment were in line with the 60%/40% ratio reported in the H1'2013 update.

- **Line of Credit:** With the respect to the line of credit established with Yorkville Advisors, Hybrigenics has a total available credit of €12MM in the form of advance payables. Post June 30, 2012, Hybrigenics has made the following drawings:-

Table 11: Line of credit – Shares issued

Date	Shares Issued	Price	Equity
10/8/2012	220,215	€ 0.9082	199,999
11/5/2012	237,557	€ 0.8419	199,999
12/5/2012	240,038	€ 0.8332	200,000
1/7/2013	253,581	€ 0.7887	199,999
1/25/2013	226,116	€ 0.8845	200,000
2/8/2013	210,903	€ 0.9483	199,999
2/25/2013	315,590	€ 0.9506	300,000
3/27/2013	225,199	€ 0.8881	199,999
10/25/2013	234,484	€ 0.6397	149,999
11/18/2013	163,934	€ 0.6100	100,000
12/13/2013	310,510	€ 0.6441	199,999
1/08/2014	493,229	€ 1.1151	550,000
2/10/2014	227,915	€ 2.1938	500,000

6. Management and Governance [xiv]

The Management and Governance team has vast experience in drug discovery in the biopharmaceutical industry particularly preclinical research and clinical development in oncology. They also have strong experience in building licensing deals with large pharmaceutical firms.

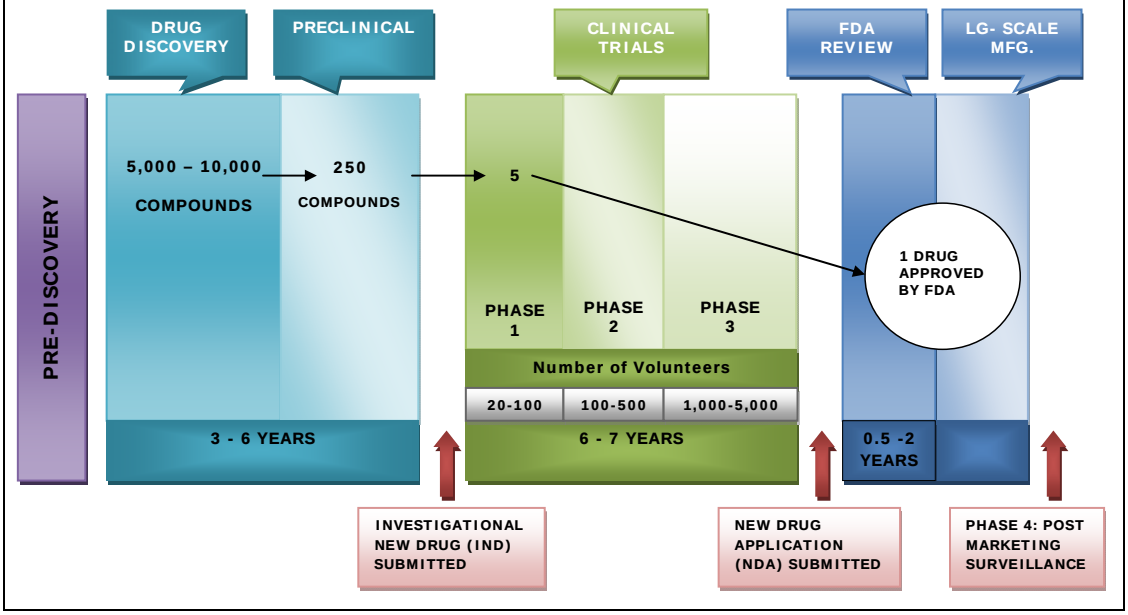
Table 12: Management and Governance

Name	Position	Past Experience	Qualifications
Dr. Rémi Delansorne	CEO	• He was working in pre-clinical R&D in Theramex from 1985 to 2000 when the Company was integrated into the Merck Group (now Merck-Serono). • In 2002, he became Merck's Global Head of Diabetes Research and was responsible for the three preclinical sites in France. • He joined Hybrigenics in 2004 as Vice-President for R&D and was appointed CEO of the Company in September 2005.	• Veterinary doctorate from "Ecole Nationale Vétérinaire d'Alfort" (D.V.M.) • PhD in life sciences from Université Pierre et Marie Curie
Dr. Jean-François Dufour-Lamartinie	Head of Clinical R&D	• He worked as Clinical Research Director at BioAlliance Pharma, a French biopharmaceutical company, for more than 3 years and contributed to the launch of their first drug on the market. • He has acquired a broad experience in the clinical development in oncology in his prior positions with pharmaceutical companies, clinical research organizations and as a Clinician at Cancer research institutes such as the Institut Gustave Roussy. • In 2006, he joined Hybrigenics as Head of Clinical Research & Development.	M.D.(Physician)
Mr. Guillaume Floch	CFO	• He joined the pharmaceutical industry in 2001 as Financial Controller at Elan France, where he became Financial and Administrative Manager. • He also took part in the creation and sale of Zeneus Pharma to Cephalon France after two years. • He subsequently joined the European headquarters of this laboratory, with the position of Manager, Business Planning & Performance. • He has served as Financial Director of Hybrigenics SA since June 2008.	• DESCF Accounting degree
Mr. Etienne Forsmtecher	CEO (Hybrigenics Services)	• He joined Hybrigenics in 2002, and served as a team leader for R&D department holding responsibility of large scale protein interaction mapping projects in human and drosophila. • In 2006, he joined the fee-for-service department and built scientific support team. Further, in 2008, he took up the managing the marketing division. • In 2010, he was appointed as Deputy General Manager of Hybrigenics Service, and was responsible for managing scientific projects, sales and marketing activities • In January 2014, he was appointed as President of Hybrigenics Services.	• PhD in Molecular and Cellular Pharmacology from Pierre and Marie Curie University • Engineer from Ecole Polytechnique (France)

7. Technologies and Markets

Drug Discovery and Development Process [xv]

Chart 11: Drug Discovery and Development Process



Drug discovery is a process by which scientists design and discover safe and effective drugs. Scientists identify the cause of the disease to be treated and work at the molecular level to understand the disease path (at the level of genes, proteins and cells). The new drug discovery and development process involves validating these targets, discovering new molecules (potential new drug) to interact with the chosen target, testing the new drug and gaining the approvals. The product development cycle is very long and it takes 10 to 15 years on an average from the time a new drug is discovered to the time it is available for treating patients. The drug development process is complex, challenging and risky with very high failure rates. It is estimated that for every 5,000–10,000 compounds taken up for study, only one receives approval.

Cost structure

The process is also very expensive and the average total cost of Research and Development (R&D) is roughly US$800MM to US$1B per molecule. [xvi]

7.1 Drug Discovery Process

7.1.1 Pre-discovery Stage

Chart 12: Chemical Pathways

In the pre-discovery stage, scientists focus on understanding the disease to be treated. They study the chemical pathways. They study how the disease affects the gene, how the genes in turn affect the proteins, how these proteins interact with each other in the cells and finally how these cells affect the tissues in the patient. Scientists identify drug molecules that could interact with molecules in the chemical pathways and make them less or more active or change their activity all together that could cure the disease. The pre-discovery stage consists of two steps; Target Identification and Target Validation.

- **Target Identification**
  In this stage, the scientists identify the target, which is a gene or a protein which is involved in a particular disease. They select the target which can be interacted with and one on which the drug molecule will work. Scientists use a variety of techniques to identify and isolate individual targets to learn more about their functions and how they influence the disease.

- **Target Validation**
  Scientists have to prove how the selected target molecule is involved in the disease and if the drug molecule can act upon it.

7.1.2 Drug Discovery

The drug discovery stage consists of three steps; Finding Lead Compounds, Conducting early safety test and Lead optimization.

- **Finding Lead Compound**
  In the drug discovery stage, scientists identify the drug molecule or 'Lead Compound' that can act on the target molecule and alter the disease course. The lead compound is one that is expected to have the potential to treat disease. Lead compounds can be found in nature, such as bacteria found in soil and plants. Molecules can be created from scratch using computer modelling. High-throughput screening process allows scientists to test large number of molecules against the target to identify the one that gives the best result. Finally, biotechnology allows scientists to genetically engineer molecules to produce drugs that can fight the target molecule.

- **Early Safety Drugs**
  Scientists test the drug molecule for Absorption, Metabolism, Excretion and Toxicology properties i.e. check if the drug is absorbed into the bloodstream, can be distributed to site of action, metabolized effectively and efficiently, successfully excreted from the body and is not toxic.

- **Lead Optimization**
  After the initial screening, selected compounds are then worked upon to change their properties to make them more effective. The purpose of changing their properties is to reduce their interaction with other chemical pathways in the body, thereby reducing the side-effects of the drug molecule.

7.1.3 Preclinical Testing

In the preclinical testing stage, an investigational drug is tested extensively in the laboratory to ensure whether it will be safe to administer to humans. The preclinical testing involves testing of the drug molecule in the laboratory on living cell cultures and animals. Post the preclinical testing stage, only one to five molecules are selected to be carried forward to the drug development stage.

7.2 Drug Development Process

7.2.1 Investigational New Drug (IND) Application

Prior to the commencement of the clinical tests, scientists file an IND application with the Food and Drug Administration (FDA). The application includes the results of the preclinical work, the potential drug's chemical structure and how it is thought to work in the body, a listing of any side effects and manufacturing information. The IND also provides a detailed clinical trial plan that outlines how, where and by whom the studies will be performed. The FDA reviews the application to make sure people participating in the clinical trials are not exposed to unreasonable risks. In addition to the IND application, all clinical trials are reviewed and approved by the Institutional Review Board (IRB) at the institutions where the trials will take place. This process includes the development of appropriate informed consent, which is required of all clinical trial participants.

7.2.2 Clinical Trials [xvii]

The clinical trials are conducted in three phases. In this stage, the drug molecule is tested on humans for the first time. These trials start 30 days after the submission of the IND if FDA has not placed a 'Clinical hold' on the development. In phase I, the drug is tested on around 20-100 healthy volunteers. In phase I, the scientist test how the drug is absorbed and distributed and how it is metabolized and eliminated from the body. They check for the desired effects of the drug as well as its side effects. Cost: US$0.1MM-US$1MM.
FDA approval is not required prior to the beginning of phase II. This stage involves 100-500 patient volunteers and takes around six months up to three years. In this stage, scientists test and determine safety and effectiveness of the drug in treating the condition and establish the minimum and maximum effective dose. Cost: US$10MM-US$100MM.
FDA consultation is required prior to the beginning of the phase III. Phase III trials confirm the effectiveness and safety of the drugs. Around 1000 – 5000 patient volunteers are tested during this stage. Phase III trials are the most expensive and the longest. Cost: US$10MM-US$500MM.

7.2.3 New Drug Application and Approval

Once all the clinical trials are successfully completed, the sponsoring company analyzes all the data to check if the drug is efficient and effective. If yes, they file a New Drug Application (NDA) with the FDA. This approval gives the company permission to manufacture and market the drug. The application must present substantial evidence that the drug will have the effect it is represented to have when people use it or under the conditions for which it is prescribed, recommended or suggested in the labelling. The FDA experts go through the application and then either approve the drug or ask for more studies or reject the drug. Since no drug has zero risk, the FDA experts need to determine that the benefits are more than the risks.

7.2.4 New French Regulatory Agency [xviii] [xix] [xx]

On April 29, 2012, the French government released an official journal which indicated that a new national drug agency would replace the beleaguered French 'Agency for the Safety of Health Products' (AFSSAPS). The new National Agency for the Safety of Medicines and Health Products (MSNA) would replace AFFSAPS and would have a higher budget to be financed entirely through state subsidy. Previously, 80% of its funding was provided by pharmaceutical companies. The new agency is likely to implement stringent approval laws going forward. Some of the initiatives that are being planned are projects to manage conflicts of interest, the public declaration of interests, the promotion of independent research on the safety of health products and improved transparency. As a part of the new initiative, it would be made necessary to publish a list of links between experts and laboratories, and the amount of money paid for services completed. This initiative has already been implemented and 19,000 drugs in France are under the scanner, out of which 12,000 are available in the market. In line with this new regulations, Takeda's drug 'Actos' was the first to be removed from the market. In addition, visits by sales representatives are also being restricted and also the pharmaceutical industry has been banned from funding medical education.

7.2.5 Manufacturing

Once all the approvals are acquired, the company can start manufacturing. The production facility must meet all the FDA guidelines for Good Manufacturing Practices (GMP).

7.2.6 Phase IV Trials

Post approval, the company has to continuously monitor the periodic reports as larger number of people start using it. Companies continue research to evaluate the long term safety of the drug.

7.3 Global Pharmaceutical Market

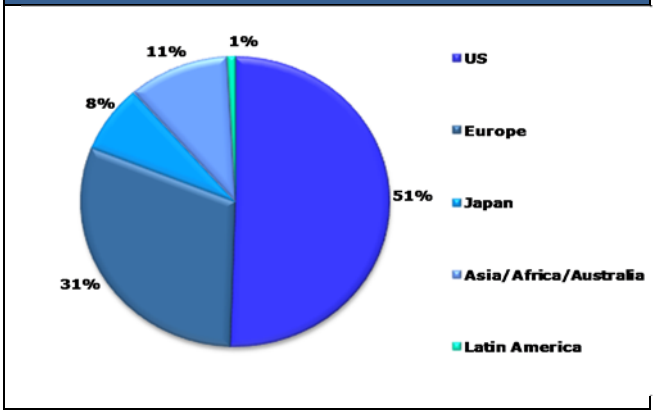
In 2012, the global pharmaceutical market sales grew only 2.4% y-o-y to US$959.0B in constant currency. The growth rate i.e. CAGR for the period FY2007-2012 was 5.3%, and further it is estimated that the global pharmaceutical market will grow at the same rate of about 5.3% during the period between FY2012-2017 in constant currency terms. Moreover, the growth rate in 2013 is expected to be around 3.3% in constant currency terms. The global pharmaceutical market is dominated by the U.S., which accounted for about 37.9% of global sales in 2012, followed by Europe with 24.4% share, and Asia/Africa/Australia together with 18.3% share. Patent expirations and limits on drug spending could weigh down the growth of drug sales in developed countries. Over 2012-2017, the size of global pharmaceutical market is expected to rise by 5.3% led by Asia/Africa/Australia & Latin America with 11.4% - 14.4% and 10%-13% growth respectively; Europe and Japan are expected to grow between -0.4% - 2.6% and 1.7% -4.7% respectively with U.S. logging a growth between 0.7% - 3.7%. [xxi]

The expiry of patents will fundamentally impact individual pharmaceutical companies during the period 2010-2014. In this period, patent expiries will impact drugs with revenue of around US$89.5B; with a majority of them being small molecules. Rising cost pressure on healthcare has resulted in an increase in generic pharmaceutical usage as generic drugs cost 30 to 80% less than their original equivalents.[xxii]

7.3.1 Global Biopharmaceutical Industry

The 'Biopharmaceuticals' industry represents a combination of 'pharmaceuticals' and 'biotechnology' industry. Biopharmaceuticals are medical drugs produced using biotechnology. The large majority of biopharmaceutical products are pharmaceuticals that are derived from life forms. Small molecule drugs are not typically regarded as biopharmaceutical in nature by the industry. However this definition is often extended to include pharmaceuticals not created through biotechnology. Thus, the term is used as an alternative for a variety of different companies producing new, apparently high-tech pharmaceutical products. [xxiii]

Chart 13: Global Biopharmaceutical Market Share by Region [xxiv]



The biopharmaceuticals market has a strong growth potential and is expected to have a bright future. According to the Market Research report from Industry Experts, biopharmaceutical products revenue contributed 10% to the total pharmaceutical industry revenue in 2006 which is expected to grow to around 15% in 2015. They also estimate that the global market for biopharmaceuticals will grow at CAGR of 12.4% over the period 2006-2015 and reach US$182.5B by 2015. [xxv]

The global biopharmaceutical market was approximately US$137B in 2009 and is expected to reach US$319B in 2020 by growing at a Compounded Annual Growth Rate (CAGR) of 9%. By 2020, at least 48 biologic products with combined estimated sales of nearly US$73B are due to go off patent.[xxvi]

7.4 Market Trends

7.4.1 Decline in Global R&D Investments [xxvii xxviii]

R&D is the most important aspect of the pharmaceutical industry. Innovation and discovery of new targets and drug compounds defines the success of the industry. After having declined for the first time in 2010, the global pharmaceutical industry is expected to increase its R&D (Drug Discovery and Development) expenditure to $149B in 2018 at a CAGR of 1.4% from to 2012 to 2018, as per World Preview report 2013 from market intelligence firm Evaluate Ltd[xxix]. According to the report, the pharmaceutical industry is expected to gradually recover from the adverse effects of the patent cliff in the U.S. with sales forecasted to reach $895B by 2018. Research budgets are also expected to show signs of improvement as the industry would benefit from improved R&D productivity. The report also predicts that an upswing in the number of drug approvals and the resulting improvement in investor confidence would be the primary drivers of expansion of the industry.
According to the Pharmaceutical R&D Fact book compiled by Thomson Reuters' unit CMR International 2013, the number of new molecular entities (NME) launched globally in 2012 reached 26 from a 10-year high of 31 in 2011[xxx].

Despite this drop, the number firmly remains above the previous 10-year average. Overall development times from the discovery to launch stage in 2012 continued its downfall from 15 years to approximately 12 years. The decline was primarily a result of changes undertaken in the R&D portfolio instead of any kind of significant improvements to the overall development methodology.

In 2000, Pharmaceutical companies contributed around 80% of the total industry R&D expenditure. Although, this investment increased by 50% since 2000, the number of new medicines developed successfully has fallen. The decline in the productivity is due to the increase in value invested in R&D and decrease in value generated. It is estimated that the industry will witness a continuing trend of decline in the R&D expenditure.

Chart 14: Decline in R&D Productivity [xxxi]

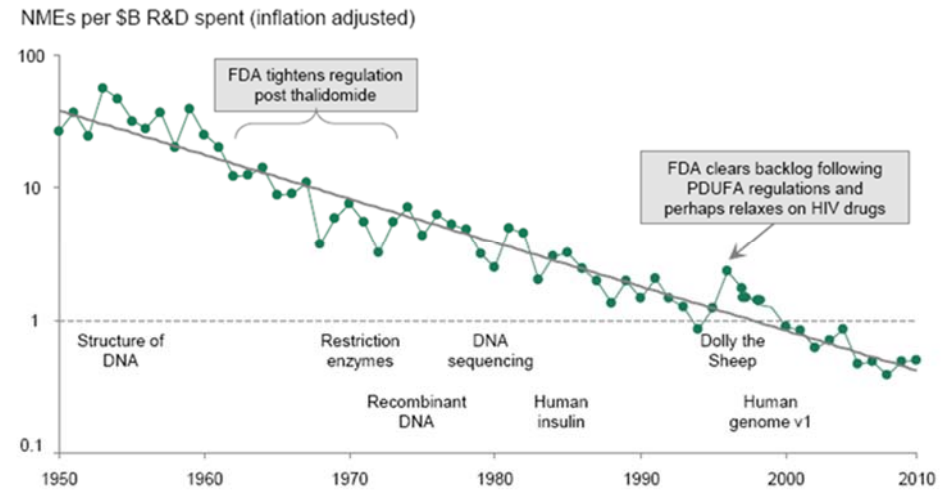
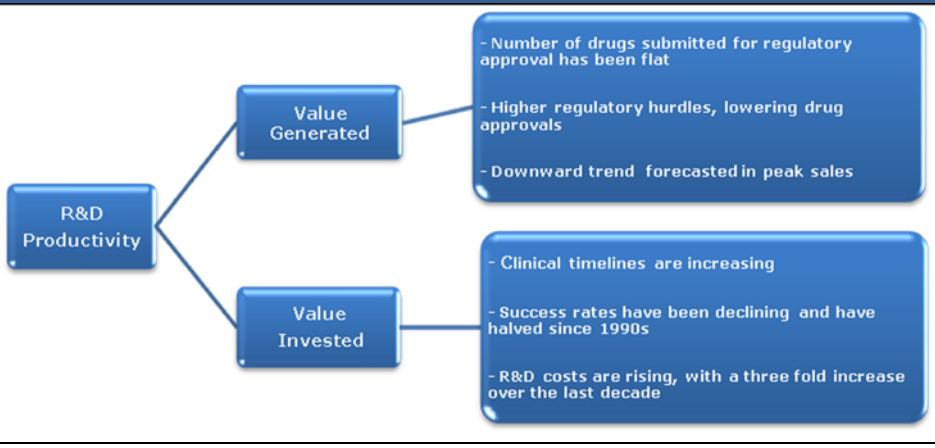


Chart 15: Decline in R&D Productivity – BCG Analysis [xxxii]



7.4.2 Need for Outsourcing – Licensing between Pharmaceutical and Biotechnology firms [xxxiii] [xxxiv]

The new drug discovery and development process is lengthy (average 15 years) and also very expensive (average cost US$800MM to US$1B per drug) and manufacturing companies have to make large R&D investments over this long period of time. It is difficult for large pharmaceutical companies to sustain such high internal R&D cost. As a result of reduced R&D productivity and the expected patent cliff (more than 110 products going off-patent) during the period 2012–2014, operating margins of large pharmaceuticals firms are expected to remain under pressure. Biosimilars pose a serious competition to the existing patented drugs (monopoly) and will be entering the market at cheaper prices eating into the market share of the existing drugs. Loss of patents impacts the sales directly and there could be price erosion up to 70% within months. [xxxv] Given the dearth of new products and increasing competition in the market from generic versions of branded drugs, pharmaceutical companies are increasingly moving towards collaborations with biotechnology companies. To make the drug discovery process more efficient and to reduce the risk of launching their own new drugs, pharmaceutical companies are using strategies such as building partnerships or licensing to bring new medicines in the market and replenish their pipelines.

Under such licensing agreements, Pharmaceutical firms get rights to use the technology combined with discovery research and/or product development activities in which both the parties have a continuing role. This enhances the productivity of their internal R&D efforts. Large players in the industry mainly cooperate with smaller players by funding their R&D process by paying them Licensing fees while sharing information. These deals involve initial payments, milestone payments based on the successful completion of the R&D stage, and royalty receipts upon product commercialization. Pharmaceutical companies mostly enter into partnerships agreements to license developmental drugs with biotechnology companies who have novel therapeutic drugs in development. Such partnership agreements give the pharmaceutical companies access to innovative new technologies, promising compounds as well as letting them focus on their core functions such as manufacturing and marketing. It also gives larger organizations the flexibility to discontinue non-profitable projects thereby enabling them to control costs. It also gives them an opportunity to enter new therapeutic areas without investing into basic drug discovery and development process. On the other hand, Biotechnology companies benefit from the funding since the pharmaceutical companies are capable of generating cash from their on-patent drugs. They also benefit from expertise in regulatory approvals, manufacturing, and marketing & distribution (established supply chains) experience of the large pharmaceutical companies.

The global pharmaceutical outsourcing market is expected to reach to US$150B by 2015 from US$85B in 2011 representing CAGR of about 12%. Further, the contribution of outsourcing strategies adopted by pharmaceutical companies is expected to grow to 67% by 2015 representing CAGR of 12.5% during the period 2011 to 2015. Presently, the percentage of R&D outsourcing adopted by pharmaceutical and biotech companies together is estimated to be around 37%. Within the outsourcing industry, the market value of Contract Research Outsourcing currently is estimated around US$40.5B, wherein chemistry- based research service contributes about 25% (approximately US$ 10.7B) and biology–based research service contributes about 75%.[xxxvi]

7.5 Trends in Prostate Cancer and CLL

7.5.1 Prostate Cancer

Prostate Cancer is one of the major causes of death among men mostly in the age group above 65 years and is the sixth largest cause of death in men worldwide. It has a very high incidence rate, much higher than lung and colorectal cancer. In 2008, it was found that Prostate cancer was the second most commonly found disease in economically developed countries. The key drivers for this market are the increasing ageing population, increasing Prostate cancer cases and rising demand for new and novel drugs that address unmet needs such as improved survival time, less toxicity, increased progression free survival, and lower cost. However, increasing pricing pressure in the developed markets and low success rates is inhibiting the growth of the global Prostate cancer market.

The Prostate cancer cases are expected to grow at a CAGR of 2.9% from 899,000 in 2008 to 1.7MM in 2030. [xxxvii] According to Datamonitor, the number of cases in the seven developed economies (U.S., Japan, France, Germany, Italy, Spain and the UK) was 518,700 in 2010 which are expected to increase by 43% by 2020. [xxxviii]

The global Prostate cancer therapeutics market is estimated to be $2.7B in 2010 and it is expected to reach $6.5B by 2020. In 2010, Europe and North America had a market share of 43% and 42% respectively. [xxxix]

Some of the key firms include Sanofi-Aventis (France), Ipsen (France), Dendreon Corporation (U.S.), Tolmar Inc (U.S.), Abbott (U.S.), Indevus Pharmaceuticals Inc (U.S.), AstraZeneca PLC (U.K.), Astellas Pharma Inc (Japan), and Ferring Pharmaceuticals (Switzerland). Currently, there are a lot of new players that are entering the market such as Active Biotech, Bristol Myers-Squibb, Teva Pharmaceuticals Industries Ltd, and Johnson & Johnson (Zytiga).

7.5.2 Leukemia

Leukemia is a type of blood cancer that affects 0.0148% of men and 0.009% of women globally and has very limited treatments available. During the time duration 2015-2020, the Leukemia therapeutics market is expected to grow at a CAGR of 3.8% to reach US$11.3B by 2020 from US$6.3B in 2010[xl]. The North American region had a market share of 61.9% (2010) and 'Gleevec' drug dominated with a market share of 55.5% of the total sales of Leukemia drugs in 2010. [xli] According to the report 'Facts and Figures 2013' published by American Leukemia and Lymphoma Society, in 2013, there were 48,610 total number of new Leukemia cases reported in the U.S. [xlii]

Chronic Lymphocytic Leukemia (CLL) is a type of Leukemia and accounts for about 35% of all leukemic patients. It is known to affect adult males and is not commonly found to affect children. Annual estimates of newly diagnosed CLL cases amount to approximately to 15,000 in the U.S. (American Leukemia Lymphoma Society, Facts 2012), 14,000 in Europe and 130,000 worldwide (Globocan 2008)[xliii]. It has been found that 90% of the patients affected by CLL are middle aged and the probability increases in the 50+ age bracket. The CLL market is expected to grow at a CAGR of 13.4% between the time duration 2015-2020. No region had a high market share of 61.2% (2010) and 'Campath' drug dominated with a market share of around 42.3% (2010).[xliv]

Acute Myeloid Leukemia, being the second most frequent form of Leukemia after CLL, constitutes about 30% of all leukemic patients. According to American Leukemia Lymphoma Society, Facts 2013, annual estimates of newly diagnosed AML cases amounted to 14,600 in the U.S., 18500 in Europe as per RARECARE Working Group, 2012. Furthermore, according to Globocan, 110,000 cases were recorded worldwide in 2008.[xlv]

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder resulting from the neoplastic transformation of the primitive hematopoietic stem cell. The disease is monoclonal in origin, affecting myeloid, monocytic, erythroid, megakaryocytic, B-cell, and, sometimes, T-cell lineages. Bone marrow stromal cells are not involved. It accounts for 15% of all leukemias in adults with approximately 5,430 new cases diagnosed in 2012 and an estimated 610 deaths in 2012.[xlvi]
According to the report 'Facts & Figures 2013' published by American Leukemia and Lymphoma Society, in all, there were approximately 2.5MM patients living in the U.S. with Acute Lymphoblastic Leukemia (ALL), AML, CLL and CML.[xlvii]

7.6 Licensing Activities

7.6.1 Licensing Activities in Q1 2014

Licensing activities have become an important strategy for large pharmaceutical and small biotech companies. The licensing activity related to Pharmaceuticals industry declined in Q1 2014 compared to Q4 2013. A total of 462 new licensing agreements were signed (34% decline Q-o-Q from 700 deals in Q4'2013, and decline 29.4% Y-o-Y from 654 deals in Q1'2013). The largest deal, potentially valued at US$2.3B took place in Q1 2014 between the Ablynx and Merck & Co.[xlviii]

7.7 French Pharmaceutical Industry [xlix] [l] [li]

The French pharmaceuticals industry contributes significantly to the French economy. In 2008, the pharmaceutical industry stood at €47B (US$58B) surpassing Germany to become the world's third-largest pharmaceutical market. Exports contribute 45% of the French pharmaceutical industry and generate a €7B (US$8.7B) trade surplus. The pharmaceutical industry has created over 100,000 direct and 310,000 indirect jobs in the country with around 2,500 jobs created per year. Moreover, According to the Business Monitor International report on "France Pharmaceutical and Healthcare Report", France's pharmaceutical industry stood at €33.02B (US$43.91B) in 2013 representing a decline of 3.4% in local currency terms from €34.17B (US$43.40B) in 2012[lii].

France is the second largest country in Europe in terms of GDP and population, and therefore, the per capita consumption of pharmaceutical drugs has been historically high. The per capita drug consumption is high. Furthermore, French patients have to pay relatively little for their medicines as a large proportion of the medicine costs are borne by statutory and supplementary health insurance, which is held by almost 90% of the population.

Given the focus on fiscal consolidation, the French government had implemented many cost containment measures in 2010 and 2011 which are expected to get more stringent in the following years. These measures could lead to savings of around €910MM and €40MM through price cuts for generic medicines and reimbursement listing respectively. This would mean lesser healthcare spending by the country impacting the pharmaceutical industry. The targeted growth for pharmaceutical spending is 2.5% for the time period 2012-2015 (lower than 2.8% in 2011).

The French generics market is expected to grow rapidly due to provision of government incentives and the loss of patent protection for several high-volume products. However, despite several patent expires in the coming years, patented medicines are still expected to represent about two-thirds of the market (€18.1B) by 2015. The high number of users of patented medicines on a per capita basis, and health needs of an aging population provides significant opportunities to new drug makers.

France is one of Europe's largest producers of drugs with over 210 production sites. This has attracted a lot of investment in France. Some of the key drivers for the industry are adoption of high-value innovative treatments driven by an aging population, physician preference for prescribing branded drugs and patient brand loyalty. However, Pharmaceutical companies in France are subject to 13 levies[liii], apart from national and local taxes, which have been imposed to provide finances to several health agencies and to control spending on health insurance. This factor is a hurdle to investment. However, the French Health Industries Strategic Advisory Board is proposing a change in the complex tax structure in the pharmaceutical industry to overcome this hurdle.

8. Valuation

The Fair Market Value for all of Hybrigenics shares stands between €76MM and €101MM as of June 23, 2014. The Fair Market Value for one of Hybrigenics's publicly traded regular shares stands between €2.93 and €3.90 as of June 23, 2014. The valuation approach followed is the Discounted Cash Flow method.

8.1 Discounted Cash Flow Method

Valuation

WACC

Risk-free rate	2.0%[liv]
Beta	0.8[lv]
Market Return	12.4%[lvi]
Additional Risk Premium	3.0%
Cost of Equity	12.7%
Cost of Debt	2.3%
Terminal Growth Rate	1.0%
WACC (Discount Rate)	12.5%

Figures are in '000 €, unless indicated otherwise.

KEY VARIABLES

Market share in terms of patients tapped	Licensing Revenue (Upfront, Milestone) and Royalty receipts	Success Rates
Refer to *Key Variables Analysis* section		

Year Ending - December	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
FCFF (High)*								
Net cash from operating activities	(4,166)	4,365	11,848	7,299	1,697	9,109	10,731	5,265
Capital Expenditure	-	-	-	-	-	-	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	(4,166)	4,365	11,848	7,299	1,697	9,109	10,231	4,765
Discount factor	0.89	0.79	0.70	0.62	0.55	0.49	0.44	0.39
Present Value of FCFF	(3,703)	3,448	8,318	4,555	941	4,490	4,483	1,855
FCFF (Low)*								
Net cash from operating activities	(4,278)	2,878	7,827	4,777	276	5,695	7,189	3,785
Capital Expenditure	-	-	-	-	-	-	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	(4,278)	2,878	7,827	4,777	276	5,695	6,689	3,285
Discount factor	0.89	0.79	0.70	0.62	0.55	0.49	0.44	0.39
Present Value of FCFF	(3,802)	2,274	5,496	2,981	153	2,807	2,931	1,279

** In the model, the valuation is continued to the year 2032, from which point the terminal value is established. For all data refer to the Appendix section 9.*

Arrowhead Fair Value Bracket	High	Low	
Terminal Value (TV)	248,035	205,710	
Present Value of TV	29,714	24,644	
Present value of FCF	69,501	49,370	
Present Value of FCF + TV	99,215	74,013	
Net Debt	(1,899)	(1,899)	lvii
Equity Value Bracket	**101,114**	**75,912**	
Shares on issue ('000)	25,921	25,921	lviii
Fair Share Value Bracket (€)	**3.90**	**2.93**	
Current Market price (€)	2.66	2.66	lix
Current Market Cap. (€) MM	69	69	
Target Market Cap. Bracket (€) MM	101	76	

Approach for DCF Valuation

Time Horizon: The Arrowhead fair valuation for Hybrigenics is based on the Discounted Cash Flow (DCF) method. The time period chosen for the valuation is 240 months (2014E-2033E).

Terminal Value: Terminal Value is estimated to depend on a terminal growth rate of 1%, as most of the drugs patents expiry following which the revenue generated from sales of these drugs is expected to drop due to price erosion.

Prudential nature of valuation: It should be noted that this Arrowhead Fair Value Bracket estimate is a relatively prudential estimate, as it discounts the eventuality of any of Hybrigenics' other R&D projects other than the Prostate Cancer and CLL drug programs.

Key variables: The upper and lower bounds in the estimation correspond to the extreme positions taken by the following key variables:

Market Share: Percentage of patients tapped– Prostate Cancer

Table 3: Market share: Percentage of patients tapped – Prostate Cancer

%	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.04%	0.18%	0.62%	1.21%	1.49%	1.56%	1.59%	1.59%	1.61%	1.21%	1.00%	0.75%
High estimate	0.05%	0.18%	0.62%	1.22%	1.50%	1.57%	1.60%	1.60%	1.61%	1.22%	1.02%	0.75%

Market Share: Percentage of patients tapped– CLL

Table 4: Market share: Percentage of patients tapped – CLL

%	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Low estimate	0.13%	0.13%	0.15%	0.17%	0.60%	0.50%	0.55%	0.70%	0.82%	0.70%	0.60%	0.52%
High estimate	0.14%	0.14%	0.15%	0.18%	0.61%	0.52%	0.60%	0.75%	0.85%	0.72%	0.62%	0.50%

Revenue from Upfront and Milestone Receipts – Prostate Cancer

Table 5: Revenue from Upfront and Milestone Payments – Prostate Cancer

€ MM	2016E	2017E	2018E	2019E	2020E	2021E	Estimated Deal value (MM)
Low estimate	29	4	18	31	31	3	**€115**
High estimate	34	4	18	36	36	3	**€130**

Revenue from Upfront and Milestone Receipts – CLL

Table 6: Revenue from Upfront and Milestone Payments – CLL

€ MM	2014E	2015E	2016E	2017E	2018E	2019E	Estimated Deal value (MM)
Low estimate	5	37	25	21	21	21	**€130**
High estimate	5	40	30	22	22	21	**€140**

Royalty Receipts – Prostate Cancer

Table 7: Royalty Receipts – Prostate Cancer

€ MM	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.5	2.2	7.9	16.1	20.8	22.8	24.3	25.4	26.9	21.2	18.3	14.4
High estimate	0.7	2.6	9.5	19.5	25.1	27.5	29.3	30.7	32.3	25.6	22.4	17.2

Royalty Receipts – CLL

Table 8: Royalty Receipts – CLL												
€ MM	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Low estimate	2.6	3.0	4.0	5.0	20.8	19.7	24.6	35.6	47.3	45.7	44.3	43.2
High estimate	3.4	3.9	4.8	6.4	25.3	24.5	32.2	45.7	58.9	56.4	54.9	49.9

Success Probability – Prostate Cancer

Table 9: Probability of Occurrence (Success) – Prostate Cancer							
%	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	25%	50%	70%	75%	80%	85%	100%
High estimate	30%	55%	75%	80%	80%	85%	100%

Success Probability - CLL

Table 9: Probability of Occurrence (Success) – CLL							
%	2014E	2015E	2016E	2017E	2018E	2019E	2020E-2033E
Low estimate	30%	67%	72%	75%	85%	85%	100%
High estimate	35%	70%	75%	80%	87%	90%	100%

Note: Refer the Key variable Section 4, for more details.

8.2 NPV Method Based on Peak Sales

Arrowhead has done an NPV valuation of Hybrigenics on the basis of peak sales for each drug program by applying success rates based on the stage of each drug program.

Valuation – NPV Based on Peak Sales

Assumptions

Current Year	2014
Discount Rate	12.5% [lx]
Shares outstanding ('000)	25,921
Pharmaceutical Industry – PE (x)	12.50x [lxi]

Table 22: NPV Based on Peak Sales

Drug Name	Indication	Current Status	Estimated launch	Years to Launch	Years to peak	Success rate		Peak Royalty - EUR '000		Deal Value (€ '000)		Risk Adjusted Total Sales (€ '000)		Profitability		Adjusted NPV - after applying success rate rNPV (€ '000)	
						Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
Inecalcitol	Prostate Cancer	Phase 2	2022	9	8	25%	30%	26,921	32,305	115,000	130,000	35,480	48,691	19.0%	21.0%	2,625	3,982
Inecalcitol	CLL	Phase 2	2020	7	8	30%	35%	47,350	58,899	130,000	140,000	53,205	69,615	19.0%	21.0%	3,937	5,693
																6,562	**9,675**

	Low	High
Fair value (Intrinsic) (€)	**3.16**	**4.67**

Sensitivity Table - High

		10.50	11.50	12.50	13.50	14.50
Discount Rate (%)	10.5%	4.52	4.95	5.39	5.82	6.25
	11.5%	4.21	4.61	5.01	5.41	5.81
	12.5%	3.92	4.29	4.67	5.04	5.41
	13.5%	3.65	4.00	4.35	4.69	5.04
	14.5%	3.40	3.73	4.05	4.38	4.70

Sensitivity Table - Low

		10.50	11.50	12.50	13.50	14.50
Discount Rate (%)	10.5%	3.07	3.36	3.65	3.94	4.24
	11.5%	2.85	3.13	3.40	3.67	3.94
	12.5%	2.66	2.91	3.16	3.42	3.67
	13.5%	2.48	2.71	2.95	3.18	3.42
	14.5%	2.31	2.53	2.75	2.97	3.19

8.3 Project NPV

Arrowhead has calculated the NPV for each of the two drug programs based on the estimated operating cash flows in the high-bracket scenario, by applying the success rates based on current stage of the drug program and then discounting the same.

8.3.1 Prostrate Cancer Drug Program

Table 23: NPV Calculations (€ '000)	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Revenue - High	-	-	33,500	3,500	18,333	36,083	36,083	2,500	686
Cost and Expenses	5,254	5,247	5,276	5,290	9,475	9,512	7,049	3,213	3,127
EBIT	**(5,254)**	**(5,247)**	**28,224**	**(1,790)**	**8,859**	**26,571**	**29,034**	**(713)**	**(2,442)**
Success Rate	100%	100%	30%	55%	75%	80%	80%	100%	100%
Risk Adjusted Cash flow	(5,254)	(5,247)	8,467	(984)	6,644	21,257	23,227	(713)	(2,442)
Year	1	2	3	4	5	6	7	8	9
Discount factor	0.89	0.79	0.70	0.62	0.55	0.49	0.44	0.39	0.35
Present Value	(4,670)	(4,145)	5,945	(614)	3,685	10,479	10,177	(278)	(845)

NPV Calculations (€'000)	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
Revenue - High	2,607	9,489	19,533	25,126	27,512	29,333	30,687	32,305	25,610	22,400
Cost and Expenses	3,603	5,561	6,452	7,603	8,857	10,163	10,342	10,437	9,288	8,934
EBIT	**(996)**	**3,928**	**13,081**	**17,522**	**18,656**	**19,170**	**20,345**	**21,868**	**16,322**	**13,466**
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	(996)	3,928	13,081	17,522	18,656	19,170	20,345	21,868	16,322	13,466
Year	10	11	12	13	14	15	16	17	18	19
Discount factor	0.31	0.27	0.24	0.22	0.19	0.17	0.15	0.13	0.12	0.11
Present Value	(306)	1,074	3,179	3,785	3,581	3,271	3,085	2,947	1,955	1,434
Net Present value of cash flow (rNPV)	**44,563**									

8.3.2 CLL Drug Program

Table 24: NPV Calculations (€ '000)	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Revenue - High	5,000	40,000	30,000	22,000	22,000	21,000	3,418	3,923	4,824
Cost and Expenses	5,254	6,997	7,035	7,053	12,633	12,683	9,399	4,284	4,170
EBIT	**(254)**	**33,003**	**22,965**	**14,947**	**9,367**	**8,317**	**(5,981)**	**(361)**	**654**
Success Rate	35%	70%	75%	80%	87%	90%	90%	90%	90%
Risk Adjusted Cash flow	(89)	23,102	17,224	11,928	8,149	7,469	(5,383)	(325)	589
Year	1	2	3	4	5	6	7	8	9
Discount factor	0.89	0.79	0.70	0.62	0.55	0.49	0.44	0.39	0.35
Present Value	(79)	18,250	12,093	7,443	4,520	3,682	(2,358)	(126)	204

NPV Calculations (€'000)	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
Revenue - High	6,396	25,338	24,548	32,190	45,728	58,899	56,419	54,885	49,855	48,292
Cost and Expenses	4,804	7,414	8,603	10,138	11,809	13,551	13,790	13,916	12,383	11,912
EBIT	**1,592**	**17,924**	**15,944**	**22,052**	**33,919**	**45,348**	**42,629**	**40,969**	**37,471**	**36,380**
Success Rate	90%	95%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	1,433	17,028	15,944	22,052	33,919	45,348	42,629	40,969	37,471	36,380
Year	10	11	12	13	14	15	16	17	18	19
Discount factor	0.31	0.27	0.24	0.22	0.19	0.17	0.15	0.13	0.12	0.11
Present Value	441	4,656	3,875	4,763	6,512	7,737	6,465	5,522	4,489	3,874
Net Present value of cash flow (rNPV)	**88,087**									

See important disclosures on page 37 of this report

Important information on Arrowhead methodology

The principles of the valuation methodology employed by Arrowhead BID are variable to a certain extent depending on the subsectors in which the research is conducted, but all Arrowhead valuation research possesses an underlying set of common principles and a generally common quantitative process.

With Arrowhead Commercial and Technical Due Diligence, Arrowhead extensively researches the fundamentals, assets and liabilities of a company, and builds solid estimates for revenue and expenditure over a coherently determined forecast period.

Elements of past performance, such as price/earnings ratios, indicated as applicable, are present mainly for reference purposes. Still, elements of real-world past performance enter the valuation through their impact on the commercial and technical due diligence.

Elements of comparison, such as multiple analyses may be to some limited extent integrated in the valuation on a project-by-project or asset-by-asset basis. In the case of this Hybrigenics report, there are no multiple analyses integrated in the valuation.

Arrowhead BID Fair Market Value Bracket

The Arrowhead Fair Market Value is given as a bracket. This is based on quantitative key variable analysis, such as key price analysis for revenue and cost drivers or analysis and discounts on revenue estimates for projects, especially relevant to those projects estimated to provide revenue near the end of the chosen forecast period. Low and high estimates for key variables are produced as a tool for valuation. The high-bracket DCF valuation is derived from the high-bracket key variables while the low bracket DCF valuation is based on the low bracket key variables.

In principle, an investor who is comfortable with the high-brackets of our key variable analysis will align with the high-bracket in the Arrowhead Fair Value Bracket, and likewise in terms of low estimates. The investor will also take into account the company intangibles – as presented in the first pages of this document in the analysis on strengths and weaknesses and on other essential company information. These intangibles serve as supplementary decision factors for adding or subtracting a premium in the investor's own analysis.

The bracket should be understood as a tool provided by Arrowhead BID for the reader of this report and the reader should not solely rely on this information to make his decision on any particular security. The reader must also understand that on one hand, global capital markets contain inefficiencies, especially in terms of information, and that on the other hand, corporations and their commercial and technical positions evolve rapidly: this present edition of the Arrowhead valuation is for a short to medium-term alignment analysis (one to twelve months). The reader should refer to important disclosures on page 37 of this report.

9. Appendix

Hybrigenics's Balance Sheet Forecast – High Estimates

Table 25: Consolidated Balance Sheet € '000	all figures in '000 € , unless stated differently					*High Bracket estimates*					
Year Ending December 31	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022A
Total current assets	6,195	6,784	7,273	19,790	32,558	36,909	41,500	53,804	60,476	59,407	60,518
Total Non-current assets	886	1,134	828	562	324	106	(100)	(295)	3	294	575
TOTAL ASSETS	**7,081**	**7,918**	**8,102**	**20,352**	**32,883**	**37,015**	**41,401**	**53,509**	**60,479**	**59,701**	**61,093**
Total current Liabilities	1,659	1,609	2,604	3,230	3,141	3,137	5,393	5,413	4,085	2,017	1,971
Total Non-current Liabilities	2,504	2,711	2,518	2,402	2,391	2,391	2,391	2,391	2,391	2,391	2,391
TOTAL LIABILITIES	**4,163**	**4,320**	**5,122**	**5,632**	**5,532**	**5,528**	**7,784**	**7,804**	**6,476**	**4,408**	**4,362**
Total Shareholder's Equity	2,918	3,598	2,980	14,720	27,351	31,487	33,617	45,705	54,003	55,293	56,731
TOTAL LIABILITIES & EQUITY	**7,081**	**7,918**	**8,102**	**20,352**	**32,883**	**37,015**	**41,401**	**53,509**	**60,479**	**59,701**	**61,093**

Hybrigenics's Balance Sheet Forecast – Low Estimates

Table 26: Consolidated Balance Sheet € '000	all figures in '000 € , unless stated differently					*Low Bracket estimates*					
Year Ending December 31	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022A
Total current assets	6,195	6,784	7,023	17,483	25,301	28,332	31,451	39,380	42,921	41,189	41,755
Total Non-current assets	886	1,134	828	562	324	106	(100)	(295)	3	294	575
TOTAL ASSETS	**7,081**	**7,918**	**7,852**	**18,045**	**25,626**	**28,437**	**31,352**	**39,085**	**42,924**	**41,483**	**42,330**
Total current Liabilities	1,659	1,609	2,604	3,230	3,141	3,137	5,393	5,413	4,085	2,017	1,935
Total Non-current Liabilities	2,504	2,711	2,518	2,402	2,391	2,391	2,391	2,391	2,391	2,391	2,391
TOTAL LIABILITIES	**4,163**	**4,320**	**5,122**	**5,632**	**5,532**	**5,528**	**7,784**	**7,804**	**6,476**	**4,408**	**4,326**
Total Shareholder's Equity	2,918	3,598	2,730	12,413	20,094	22,909	23,568	31,281	36,448	37,075	38,004
TOTAL LIABILITIES & EQUITY	**7,081**	**7,918**	**7,852**	**18,045**	**25,626**	**28,437**	**31,352**	**39,085**	**42,924**	**41,483**	**42,330**

FCFF Calculation (2022E-2032E) – Continued from page 28

Table 27: Year Ending – December (€ '000)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
FCFF (High)											
Net cash from operating activities	1,762	2,429	10,438	17,444	22,581	29,428	36,273	38,077	37,648	34,913	31,651
Capital Expenditure	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	1,262	1,929	9,938	16,944	22,081	28,928	35,773	37,577	37,148	34,413	31,151
Discount factor	0.35	0.31	0.27	0.24	0.22	0.19	0.17	0.15	0.13	0.12	0.11
Present Value of FCFF	437	594	2,717	4,118	4,769	5,553	6,104	5,699	5,007	4,123	3,317
FCFF (Low)											
Net cash from operating activities	1,225	1,691	8,239	13,795	17,421	22,561	28,286	29,936	29,581	28,256	26,125
Capital Expenditure	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	725	1,191	7,739	13,295	16,921	22,061	27,786	29,436	29,081	27,756	25,625
Discount factor	0.35	0.31	0.27	0.24	0.22	0.19	0.17	0.15	0.13	0.12	0.11
Present Value of FCFF	251	366	2,116	3,231	3,655	4,235	4,741	4,464	3,920	3,325	2,728

10. Analyst Certifications and Important Disclosures

Analyst certifications

I, Snehal Mahajan, certify that all of the views expressed in this research report accurately reflect my personal views about the subject security and the subject company, based on the collection and analysis of public information and public company disclosures

Important disclosures

Arrowhead Business and Investment Decisions, LLC received fees in 2012, 2013 and 2014 from Hybrigenics for researching and drafting this report and for a series of other services to Hybrigenics including distribution of this report and networking services. Neither Arrowhead BID nor any of its principals or employees own any long or short positions in Hybrigenics.

Aside from certain reports published on a periodic basis, the large majority of reports are published by Arrowhead BID at irregular intervals as appropriate in the analyst's judgment.

Any opinions expressed in this report are statements of Arrowhead BID's judgment to this date and are subject to change without notice.

This report was prepared for general circulation and does not provide investment recommendations specific to individual investors. As such, any of the financial or other money-management instruments linked to the company and company valuation described in this report, hereafter referred to as "the securities", may not be suitable for all investors.

Investors must make their own investment decisions based upon their specific investment objectives and financial situation utilizing their own financial advisors as they deem necessary.

Investors are advised to gather and consult multiple sources of information while preparing their investment decisions. Recipients of this report are strongly advised to read the *Information on Arrowhead Methodology* section of this report to understand if and how the Arrowhead Due Diligence and Arrowhead Fair Value Bracket integrate alongside the rest of their stream of information and within their decision making process.

Past performance of securities described directly or indirectly in this report should not be taken as an indication or guarantee of future results. The price, value of, and income from any of the financial securities described in this report may rise as well as fall and may be affected by simple and complex changes in economic, financial and political factors.

Should a security described in this report be denominated in a currency other than the investor's home currency, a change in exchange rates may adversely affect the price of, value of, or income derived from the security.

This report is published solely for information purposes, and is not to be considered in any case as an offer to buy any security, in any state.

Other than disclosures relating to Arrowhead Business and Investment Decisions, LLC, the information herein is based on sources Arrowhead BID believes to be reliable but is not guaranteed by Arrowhead BID and does not purport to be a complete statement or summary of the available data.

Arrowhead Business and Investment Decisions, LLC is not responsible for any loss, financial or other, directly or indirectly linked to any price movement or absence of price movement of the securities described in this report.

11. Notes and References

[i] Source: Bloomberg, June 20, 2014
[ii] 52 weeks to June 20, 2014. Source: Bloomberg June 20, 2014
[iii] 3 months to June 20, 2014. Source: Bloomberg June 20, 2014
[iv] Arrowhead Business and Investment Decisions Fair Value Bracket – AFVBTM. See information on valuation on pages 28-33 of this report and important disclosures on page 37 of this report.
[v] Source: http://www.reuters.com/article/2011/06/26/pharmaceuticals-rd-idUSL6E7HO1BL20110626
[vi] Source: http://www.evaluategroup.com/public/PressReleases/Return-to-Growth-for-Pharmaceutical-Sector-World-Preview-2013-Outlook-to-2018.aspx
[vii] Source: http://www.espicom.com/prodcat2.nsf/Product_ID_Lookup/00000341?OpenDocument
[viii] Source: http://www.thefreelibrary.com/Research+and+Markets%3A+France+Pharmaceuticals+and+Healthcare+Report+Q1...-a0277263302
[ix] Source: Company Website and Company Documents
[x] Source: Company Management
[xi] Source: Arrowhead BID estimate
[xii] Source: Arrowhead BID estimate
[xiii] Source: Company website – Press Release section
[xiv] Source: Company Documents and website
[xv] Source: Drug Discovery and Development Report, "Understanding the R&D process" By Innovation.org (http://www.innovation.org/drug_discovery/objects/pdf/RD_Brochure.pdf)
[xvi] Source: Drug Discovery and Development Report, "Understanding the R&D process" By Innovation.org (http://www.innovation.org/drug_discovery/objects/pdf/RD_Brochure.pdf)
[xvii] Source: Drug Development Process, Addie D. Anderson, CRB Consulting Engineers Inc.
[xviii] Source: http://www.pharmatimes.com/mobile/12-05-17/EU_Parliament_seeks_urgent_review_of_drug_monitoring.aspx
[xix] Source: http://www.raps.org/focus-online/news/news-article-view/article/1426/new-french-regulatory-agency-announces-transition-of-leadership.aspx
[xx] Source: http://www.espicom.com/
[xxi] Source: http://www.imshealth.com
[xxii] Source: http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf
[xxiii] Source: http://en.wikipedia.org/wiki/Biopharmaceutical
[xxiv] Source: " Leadership in affordable therapeutic products, A Biopharma Strategy for India", Report by Association of Biotechnology Led Enterprises and PWC (Vision 2020)
[xxv] Source: http://www.prlog.org/10979786-biopharmaceuticals-market-is-projected-to-grow-by-cagr-2006-2015-of-124-to-touch-1825bn.html
[xxvi] Source: " Leadership in affordable therapeutic products, A Biopharma Strategy for India", Report by Association of Biotechnology Led Enterprises and PWC (Vision 2020)
[xxvii] Source: http://cmr.thomsonreuters.com/pdf/fb-exec-2013.pdf
[xxviii] Source: http://www.evaluategroup.com/public/PressReleases/Return-to-Growth-for-Pharmaceutical-Sector-World-Preview-2013-Outlook-to-2018.aspx
[xxix] Source: http://www.evaluategroup.com/public/PressReleases/Return-to-Growth-for-Pharmaceutical-Sector-World-Preview-2013-Outlook-to-2018.aspx
[xxx] Source: http://cmr.thomsonreuters.com/pdf/fb-exec-2013.pdf
[xxxi] Source: Bernstein Research "The Long view – R&D Productivity", September 30, 2010, Boston Consulting Group (http://www.bcg.com/documents/file80247.pdf)
[xxxii] Source: BCG analysis: http://www.bcg.com/documents/file80247.pdf
[xxxiii] Source: Drug Discovery and Development Report, "Understanding the R&D process" By Innovation.org (http://www.innovation.org/drug_discovery/objects/pdf/RD_Brochure.pdf)
[xxxiv] Source: "Drug discovery industry must embrace open source innovation to speed process, boost bottom lines" Report, by Frost & Sullivan (http://www.centerwatch.com/news-online/headline-details.aspx?HeadlineID=1021)

[xxxv] Source: http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf
[xxxvi] Source: http://www.lifescienceleader.com/
[xxxvii] Source: http://www.prnewswire.com/news-releases/marketsandmarkets-global-prostate-cancer-therapeutics-market-worth-6457-million-by-2020-134024528.html
[xxxviii] Source: www.datamonitor.com/
[xxxix] Source: http://www.prnewswire.com/news-releases/marketsandmarkets-global-prostate-cancer-therapeutics-market-worth-6457-million-by-2020-134024528.html
[xl] Source: http://www.prnewswire.com/news-releases/marketsandmarkets-leukemia-therapeutics-market-worth-113-billion-by-2020-134228963.html
[xli] Source: http://www.marketsandmarkets.com/Market-Reports/chronic-lymphocytic-leukemia-223.html
[xlii] Source: Company Presentation, May 2014
[xliii] Source: Company Press Release
[xliv] Source: http://www.marketsandmarkets.com/Market-Reports/chronic-lymphocytic-leukemia-therapeutics-market-519.html
[xlv] Source: Company Press Release
[xlvi] Source: http://www.cancernetwork.com/cancer-management/CML
[xlvii] Source: Company Presentation, May 2014
[xlviii] Source: https://lsconnect.thomsonreuters.com/top-pharma-deals-q1-2014/
[xlix] Source: http://www.thefreelibrary.com/Research+and+Markets%3A+France+Pharmaceuticals+and+Healthcare+Report+Q1...-a0277263302
[l] Source: http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=715249&pageID=1&sk=&date=
[li] Source: http://www.espicom.com
[lii] Source: http://store.businessmonitor.com/france-pharmaceuticals-healthcare-report.html
[liii] Source: http://www.reportlinker.com/p0187683/France-Pharmaceuticals-and-Healthcare-Report-Q2.html
[liv] Source: Bloomberg
[lv] Source: Bloomberg
[lvi] Source: Bloomberg
[lvii] Source: Company Documents, Cash (as on December 31, 2013) and Arrowhead estimates, Debt (As on December 31, 2013)
[lviii] Shares as on June 20, 2014
[lix] Source: Bloomberg, June 20, 2014
[lx] Source: WACC calculation Shown on Page 28
[lxi] Source: Arrowhead estimates