ARROWHEAD
BUSINESS AND INVESTMENT DECISIONS

Diligence and Valuation Report

Arrowhead Code:	69-02-05
Coverage initiated:	29 April 2012
This document:	02 June 2015
Fair share value bracket – DCF:	€2.50– €3.05
Share price: 01 June 2015:	€1.86[i]

Analyst Team

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

NYSE Alternext

HYBRIGENICS

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

Market Data

52-Week Range:	€1.17– €2.78[ii]
Average Daily Volume (3M Avg.):	695,452[iii]
Market Cap (01 June. 2015) :	€66.5 MM

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

	'15E	'16E	'17E	'18E	'19E	'20E	'21E
High NI (MM)	(15.75)	8.52	2.34	6.46	17.07	14.41	6.60
High EPS	(4.40)	2.38	0.65	1.81	4.77	4.03	1.84
Low NI (MM)	(15.75)	3.35	0.54	4.58	11.89	10.40	5.93
Low EPS	(4.40)	0.94	0.15	1.28	3.32	2.91	1.66

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 R&D 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 completed, Chronic Myeloid Leukemia (CML) – Phase II and Acute Myeloid Leukemia (AML). In addition, Hybrigenics' research program also investigates the action of 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 €2.50 in the low bracket and €3.05 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. It has 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 rare diseases such as Prostate Cancer, CLL, CML, and AML; **(3)** Inecalcitol for CLL has been designated with Orphan drug status in Europe and the U.S.; **(4)** In addition to CLL, other indications such as AML and CML are also identified as potential orphan therapeutic indications for Inecalcitol **(5)** Completed phase II clinical trials pertaining to Inecalcitol in CLL, and commenced Phase II study in CML; **(6)** 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; **(7)** The Company's genomic studies and services division, Helixio acquired Illumina® NextSeq500 sequencer to offer tailor-made services to various researchers from life sciences based on next generation sequencing; **(8)** In the field of USPs inhibitors, Hybrigenics extended partnership with Servier, validating its belief on the Company's first-in-class mechanism applied to drug discovery against cancer; **(9)** The Company's has also licensed its patented USP inhibitors, HBX 41,108, to the Bio-Techne group as a reference pharmacological research tool.

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 €2.50 to €3.05 bracket calculated using the DCF method. Based on the Risk Adjusted Net Present Value (rNPV) 'Peak Sales' method, the fair value lies in the €2.36 to €3.12 bracket. The rNPV for the drug R&D programs for oral Inecalcitol for Prostate Cancer and CLL is €57MM and €55MM respectively.

See important disclosures on page 38 of this report

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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 €2.50 in the low bracket scenario and €3.05 in the high bracket scenario (DCF Valuation Method). Based on the NPV 'Peak Sales' method, the fair value lies in the €2.36 to €3.12 bracket. The rNPV for the drug R&D programs for oral Inecalcitol for Prostate Cancer and CLL is €57MM and €55MM, respectively.

Key Highlights:

1. Hybrigenics' clinical programs are based on 'Inecalcitol', for which the Company has received global exclusivity with respect to all therapeutic indications. Inecalcitol is recognized as a key ingredient in developing drugs for treating diseases such as Prostate Cancer, CLL, CML and AML. The Company has also recently acquired patents in the U.S. and Europe for the use of high doses of Inecalcitol.
2. Hybrigenics key drug, Inecalcitol for CLL, has been designated with an 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.
3. In addition to CLL; AML and CML are also identified as potential orphan therapeutic indications for Inecalcitol.
4. Phase II clinical trials pertaining to Inecalcitol in CLL have been completed. The encouraging results support the idea to test Inecalcitol in CML and AML as well.
5. The Company commenced Phase II clinical studies to evaluate the potential of Inecalcitol in combination with Imatinib (Geevec®) in CML patients and soon plans to initiate Phase II study on Inecalcitol in AML.
6. Hybrigenics has been awarded global exclusivity of 'Yeast Two-hybrid (Y2H) Screening' technology valid up to 2022, a specialized scientific service to identify and validate protein interactions in animals, plants or microbiological cells.
7. The Company's genomic studies and services division, Helixio acquired Illumina® NextSeq500 sequencer to offer tailor-made services to various researchers from life sciences based on next generation sequencing.
8. In the field of USPs inhibitors, Hybrigenics extended its partnership with Servier, validating its belief on the Company's first-in-class mechanism applied to drug discovery against cancer.
9. Hybrigenics has out-licensed its first lead compound, HBX 41,108 (lead compound of ubiquitin-specific protease n°7 (USP7) inhibitors), a reference USP inhibitor for commercialization by Bio-Techne group and distributed by Fisher Scientific. This out-licensing deal exhibits the Company's ability to successfully transform its research on USP inhibitors into definitive valuable intellectual property assets for the next 12 to 17 years. Hybrigenics' total intellectual property on USP inhibitors amounts to 56 patents protecting four chemical families and is spread over more than 30 countries.
10. Global Pharmaceutical Industry Overview: The global pharmaceutical market is expected to grow at a CAGR of 3.9% to reach $1.2T over 2012-2017.[v] As per the 'World Preview report 2014' from market intelligence firm, Evaluate Ltd, the global pharmaceutical industry's R&D expenditure is expected to increase at a CAGR of 2.4% to reach $162B during the period 2013-2020. Primary drivers of recovery in the R&D expenditure is led by the improvement in R&D productivity, two years of excellent new drug approvals, and a replenished industry R&D pipeline. 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 $1,017B by 2020, equating to average annual growth of 5.1% over 2013-2020. [vi]
11. French Industry Overview: According to GlobalData, the French Pharmaceutical market is expected to grow at a slow pace i.e. CAGR of 0.7% from $46.2B in 2014 to $48.2B in 2020 owing to the growing focus on generic drugs.[vii] Factors leading to shift in preference for generic drugs in France are patent expirations, favourable regulatory regime, and several government incentives for physicians, pharmacists and patients to select generics drugs over branded drugs.

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.

2. Business Overview [viii]

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 CLL by oral administration.

In 2011, the Company collaborated with Necker Institute in Paris to conduct a basic research and design a clinical trial for 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 for conducting CLL trials. In July 2014, the Company completed the Phase II clinical trials. The observations from the results are expected to help the Company in designing the next step of clinical development of Inecalcitol for CLL. Also, in 2014, Inecalcitol was designated with Orphan drug status for the treatment of CLL in Europe and the U.S.

In addition to Inecalcitol for CLL, several researchers conducted a study on Inecalcitol's efficacy on the growth of human AML and 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. Further, following the positive results observed in the Phase II for CLL, the Company initiated a Phase II trial in CML on January 19, 2015 in combination with Imatinib (Gleevec®) and has plans to initiate a study on AML as well. To finance these expenses, the Company has raised €10.7MM (€6.1MM through a private placement and €4.6MM from the Crede Capital Group).

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'Oreal, 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.

On January 26, 2015, the Company extended its partnership with Servier, validating its belief on the Company's first-in-class mechanism applied to drug discovery against cancer. In September 2012, Hybrigenics Services had 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, to finance the acquisition cost and to enhance its genomics activities, the Company raised €1.3MM through private placement from Pradeyrol Development.

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:

Exhibit 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	Filing in 2009: already granted in Europe	2030	European Patent Office	According to Patent Cooperation Treaty (PCT), the same patent application is still

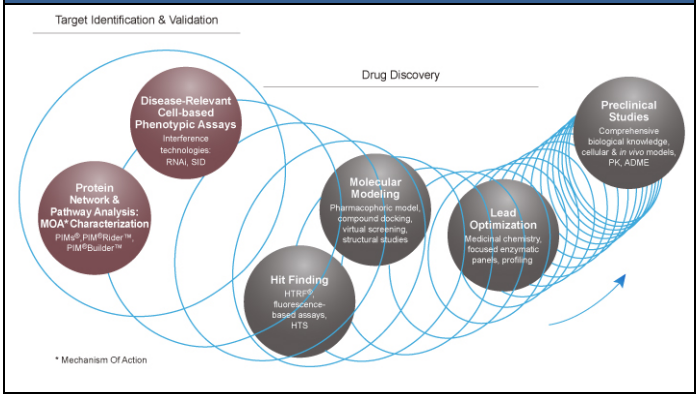
	milligram (mg) per day)				under process in countries such as Australia, Brazil, Canada, China, South Korea, India, Israel, Japan, Mexico, New-Zealand, Ukraine, Russia, and Singapore.
2	Therapeutic uses of high doses of Inecalcitol (doses higher than 1mg per day)	Filing in 2009: granted in the United States	2031	US Patent and Trademark Office	
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 oral drinking solutions	Filing in 2010: already granted in Europe for tablets and new generation of soft gelatine capsules	2031	European Patent Office	Tablets & New generation soft gel and capsules: Pending in the U.S. and rest of the world. Oral drinking solutions: ongoing PCT examination
5	Five patent families in total on USP inhibitors	Filed between 2005 and 2011: First chemical family granted in the U.S., Europe and rest of the world Fourth chemical family granted in Europe	First chemical family: mid 2029 in the US and mid – 2026 in Europe and rest of the world Fourth chemical family – 2031	European Patent Office	56 USP inhibitors are granted patents protecting four chemical families and spread over in 30+ countries. A fifth chemical family and a total of 38 patent applications are still pending examination worldwide.

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 constitutes about 18.4% of the revenue of the group in 2014.

Exhibit 2: 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.

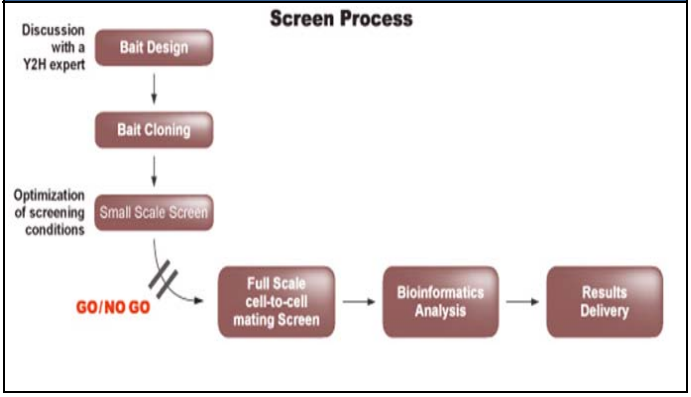
2.1.2 'Yeast Two-Hybrid' system (Protein Interaction Studies):

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 constitutes about 81.2% of the revenue of the group in 2014.

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

Exhibit 3: 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.

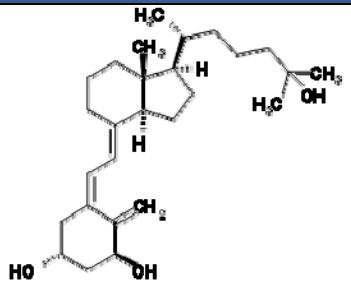
The Company has recently introduced new services to identify interactions between small molecules and protein targets. Using the Y2H model, small molecules can be used as "bait" against the cDNA or genomics libraries involving millions of "prey" protein fragments helping in identifying target proteins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

2.2 Technology

2.2.1 Inecalcitol, a Vitamin D3 Analogue

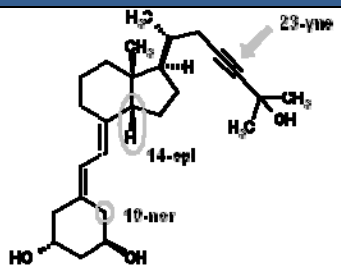
Inecalcitol is a synthetic chemical derivative of Calcitriol, the naturally active metabolite of vitamin D. Inecalcitol has been optimized to be more potent than Calcitriol and to play an active role in slowing down the growth of cancerous cells as well as hyper-proliferating normal cells, such as cells 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.

Exhibit 4: Calcitriol Chemical Structure



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

Exhibit 5: Inecalcitol Chemical Structure



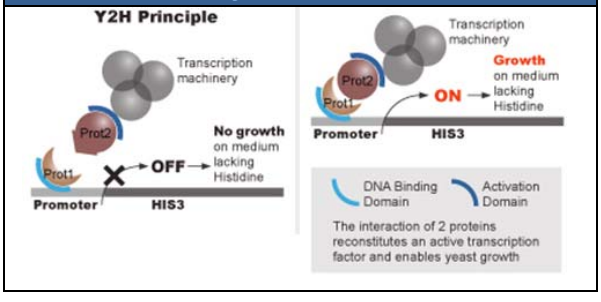
- Analogue of Calcitriol
- 10 times more potent on cell lines and 100 times less toxic than Calcitriol

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

Exhibit 6 : 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. Earlier, Prostate Cancer and CLL were identified for treatment by oral administration of Inecalcitol. Recently, studies conducted by researchers have inferred Inecalcitol to be effective for the treatment of CML and AML.

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 mg 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)

CLL is characterised by the hyper-proliferation of single kind of white blood cells called lymphocytes. 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 II clinical trials of oral Inecalcitol in patients with CLL. The funding for these trials was secured through a €3.3MM PIPE in March 2012. The open-label clinical study was 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.

In 2014, Inecalcitol, a key drug for the treatment of CLL was designated with Orphan drug status in Europe and the U.S. On July 16, 2014, the Company announced the end of 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: 21 out of 24 patients were treated with oral Inecalcitol (2 mg per day) for at least 4 to 23 months. The Blood Lymphocytes Counts (BLC) of 11 patients (52%) decreased or stabilized. Moreover, after 10 months of treatment, one out of these 11 patients experienced a -95% decrease in BLC and another patient showed -45% BLC reduction after 4 and 5 months of treatment. In case of 10 patients (48%), the BLC has increased at a regular exponential pace without any influence of treatment. Two patients experienced hypercalcemic adverse events attributable to Inecalcitol after 15 and 17 months of treatment.

2.3.3 Chronic Myeloid Leukemia (CML)

CML is a disease in which patients have many mature white blood cells and is characterized as a myeloproliferative disorder. In December 2013, preliminary studies conducted by Prof. Ali Turhan, Head of the Division of Hematology, Paris-sud 11 Kremlin-Bicetre University Hospital, inferred that Inecalcitol could be tested in CML patients in combination with Imatinib (Gleevec®) as a therapeutic indication for Inecalcitol. In July 2014, the French drug agency, authorized the Company to start Phase II clinical trials to study oral Inecalcitol in CML patients undergoing treatment using oral Imatinib with a stable but sub-maximal level of efficacy, as measured in blood by the BCR-ABL biomarker. The Company was granted authorization based on 1) antiproliferative effects of Inecalcitol and its synergy with Imatinib as validated by Prof. Thuran, and 2) positive results obtained in the clinical phase II study of Inecalcitol in CLL, where, blood leukemic lymphocytes counts stabilized or decreased in 52% of patients.

In January 2015, the Company announced the commencement of clinical phase II study of Inecalcitol in CML. The study is expected to enrol 54 CML patients within one year at across five centres in France, including Paris-Sud 11 Kremlin-Bicetre University Hospital and co-ordinated by Prof. Johnson-Ansah from Caen University Hospital. The study is expected to last until 2Q'2016. Application for orphan drug application is expected to be filed in 4Q'2015.

In the clinical phase II study in CML, oral Inecalcitol will be administered daily for one year with the dose of 4 mg in the patients undergoing treatment by oral Imatinib (Gleevec®) for more than two years. The objective of the clinical trial is to improve the CML patients' condition by reducing the BCR-ABL biomarker to 10 times lower or undetectable levels indicating prolong CML remission or even cure the disease by eliminating the stem cells.

2.3.4 Acute Myeloid Leukemia (AML)

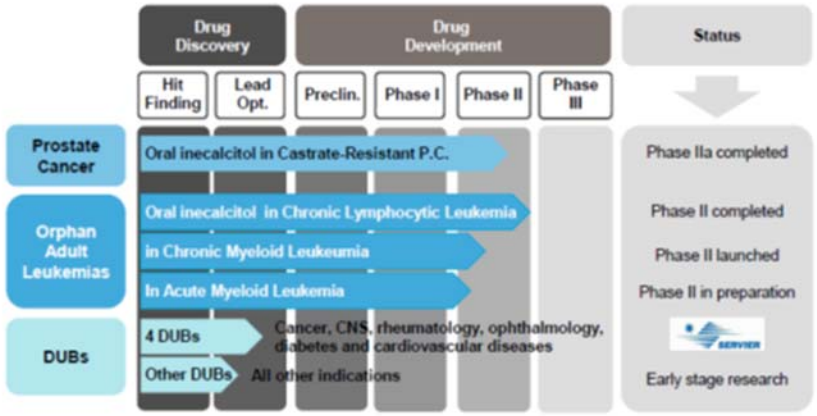
AML is a disorder wherein patients' have many immature white blood cells in their bone marrow that are not capable of maturing properly. In March 2014, the Company announced the results of the international group of researchers from France (Necker and Saint-Louis Hospitals in Paris), Belgium (Katholieke Universiteit Leuven), the United Kingdom (Wellcome Trust Sanger Institute in Hinxton) and Japan (National Cancer Research Institute in Tokyo) on the activity of Inecalcitol in 'in-vitro' and 'in-vivo' preclinical models of AML. The study concluded that Inecalcitol has demonstrated to be 1,000 fold more potent in 'in vitro' than the active metabolite of vitamin D to inhibit human AML cell lines. Also, treatment by Inecalcitol resulted in long delay to contract AML in genetically AML induced mice.

In June 2014, international group of researchers from France, Belgium and the United Kingdom concluded that Inecalcitol in combination with Azacytidine could inhibit the growth of human AML cell lines. Treatment of AML patients' (>65 years old or frail patients) with Inecalcitol in combination with hypomethylating agents, Azacytidine (Vidaza®, Celgene) and decitabine (Dacogen®, Janssen-Cilag) are inferred to have prolonged survival.

Currently the Company is planning to conduct Phase II study in 8 to 12 specialized centres by enrolling around 50 patients. The study is expected to commence in 4Q'2015. In parallel, an application for orphan drug designation based on preclinical evidence is expected to be filed in April 2015.

2.4 R&D Pipeline

Exhibit 7 : 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 (granted Orphan drug status). In addition, the company is planning/undergoing clinical trials 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.

- **Intellectual Property on USP Inhibitors:** The Company is considered as a pioneer in conducting research work in the field of USP inhibition by the scientific community. In 2014, its USP inhibitors were announced to have been transformed into a valuable intellectual property assets. Currently, Intellectual Property on USP inhibitors includes 56 granted patents protecting four chemical families and is spread across 30+ countries.

  In 2014, the Company's first patent on USP inhibitors in the U.S. was granted a three-year extension to mid-2029 as compared to mid-2026 in Europe and in the rest of the world. Further, its first family including HBX 41,108 is announced to be commercialized by the Bio-Tech group of companies and is distributed by Fischer Scientific, under Hybrigenics' worldwide license as a reference pharmacological research tool.

- **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

Exhibit 8: 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.

- **Strong Cash Position:** At the end of 2014, the Company recorded the strongest cash position of €9.4MM, since 2006. It successfully raised €11.75MM funding through two private placements (€6.1MM from French and Swiss investors, €4.6MM from US-based CREDE Capital Group, and €1.05MM from equity line agreement with the American fund Yorkville Global Advisors). As a result of this, Hybrigenics' is fully funded to bear the costs associated with the clinical development of Inecalcitol and business expansion activities pertaining to proteomic and genomic services.

- **Partnership with Servier extended:** Extension of partnership agreement with Servier validates its confidence in Hybrigenics' expertise in the field of USPs applied to drug discovery against cancer. Additionally, Servier has committed to provide the Company with an additional amount of €0.92MM.

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.

  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.

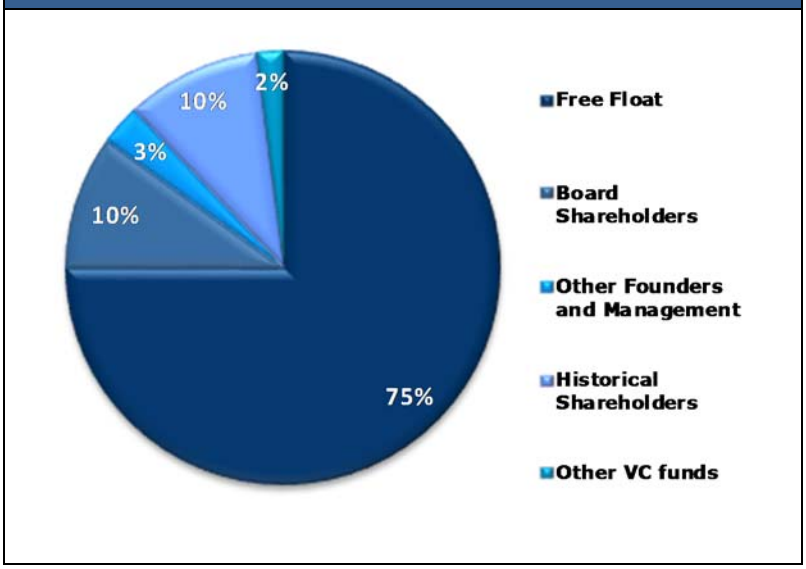
- **Increased Investments in Genomic Capabilities:** With the development of genomics in all the areas of life sciences, the use of genomic technologies too has gained importance in the fields of personalized medicine, quality control of biological pharmaceuticals or cosmetic, etc. Considering the increasing demand, Hybrigenics entered this segment by acquiring genomics division of Imaxio in 2013 and gained access to technologies based on DNA or RNA microarrays and on next generation sequencing.

  In order to expand its marketing activities, the Company in April 2014, established a new brand, Helixio®. Further to expand and intensify its services, in October 2014, the Company through Helixio acquired NextSeq500® sequencer from Illumina®, the world leader in next generation sequencing technologies. Through this acquisition, the Company intends to deliver customized sequencing services to meet the evolving needs of researchers from all life sciences.

2.8 Shareholding Pattern

The total basic shares outstanding are 35.8 MM as on 30 April, 2015 with a free float of 75%.

Exhibit 9 : Shareholding Pattern (As on December 31, 2014)
ix



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. Key variable analysis [x]

3.1 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 has recently completed with Phase II study. 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.

3.1.1 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:

Exhibit 10: 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%

3.1.2 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:

Exhibit 11: Market share: Percentage of patients tapped – CLL

%	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.13%	0.13%	0.15%	0.17%	0.60%	0.50%	0.55%	0.70%	0.82%	0.60%	0.52%	0.43%	0.35%	0.30%
High estimate	0.14%	0.14%	0.15%	0.18%	0.61%	0.52%	0.60%	0.75%	0.85%	0.61%	0.52%	0.44%	0.36%	0.32%

3.2 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 and CLL. The revenue from these partnerships 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

3.2.1 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.

Exhibit 12 : 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	2	**€115**
High estimate	34	4	18	36	36	2	**€130**

3.2.2 Revenue from Upfront and Milestone Payments – CLL

According to Arrowhead estimates, the expected deal value for CLL drug program lies between €122MM – €132MM. The upfront payments are expected to be in the range of €27MM in the low bracket and €30MM in the high bracket.

Exhibit 13: Revenue from Upfront and Milestone Payments – CLL

€ MM	2015E	2016E	2017E	2018E	2019E	Estimated Deal value (MM)
Low estimate	36	24	20	20	22	€122
High estimate	39	29	21	21	22	€132

3.3 Royalty Receipts

Royalty will be received on the annual revenue earned through sales. The forecasted sales are based on Arrowhead's estimate for (a) the market share for each drug (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.

3.3.1 Royalty Receipts – Prostate Cancer

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

Exhibit 14: 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	21.1	18.1	14.1
High estimate	0.7	2.6	9.5	19.5	25.1	27.5	29.3	30.7	32.3	25.5	22.2	17.0

3.3.2 Royalty Receipts – CLL

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

Exhibit 15: Royalty Receipts – CLL

€ MM	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	2.6	3.0	4.0	5.0	20.8	19.7	24.6	35.6	47.3	39.2	38.4	35.7	32.7	31.5
High estimate	3.4	3.9	4.8	6.4	25.3	24.5	32.2	45.7	58.9	47.8	46.0	43.8	40.4	40.4

3.4 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 i.e. 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).

3.4.1 Success Probability – Prostate Cancer

Exhibit 16: Probability of Occurrence (Success) – Prostate Cancer

%	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	25%	60%	70%	75%	82%	100%	100%
High estimate	30%	60%	75%	80%	85%	100%	100%

3.4.2 Success Probability – CLL

Exhibit 34: Probability of Occurrence (Success) – CLL

€ MM	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	45%	60%	85%	85%	85%	90%	100%
High estimate	45%	70%	90%	95%	90%	95%	100%

4. News [xi]

- **Hybrigenics presented new in vitro results on Inecalcitol in breast cancer at the ASCO meeting in Chicago, USA:** On May 29, 2015, Hybrigenics announced the results of tests conducted by Irish group of researchers to study the in vitro effects of Inecalcitol on the growth of human breast cancer cell lines in culture. It was found that both Inecalcitol and calcitriol effectively inhibited the proliferation and induced the death of breast cancer cells. There is a significant positive correlation between the effects of Inecalcitol and calcitriol and the levels of vitamin D receptors present in the cell lines: the more vitamin D receptors, the more cellular sensitivity. Both Inecalcitol and calcitriol were also significantly more active on breast cancer cell lines with estrogens receptors (ER-positive) than without (ER-negative). Inecalcitol was found to be at least 14 times more potent than calcitriol in vitro.

- **A joint project between PicoSeq, Hybrigenics, Ecole Normale Supérieure and CNRS is selected for the second phase of the French Worldwide Innovation Challenge:** On April 28, 2015, Hybrigenics announced the selection of their joint project for the second phase of the French Worldwide Innovation Challenge, which will focus on the development of a breakthrough technology for epigenetic analysis of DNA. The project is named "EPIGENETIX2", it will receive EUR1.2MM from BPIFrance and it has also been selected within the category of 'personalized medicine', one of the seven French strategic innovation goals for 2030.

- **Hybrigenics presented new in vitro results on Inecalcitol in CML at the American Association for Cancer (AACR) Research in USA:** On April 20, 2015, Hybrigenics announced the presentation by Prof. A. Turhan, from Inserm U935 and Paris-Sud University. In the study by the researchers it was observed, that Inecalcitol synergizes in vitro with dasatinib and nilotinib to inhibit the growth of stem cells isolated from CML patients.

- **Hybrigenics reaffirms its eligibility for the PEA-SMEs:** On April 9, 2015, Hybrigenics announced its eligibility for the PEA feature for SMEs. Investors can continue to integrate the actions within Hybrigenics accounts PEA-SME device dedicated to investment in small and mid-caps, benefiting the same tax advantages as the classic PEA.

- **Hybrigenics extended its partnership with Servier:** On January 26, 2015, Hybrigenics announced that it has extended its partnership with Servier to discover new drug inhibiting USPs. Since the initiation of its partnership in 2011, Servier has helped the Company to earn a revenue of around €4.3 MM. With the extension of this partnership agreement by one year, Servier has committed to help the Company earn additional revenue of €0.92MM.

- **Hybrigenics launched phase II study of Inecalcitol in CML:** On January 19, 2015, Hybrigenics announced that it has launched the clinical phase II study of Inecalcitol in CML, an orphan blood cancer. Initiation of this trial is primarily due to positive results such as antiproliferative effects of Inecalcitol and its synergy with Imatinib as validated by Prof. A. Thuran's INSERM U935 research group on 'in vitro' cultures of CML stem cells directly taken from CML patients. Further, results obtained from the clinical phase II study of Inecalcitol in CLL at the dose of 2 mg per day supported the idea to conduct clinical trials of Inecalcitol in CML patients.

- **Hybrigenics raised €4.6MM through private placement:** On October 22, 2014, Hybrigenics announced that it raised €4.62MM from the Crede Capital Group, llc, a U.S. based investment firm. The deal was completed through the issuance of 3.5MM new shares valued at €1.32 per share.

- **Hybrigenics Subsidiary Helixio invested in an Illumina sequencer:** On October 01, 2014, Hybrigenics announced that its subsidiary, Helixio acquired a NextSeq500® next generation sequencer from Illumina®, a global leader in next generation sequencing technologies. Attractive features of this technology are: It can sequence the human whole genome or of most plant or animal individual organisms in less than two days, and has flexibility to adapt to the parallel sequencing of the desired number of exomes or transcriptomes with the optimal level of accuracy. Through this acquisition, Helixio, intends to offer customized state-of-art sequencing services to its free-for-service customers from all life sciences, and also plans to support Hybrigenics' internal R&D studies by providing new information on genomics.

- **Hybrigenics received patent for USP:** On September 04, 2014, Hybrigenics announced that it has received a patent until 2031 from European Patent Office covering the fourth chemical family inhibitors of USP in Europe. It also announced the extension of three years of the life of patent for its first family of USP inhibitors in the U.S. until mid-2029 instead of mid-2026 in Europe in the rest of the world. The first family includes its first lead compound HBX 41,108, a reference USP inhibitor commercialized by the Bio-Techne group of companies (Tocris, Boston Biochem, and R&D Systems) and distributed by Fischer Scientific, under Hybrigenics' worldwide license. Also, it is

sold as a pharmacological tool to scientific laboratories only for experimental research use in vitro and in vivo, but not for tests in humans.

- **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.

5. Management and Governance [xii]

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.

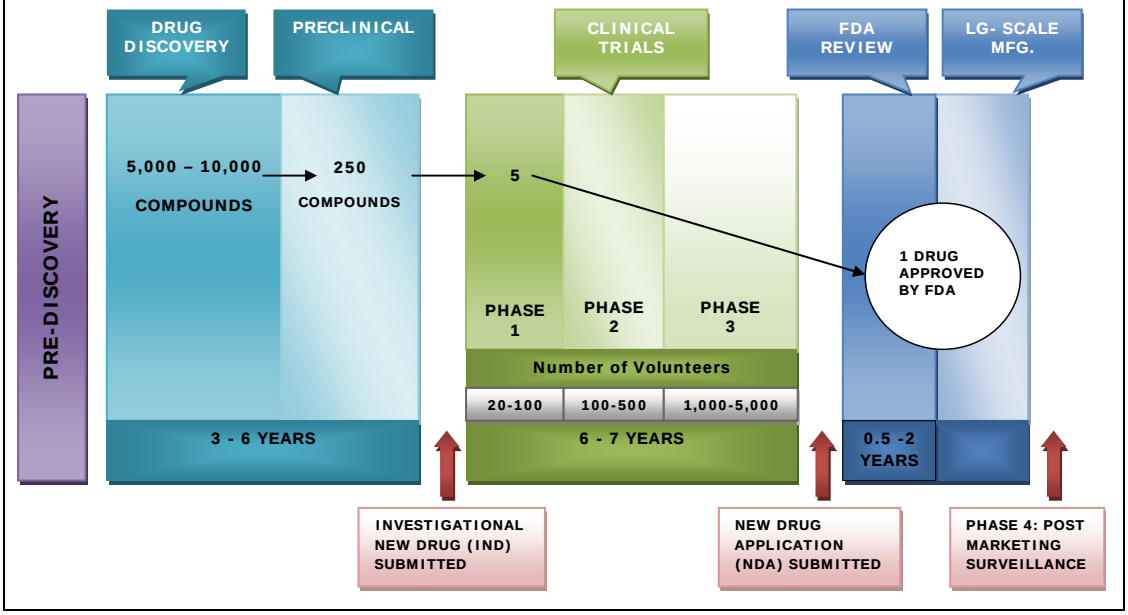
Exhibit 19: Management and Governance

Name	Position	Past Experience	Qualifications
Dr. Remi 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	Managing Director	• 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)

6. Technologies and Markets

Drug Discovery and Development Process [xiii]

Exhibit 20: 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. [xiv]

6.1 Drug Discovery Process

6.1.1 Pre-discovery Stage

Exhibit 21: 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.

6.1.2 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.

6.1.3 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.

6.2 Drug Development Process

6.2.1 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.

6.2.2 Clinical Trials [xv]

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 1,000 – 5,000 patient volunteers are tested during this stage. Phase III trials are the most expensive and the longest. Cost: US$10MM-US$500MM.

6.2.3 New Drug Application and Approval

Once all the clinical trials are successfully completed, the sponsoring company analyses 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.

6.2.4 New French Regulatory Agency [xvi] [xvii] [xviii]

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.

6.2.5 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).

6.2.6 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.

6.3 Global Pharmaceutical Market

The global spending on medicine is expected to grow at a CAGR of 1.8% to reach $1T in 2014 on constant currency basis from $965B in 2012. Further, the global pharmaceutical market is expected to exceed $1.2T by 2017, by growing at a CAGR of 3.9% over 2012.

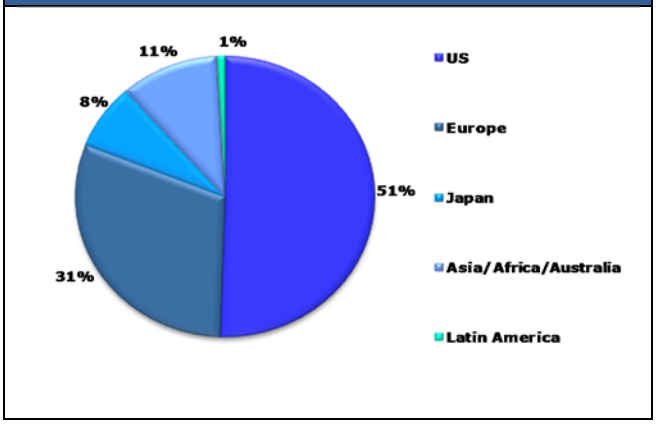
The global pharmaceutical market is dominated by the U.S., which accounted for about 34% of global sales in 2012, followed by Asia/Africa/Australia together with 31%, Europe with 15% share and China with 8%. This geographic distribution of medicine spending is expected to change in 2017 with U.S. contributing 31% (-300 bps over 2012), Asia/Africa/Australia together contributing 33% (+200 bps), Europe 13% (-200 bps) and China 15% (+700 bps). Patent expirations and limits on drug spending could weigh down the growth of drug sales in developed countries. The U.S., EU5 (the aggregate of Germany, France, Italy, U.K. and Spain), Japan and China are expected to account for 67% of global spending on medicines in 2017, contributing 59% of the global growth in the 5 year period to 2017. [xix]

The expiry of patents will fundamentally impact individual pharmaceutical companies during the period 2014-2017. In 2014, due to loss of exclusivity, total pharma sales at risk was anticipated to be around $38.7B and by 2015 total sales at risk of patent expiry is expected to reach $47.5B (nearly matching loss of about $54.7 in 2012). [xx] Rising cost pressure on healthcare has resulted in an increase in generic pharmaceutical usage as generic drugs cost 80% less than their original equivalents.[xxi]

6.3.1 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. [xxii]

Exhibit 22: Global Biopharmaceutical Market Share by Region [xxiii]



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. [xxiv]

According to Research and Markets, in 2013, the global biopharmaceuticals market was estimated at US$199.7B, which is expected to grow at a CAGR of 13.9% over the period 2013-2020 to reach US$497.9B by 2020. [xxv]

6.4 Market Trends

6.4.1 Decline in Global R&D Investments [xxvi] [xxvii]

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 $162B in 2020 at a CAGR of 2.4% from to 2013 to 2020, as per World Preview report 2014 from market intelligence firm Evaluate Ltd. [xxviii] 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 $1.017B by 2020. 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[xxix]. 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.

Exhibit 23: Decline in R&D Productivity [xxx]

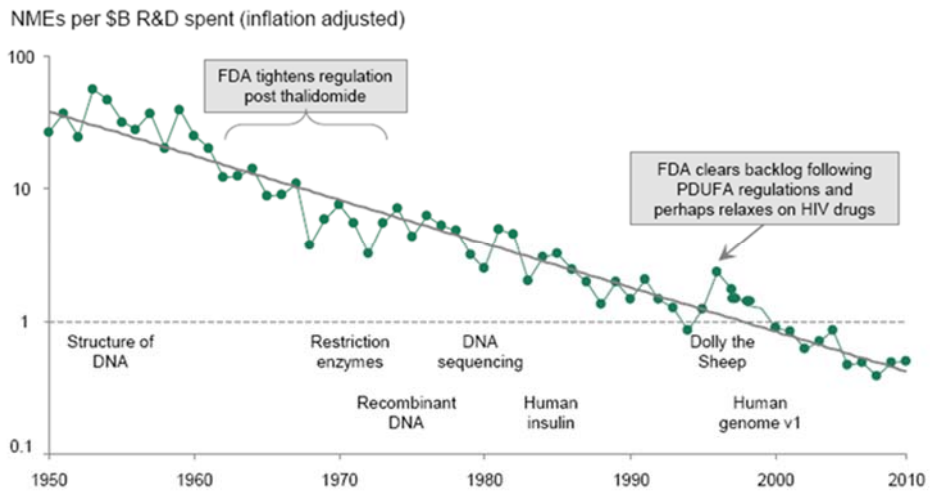
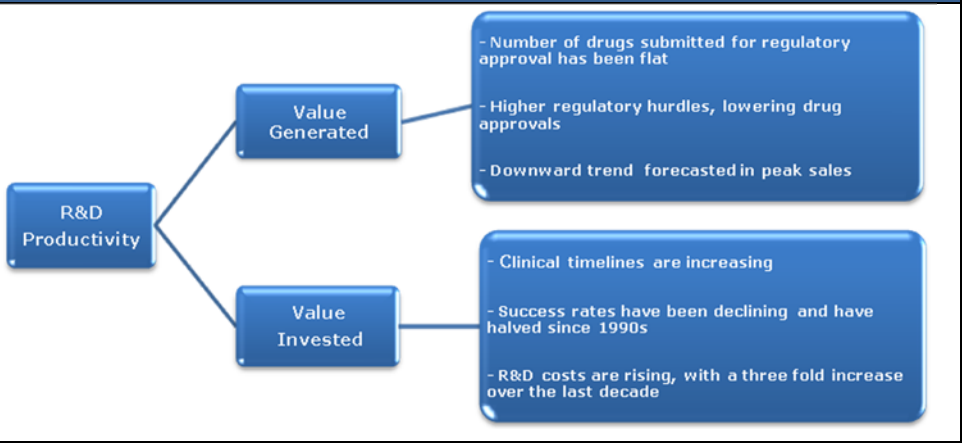


Exhibit 24: Decline in R&D Productivity – BCG Analysis [xxxi]



6.4.2 Need for Outsourcing – Licensing between Pharmaceutical and Biotechnology firms [xxxii] [xxxiii]

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. [xxxiv] 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%.[xxxv]

6.5 Trends in Prostate Cancer and CLL

6.5.1 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. [xxxvi] 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. [xxxvii]

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. [xxxviii]

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).

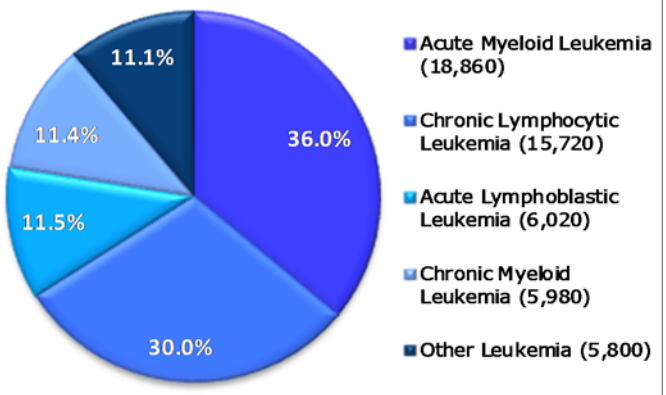
6.5.2 Leukemia

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. North America dominates the Leukemia drug market in the U.S. with 62.0% share while Germany dominates the European market with 31.1% share.[xxxix]

According to the report 'Facts and Figures 2013' published by American Leukemia and Lymphoma Society, in 2014, new cases of Leukemia are expected to be around 52,380 in the U.S.[xl]

The Leukemia market is categorized into four types 1) Acute Lymphocytic Leukemia (ALL), 2) Chronic Lymphocytic Leukemia (CLL), 3) Acute Myeloid Leukemia (AML), and 4) Chronic Myeloid Leukemia (CML). In 2014, an estimated 327,520 number of patients were either living with ALL, AML, ALL or CML or were in remission from Leukemia. [xlii]

Exhibit 25: Total Estimated Number of New Leukemia Cases in the U.S. – 2014 [xli]



CLL is a type of Leukemia, which is expected to accounts for about 30% of all leukemic patients in the U.S. in 2014.[xliii] 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 15,720 in the U.S. (American Leukemia Lymphoma Society, Facts 2014-2015), 14,000 in Europe and 130,000 worldwide (Globocan 2008). [xliv] 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).[xlv]

AML is expected to witness the highest number of new cases in 2014, accounting for around 36% of all leukemic patients.[xlvi] According to American Leukemia Lymphoma Society, Facts 2014-15, annual estimates of newly diagnosed AML cases amounted to 18,860 in the U.S., 18,500 in Europe as per RARECARE Working Group, 2012. Furthermore, according to Globocan, 110,000 cases were recorded worldwide in 2008.[xlvii]

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 15.0% of all types of leukemia in adults with approximately 5,430 new cases diagnosed in 2012 and an estimated 610 deaths in 2012.[xlviii]

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.[xlix]

According MarketsandMarkets, in 2010, Leukemia therapeutic market was dominated by CML, and by 2020, it is expected to be dominated by ALL and CML sales of around $3.9B and $3.6B respectively.[l]

Exhibit 26: The Four Major Types of Leukemia: Acute or Chronic and Lymphoid or Myeloid [li]

Type of Leukemia	Lymphoid	Myeloid
Chronic	**Chronic Lymphocytic Leukemia** 30% annual incidence 47% total prevalence Most frequent > 50 years 5-year survival rate = 83.5%	**Chronic Myeloid Leukemia** 11.4% annual incidence 13% total prevalence Most frequent > 65 years 5-year survival rate = 60%
Acute	**Acute Lymphoblastic Leukemia** 11.5% annual incidence 26% total prevalence Most frequent < 20 years 5-year survival rate = 70%	**Acute Myeloid Leukemia** 36% annual incidence 14% total prevalence Most frequent > 50 years 5-year survival rate = 25%

6.6 Licensing Activities

6.6.1 Licensing Activities in Q3 2014

Licensing activities have become an important strategy for large pharmaceutical and small biotech companies. The licensing activity related to Pharmaceuticals industry in Q3 2014 were reported to be 651 new deals representing 11.7% increase Q-o-Q and 5.9% decline Y-o-Y. Approximately, 19 high value new partnerships, worth in excess of $100 MM, were entered into during the Q3 2014. Of these, nine could potentially generate $0.5B or more in revenue for their primary collaborators. [lii]

6.7 French Pharmaceutical Industry [liii] [liv]

According to GlobalData, the French Pharmaceutical market is expected to grow at a very slow pace i.e. CAGR of 0.7% to $48.2B in 2020 from $46.2B in 2014 owing to the growing focus on generic drugs. Shift in increased usage of generic medicine can be made evident from the fact that in terms of volume, generic drugs accounted for 21.7% of the French Pharmaceutical industry in 2008 which grew to 30.2% by 2013. [lv] [lvi]

As compared to European countries such as UK and Germany, France is considered to very late in picking up the usage of generic drugs. Primary reason for this restricted usage was the consumer's preference for patented medicines and the economy's reliance on big pharma companies such as Sanofi, Ipsen and Servier. High healthcare expenditure has compelled the French government to promote increased use of generics drugs as a cost-cutting measure. With reference to this, the government in 2012, introduced a scheme where patients who preferred generic substitution would be free from paying the price of the drugs. Additionally, the government introduced stricter rules for determining the reimbursement rates and pricing for drugs in the form of the Relative Therapeutic Index (ITR). Based on the rules defined by Transparency Commission, assessment of the index will be based on the analysis of the following criteria's:

- The clinical relevance of comparators,
- The clinical relevance of primary and secondary endpoints, and
- The validity of methodological studies presented for demonstration

Further, the rule was passed that if the drugs were approved for reimbursement, then the drug would be allowed to retain this status for five years before being evaluated again for determining the reimbursement rates and pricing for drugs. Typically, drugs in France have a reimbursement rate of 65%, but then can be in the range of 15% to 100% depending on factors such as benefit, cost, and innovation of the treatment.

Clearly, factors that led to shift in preference for generic drugs in France are patent expirations, favourable regulatory regime, and several government incentives for physicians, pharmacists and patients to select generics drugs over branded drugs.

Though shift in preference for generic drugs had affected the France Pharmaceutical market, going forward, factors such as large and aging population, tax incentives (elimination of corporate tax and the Research Tax Credit to support research and development is creating healthy competition between healthcare companies), and high public healthcare expenditure are expected to be favourable.

See important disclosures on page 38 of this report

7. Valuation

The Fair Market Value for all of Hybrigenics shares stands between €89MM and €109MM as of June 2, 2015. The Fair Market Value for one of Hybrigenics's publicly traded regular shares stands between €2.50 and €3.05 as of June 2, 2015. The valuation approach followed is the Discounted Cash Flow method.

7.1 Discounted Cash Flow Method

Valuation	
WACC	
Risk-free rate	1.00%[lvii]
Beta	0.82[lviii]
Market Return	9.4%[lix]
Additional Risk Premium	8.8%
Cost of Equity	15.1%
Cost of Debt	2.3%
Terminal Growth Rate	0.5%
WACC (Discount Rate)	14.98%

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	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
FCFF (High)*								
Net cash from operating activities	(7,580)	(1,059)	4,007	4,056	12,561	16,624	11,194	7,882
Capital Expenditure	(100)	(100)	(100)	(100)	(100)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	(7,680)	(1,159)	3,907	3,956	12,461	16,124	10,694	7,382
Discount factor	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33
Present Value of FCFF	(6,679)	(877)	2,570	2,264	6,202	6,980	4,026	2,417
FCFF (Low)*								
Net cash from operating activities	(7,580)	(3,010)	1,489	2,212	8,818	12,105	9,076	7,325
Capital Expenditure	(100)	(100)	(100)	(100)	(100)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	(7,680)	(3,110)	1,389	2,112	8,718	11,605	8,576	6,825
Discount factor	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33
Present Value of FCFF	(6,679)	(2,352)	914	1,208	4,339	5,024	3,229	2,235

** 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)	321,212	278,644	
Present Value of TV	22,660	19,657	
Present value of FCF	77,488	60,672	
Present Value of FCF + TV	100,148	80,329	
Net Debt	(8,993)	(8,993)	lx
Equity Value Bracket	**109,141**	**89,322**	
Shares on issue ('000)	35,778	35,778	lxi
Fair Share Value Bracket (€)	**3.05**	**2.50**	
Current Market price (€)	1.86	1.86	lxii
Current Market Cap. (€) MM	67	67	
Target Market Cap. Bracket (€) MM	109	89	

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 228 months (2015E-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

Exhibit 27: 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

Exhibit 28: Market share: Percentage of patients tapped – CLL

%	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	0.13%	0.13%	0.15%	0.17%	0.60%	0.50%	0.55%	0.70%	0.82%	0.60%	0.52%	0.43%	0.35%	0.30%
High estimate	0.14%	0.14%	0.15%	0.18%	0.61%	0.52%	0.60%	0.75%	0.85%	0.61%	0.52%	0.44%	0.36%	0.32%

Revenue from Upfront and Milestone Receipts – Prostate Cancer

Exhibit 29 : 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	2	**€115**
High estimate	34	4	18	36	36	2	**€130**

Revenue from Upfront and Milestone Receipts – CLL

Exhibit 30: Revenue from Upfront and Milestone Payments – CLL

€ MM	2015	2016E	2017E	2018E	2019E	Estimated Deal value (MM)
Low estimate	36	24	20	20	22	**€122**
High estimate	39	29	21	21	22	**€132**

Royalty Receipts – Prostate Cancer

Exhibit 31: 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	21.1	18.1	14.1
High estimate	0.7	2.6	9.5	19.5	25.1	27.5	29.3	30.7	32.3	25.5	22.2	17.0

Royalty Receipts – CLL

Exhibit 32: Royalty Receipts – CLL														
€ MM	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Low estimate	2.6	3.0	4.0	5.0	20.8	19.7	24.6	35.6	47.3	39.2	38.4	35.7	32.7	31.5
High estimate	3.4	3.9	4.8	6.4	25.3	24.5	32.2	45.7	58.9	47.8	46.0	43.8	40.4	40.4

Success Probability – Prostate Cancer

Exhibit 33: Probability of Occurrence (Success) – Prostate Cancer							
%	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	25%	60%	70%	75%	82%	100%	100%
High estimate	30%	60%	75%	80%	85%	100%	100%

Success Probability – CLL

Exhibit 34: Probability of Occurrence (Success) – CLL							
€ MM	2016E	2017E	2018E	2019E	2020E	2021E	2022E-2033E
Low estimate	45%	60%	85%	85%	85%	90%	100%
High estimate	45%	70%	90%	95%	90%	95%	100%

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

7.2 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	2015
Discount Rate	14.9% [lxiii]
Shares outstanding ('000)	35,778
Pharmaceutical Industry – PE (x)	13.00x [lxiv]

Exhibit 35: 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	7	8	30%	32%	26,921	32,305	115,000	130,000	42,576	51,938	21.0%	23.0%	2,928	3,912
Inecalcitol	CLL	Phase 2	2020	5	8	30%	32%	47,350	58,899	125,000	135,000	51,705	62,048	21.0%	23.0%	3,555	4,673

	Low	High
Fair value (Intrinsic) (€)	2.36	3.12

Sensitivity Table - High

		11.00	12.00	13.00	14.00	15.00
Discount Rate (%)	13.0%	3.04	3.31	3.59	3.87	4.14
	14.0%	2.83	3.09	3.34	3.60	3.86
	15.0%	2.64	2.88	**3.12**	3.36	3.60
	16.0%	2.46	2.69	2.91	3.13	3.36
	17.0%	2.30	2.51	2.72	2.93	3.14

Sensitivity Table - Low

		11.00	12.00	13.00	14.00	15.00
Discount Rate (%)	13.0%	2.29	2.50	2.71	2.92	3.13
	14.0%	2.14	2.33	2.53	2.72	2.91
	15.0%	1.99	2.17	**2.36**	2.54	2.72
	16.0%	1.86	2.03	2.20	2.37	2.54
	17.0%	1.74	1.89	2.05	2.21	2.37

7.3 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.

7.3.1 Prostrate Cancer Drug Program

Exhibit 36: NPV Calculations (€ '000)	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Revenue - High	33,500	3,500	18,333	36,333	36,333	2,000	686	2,607	9,489
Cost and Expenses	5,576	5,829	8,870	9,414	6,677	3,439	3,379	3,855	5,812
EBIT	27,924	(2,329)	9,463	26,919	29,657	(1,439)	(2,694)	(1,248)	3,677
Success Rate	30%	60%	75%	80%	85%	100%	100%	100%	100%
Risk Adjusted Cash flow	8,377	(1,397)	7,098	21,536	25,208	(1,439)	(2,694)	(1,248)	3,677
Year	1	2	3	4	5	6	7	8	9
Discount factor	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33	0.28
Present Value	7,286	(1,057)	4,670	12,323	12,546	(623)	(1,014)	(409)	1,047

NPV Calculations (€ '000)	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Revenue - High	19,533	25,126	27,512	29,333	30,687	32,305	25,483	22,179	16,977
Cost and Expenses	6,731	7,911	9,218	10,570	10,266	10,376	9,430	8,979	8,659
EBIT	12,802	17,214	18,294	18,763	20,421	21,929	16,053	13,199	8,317
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	12,802	17,214	18,294	18,763	20,421	21,929	16,053	13,199	8,317
Year	10	11	12	13	14	15	16	17	18
Discount factor	0.25	0.22	0.19	0.16	0.14	0.12	0.11	0.09	0.08
Present Value	3,171	3,709	3,428	3,058	2,895	2,703	1,721	1,231	675
Net Present value of cash flow (rNPV)	**57,360**								

7.3.2 CLL Drug Program

Exhibit 37: NPV Calculations (€ '000)	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Revenue - High	29,000	21,000	21,000	22,000	3,418	3,923	4,824	6,396	25,338
Cost and Expenses	7,435	7,772	11,827	12,552	8,902	4,585	4,505	5,140	7,749
EBIT	21,565	13,228	9,173	9,448	(5,484)	(662)	319	1,256	17,589
Success Rate	25%	45%	70%	95%	85%	90%	90%	90%	95%
Risk Adjusted Cash flow	5,391	5,953	6,421	8,976	(4,662)	(596)	287	1,131	16,710
Year	1	2	3	4	5	6	7	8	9
Discount factor	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33	0.28
Present Value	4,689	4,503	4,225	5,136	(2,320)	(258)	108	370	4,759

NPV Calculations (€'000)	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Revenue - High	24,548	32,190	45,728	58,899	47,799	46,033	43,828	40,350	40,358
Cost and Expenses	8,975	10,548	12,291	14,094	13,688	13,835	12,573	11,973	11,546
EBIT	15,573	21,642	33,438	44,805	34,111	32,198	31,256	28,377	28,813
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	15,573	21,642	33,438	44,805	34,111	32,198	31,256	28,377	28,813
Year	10	11	12	13	14	15	16	17	18
Discount factor	0.25	0.22	0.19	0.16	0.14	0.12	0.11	0.09	0.08
Present Value	3,857	4,662	6,265	7,302	4,835	3,969	3,351	2,646	2,337
Net Present value of cash flow (rNPV)	**55,455**								

See important disclosures on page 38 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 38 of this report.

8. Appendix

Hybrigenics's Balance Sheet Forecast – High Estimates

Exhibit 38: Consolidated Balance Sheet € '000	all figures in '000 € , unless stated differently						*High Bracket estimates*				
Year Ending December 31	2012A	2013A	2014A	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Total current assets	6,195	6,784	15,650	11,552	20,113	22,765	31,904	49,480	61,209	64,700	72,755
Total Non-current assets	886	1,134	1,296	1,197	1,103	1,013	926	841	1,150	1,452	1,748
TOTAL ASSETS	**7,081**	**7,918**	**16,946**	**12,749**	**21,216**	**23,778**	**32,829**	**50,321**	**62,359**	**66,153**	**74,503**
Total current Liabilities	1,659	1,609	2,591	5,180	5,122	5,387	8,021	8,447	6,076	3,272	3,220
Total Non-current Liabilities	2,504	2,711	2,688	2,688	2,688	2,643	2,597	2,597	2,597	2,597	2,597
TOTAL LIABILITIES	**4,163**	**4,320**	**5,279**	**7,868**	**7,810**	**8,030**	**10,618**	**11,044**	**8,673**	**5,869**	**5,817**
Total Shareholder's Equity	2,918	3,598	11,667	4,882	13,406	15,749	22,211	39,277	53,686	60,284	68,686
TOTAL LIABILITIES & EQUITY	**7,081**	**7,918**	**16,946**	**12,749**	**21,216**	**23,778**	**32,829**	**50,321**	**62,359**	**66,153**	**74,503**

Hybrigenics's Balance Sheet Forecast – Low Estimates

Exhibit 39: Consolidated Balance Sheet € '000	all figures in '000 € , unless stated differently						*Low Bracket estimates*				
Year Ending December 31	2012A	2013A	2014A	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Total current assets	6,195	6,784	15,650	11,552	14,938	15,790	23,051	35,449	43,166	45,994	53,481
Total Non-current assets	886	1,134	1,296	1,197	1,103	1,013	926	841	1,150	1,452	1,748
TOTAL ASSETS	**7,081**	**7,918**	**16,946**	**12,749**	**16,041**	**16,803**	**23,976**	**36,290**	**44,316**	**47,446**	**55,229**
Total current Liabilities	1,659	1,609	2,591	5,180	5,122	5,387	8,021	8,447	6,076	3,272	3,162
Total Non-current Liabilities	2,504	2,711	2,688	2,688	2,688	2,643	2,597	2,597	2,597	2,597	2,597
TOTAL LIABILITIES	**4,163**	**4,320**	**5,279**	**7,868**	**7,810**	**8,030**	**10,618**	**11,044**	**8,673**	**5,869**	**5,759**
Total Shareholder's Equity	2,918	3,598	11,667	4,882	8,231	8,774	13,358	25,246	35,643	41,578	49,470
TOTAL LIABILITIES & EQUITY	**7,081**	**7,918**	**16,946**	**12,749**	**16,041**	**16,803**	**23,976**	**36,290**	**44,316**	**47,446**	**55,229**

FCFF Calculation (2023E-2033E) – Continued from page 31

Exhibit 40:Year Ending – December (€ '000)	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
FCFF (High)											
Net cash from operating activities	10,248	19,230	29,307	36,827	46,410	56,618	58,482	56,021	54,542	51,360	48,767
Capital Expenditure	(500)	(500)	(500)	(500)	(500)	(500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	9,748	18,730	28,807	36,327	45,910	56,118	55,982	53,521	52,042	48,860	46,267
Discount factor	0.28	0.25	0.22	0.19	0.16	0.14	0.12	0.11	0.09	0.08	0.07
Present Value of FCFF	2,776	4,640	6,206	6,807	7,482	7,954	6,901	5,739	4,853	3,963	3,264
FCFF (Low)											
Net cash from operating activities	9,545	17,236	25,759	31,841	39,703	48,714	50,870	49,242	47,956	45,037	42,636
Capital Expenditure	(500)	(500)	(500)	(500)	(500)	(500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	9,045	16,736	25,259	31,341	39,203	48,214	48,370	46,742	45,456	42,537	40,136
Discount factor	0.28	0.25	0.22	0.19	0.16	0.14	0.12	0.11	0.09	0.08	0.07
Present Value of FCFF	2,576	4,146	5,442	5,873	6,389	6,834	5,963	5,012	4,239	3,450	2,831

See important disclosures on page 38 of this report

9. 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

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10. Notes and References

[i] Source: Bloomberg, June 1, 2015

[ii] 52 weeks to June 1, 2015. Source: Bloomberg June 1, 2015

[iii] 3 months to June 1, 2015. Source: Bloomberg June 1, 2015

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[lxii] Source: Bloomberg, June 1, 2015
[lxiii] Source: WACC calculation Shown on Page 31
[lxiv] Source: Arrowhead estimates