ARROWHEAD
BUSINESS AND INVESTMENT DECISIONS

Diligence and Valuation Report

Arrowhead Code:	69-02-11
Coverage initiated:	29 April 2012
This document:	20 September 2018
Fair share value bracket – DCF:	€1.98– €2.66
Share price: (20 September 2018):	€0.45[i]

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NYSE Alternext

HYBRIGENICS PHARMA

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

Market Data

52-Week Range:	€0.41– €0.75[ii]
Average Daily Volume (3M Avg.):	37,244[iii]
Market Cap (20 September 2018):	€21.03 MM

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

	'18E	'19E	'20E	'21E	'22E	'23E	'24E
High NI(MM)	29.1	18.0	13.1	(18.0)	(2.7)	12.0	21.0
High EPS	0.62	0.38	0.28	(0.39)	(0.06)	0.26	0.45
Low NI(MM)	25.1	11.4	8.5	(20.9)	(5.7)	10.5	15.5
Low EPS	0.54	0.24	0.18	(0.45)	(0.12)	0.22	0.33

Company Overview: Hybrigenics SA is a France-based biopharmaceutical group 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; it was 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 (a naturally active form of vitamin D). The Company's R&D pipeline includes the development of oral Inecalcitol for Prostate Cancer, Chronic Lymphocytic Leukemia (CLL), Chronic Myeloid Leukemia (CML) 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. 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. The R&D partnership has now reached its objectives - triggering a € 1.5 million milestone payment by Servier Laboratories to Hybrigenics. Hybrigenics S.A. has sold its controlling stakesin Hybrigenics Services S.A.S., its subsidiary dedicated to scientific proteomic services.

Arrowhead is updating coverage on Hybrigenics SA with a fair value bracket of € 1.98 in the low bracket and € 2.66 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; **(2)** Inecalcitol is recognized as a key ingredient for developing drugs for treating diseases such as Prostate Cancer, CLL, CML and AML; **(3)** Inecalcitol for CLL and AML has been designated Orphan drug status in Europe and U.S.; **(4)** If the remaining phases of clinical development in each indication are successful, inecalcitol could be commercialized for AML, CML or CLL in 2023, 2024 or 2025, respectively **(5)** Hybrigenics sold off its genomics division, Helixio which completes the company's refocusing on R&D initiated last year **(6)** Hybrigenics closed recruitment in Phase II International Trial of Inecalcitol in Acute Myeloid Leukemia (AML); **(7)**The company did not make any revenue in FY 2017 in comparison to € 1,492K in FY 2016 **(8)** The operating loss increased from € 4,036K in 2016 to € 7,377K in 2017 **(9)** The net loss increased from € 5,252K in FY 2016 to € 7,957K in FY 2017 **(10)** The company restored its eligibility for the PEA-PME scheme for 12 months forthcoming. Investors can continue to integrate Hybrigenics shares into PEA-PME accounts, device dedicated to investing in small and medium-sized companies

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 € 1.98 to € 2.66 bracket calculated using the DCF method. Based on the Risk Adjusted Net Present Value (rNPV) 'Peak Sales' method, the fair value lies in the € 1.21 to € 1.64 bracket. The rNPV for High bracket for the drug R&D programs for oral Inecalcitol for CLL, AML and CML is € 39.49 MM, € 92.60 MM and € 36.06 MM respectively.

See important disclosures on page 42 of this report

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1. Summary and Outlook

We are updating coverage on Hybrigenics SA. The Company headquartered in Paris, France, is 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 € 1.98 in the low bracket scenario and € 2.66 in the high bracket scenario (DCF Valuation Method). Based on the NPV 'Peak Sales' method, the fair value lies in the € 1.21 to € 1.64 bracket. The rNPV based on high bracket method for the drug R&D programs for oral Inecalcitol for CLL, AML and CML is € 39.49 MM, € 92.60 MM and € 36.06 MM 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 for 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 and AML, has been designated with an Orphan drug status in Europe, the U.S. and Japan. The Company enjoys several benefits due to the orphan drug status, such as 10 years of marketing exclusivity, protocol assistance at discounted rates and faster registration process in the country.
3. Besides CLL and AML, CML has also been identified as potential orphan therapeutic indication for Inecalcitol. If the remaining phases of clinical development in each indication are successful, inecalcitol could be commercialized for AML, CML or CLL in 2023, 2024 or 2025, respectively.
4. Hybrigenics completed the recruitment of the clinical study Phase II International Trial of Inecalcitol in Acute Myeloid Leukemia (AML). Inecalcitol has received the orphan drug designation for AML in Europe and United States. 115 patients have been recruited in 31 hospitals across 5 countries.
5. The company did not generate any revenue in 2017 in comparison to € 1.4 million in 2016. Hybrigenics' operating loss increased further by 82.2 % that is from € 4 million in 2016 to € 7.4 million in 2017. There has been an increase in net loss of 51.5 % from € 5.3 million in 2016 to € 7.9 million in 2017.
6. Phase II clinical trial of double-blind placebo-controlled has been approved by the National Agency of Drug Safety in France and the Food and Drug Administration in the United States, with the same protocol.
7. Hybrigenics successfully raised € 6.8 MM of capital via preferential subscription right of the shareholders (DPS). The transaction results in the creation of 10.9 MM new shares at a unit price of € 0.62. This operation will allow Hybrigenics to extend its clinical study of phase 2 of Inecalcitol in acute myeloid Leukemia (AML) to other European countries which is currently on-going in United States and France.
8. An interim milestone payment released in February 2017 for Chronic myeloid Leukemia (CML), which is currently in phase II. The ongoing Phase II study is assessing the usefulness of oral Inecalcitol added to Imatinib in patients with CML. After at least two years of treatment with imatinib have finally reached the stage of RMM (Major Molecular Response) but not yet RMP (Deep Molecular Response). The goal is to make them reach the stage of RMP in one year maximum of treatment combining Inecalcitol and imatinib.
9. Hybrigenics has been awarded global exclusivity for '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.
10. The Company also received two new patents from U.S. Patent and Trademark Office (USPTO) - one on the 14-epimerisation step in the chemical synthesis of Inecalcitol and the other on its convenient formulation as tablets, soft gel capsules and oral drinking solutions, enabling more patient-friendly administration of Inecalcitol. A third patent on the therapeutic use of Inecalcitol at high doses had already been granted earlier in the U.S. These three American patents are all valid up to 2031, with the earliest expiring on September 10, 2031.
11. The Company's genomic scientific services division, Helixio acquired Illumina® NextSeq500 sequencer to offer tailor-made services to various researchers from life sciences based on next generation sequencing.
12. Hybrigenics has a licence agreement with Servier for de-ubiquitination (DUB) identification and validation, screening and profiling of development candidates in oncology, neurology, psychiatry, rheumatology, ophthalmology, diabetes and cardiovascular diseases. Per the Company, the agreement provides potential preclinical, clinical and registration milestones totalling € 9.5 MM or € 11.5 MM for each target yielding a DUB inhibitor, which becomes a commercialized drug. It has already reached the first preclinical milestone (€ 500,000) and it has potential offers of royalties to the Company on future sales of companion diagnostic kits.

13. Hybrigenics announced a new development in its R&D partnership with Servier in the field of USPs. The research collaboration, which started in 2011 and had focused on one USP especially relevant to oncology, has now reached its objectives, triggering a €1.5 MM milestone payment to Hybrigenics. Servier will take charge of the continuation of the R&D program in oncology, while Hybrigenics will remain associated with its success, with a total of up to € 12 MM further payments linked to potential additional milestones until drug registration. Further, Hybrigenics will intensify its research to validate other USPs as innovative therapeutic targets and to discover new chemical series to efficiently inhibit them.

14. Hybrigenics sold 75.8% of its services business to Biofiteam, due to which the revenue has declined to € 0.4 MM in the first half of FY 2017. However, operating cost has increased primarily due to 81% rise in R&D expenditure.

15. Strategic refocusing on biopharmaceutical R&D: Hybrigenics S.A. has sold its controlling stakes in Hybrigenics Services S.A.S., its subsidiary dedicated to scientific proteomic services. The Company changed its strategic perspective to refocusing on biopharmaceutical R&D, given (a) the success of the research collaboration with Servier in the field of USPs, (b) the launch of the Phase II clinical study of inecalcitol in AML both in France and the U.S., and (c) the encouraging results of the Phase II clinical study of inecalcitol in CML in France. Hybrigenics S.A. retains 20% of Hybrigenics Services' capital. Hybrigenics' CEO, Remi Delansorne, said that the Company's past dual services and R&D business model is being simplified for a clearer perception of its new profile of pure biotechnology therapeutic player. Management buy-out of 75.8% of Hybrigenics Services' share capital is for a total amount of € 0.796 MM which includes down payment of € 0.196 MM and three earn-out payments for a maximum amount of € 0.200 MM each contingent to net result of Hybrigenics Services in 2018, 2019 and 2020.

16. Hybrigenics presented new results at American Association for Cancer Research (AACR 2017) on the specificity of inecalcitol in AML and MM. Hybrigenics' CEO, Remi Delansorne, said that the results will support the ongoing clinical Phase II study of inecalcitol in AML and finding similar results on human MM cell lines will encourage to investigate the therapeutic role that inecalcitol could play in the new indication.

17. The ongoing, open-label Phase II study evaluates the efficacy of oral inecalcitol added to oral imatinib in CML patients, with the objective to reach deep molecular response (DMR) within one year of treatment, presented encouraging results. At this intermediate stage of study, (a) 43% of the patients (6 out of 14) have shown further decrease in BCR-ABL from major molecular response (MMR) at three months, and (b) 33% (3 out of 9) have demonstrated undetectable biomarker traces after one year of treatment. These results are in comparison to 7.5% yearly increase in patients reaching DMR under imatinib alone, as per two independent reports.

18. 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 distribution 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 in more than 30 countries.

19. Global Pharmaceutical Industry Overview: The global pharmaceutical market crossed $1T in 2014 and is expected to grow at CAGR of 4.7% to reach $1.3T in 2018 led by U.S. and Pharmerging markets. As per the 'World Preview report 2014' from market intelligence firm, Evaluate Ltd, the global pharmaceutical industry's R&D expenditure is expected to increase at a CAGR of 2.4% to reach US$ 160 B during the period 2014-2020. 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. Per 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 US$ 1,415 B by 2020.[v]

20. French Industry Overview: Per GlobalData, the French Pharmaceutical market is expected to grow at a slow pace, i.e., at a CAGR of 0.7% from US$ 46.2 B in 2014 to US$ 48.2 B in 2020 owing to the growing focus on generic drugs.[vi] Factors leading to shift in preference toward 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; risks associated with the success of pipeline, drug approval and commercialization of drugs; and inadequate experience in global development.

2. Business Overview [vii]

Incorporated in 1997, Hybrigenics SA is a French biotechnology and pharmaceutical company, which discovers and develops novel drugs 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 that 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, CML and AML 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 started. The trial was funded by a private placement of € 3.3 MM in two tranches of € 1.45 MM and € 1.85 MM, 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. In this trial, 21 patients were treated for at least 15 months and 52% of the patients showed some effect of the Inecalcitol treatment. The insights gained from the trial are expected to help the Company in designing the next step of clinical development of Inecalcitol for CLL. In 2014, Inecalcitol was designated the Orphan drug status for the treatment of CLL in Europe, the U.S. and Japan, and it was designated the Orphan drug status for AML in 2015 in Europe and the U.S.

Several researchers also 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 CML may possibly be the new additional orphan therapeutic indication. Further, following the positive results observed during the Phase II for CLL, the Company initiated a Phase II trial in CML on January 19, 2015 in combination with Imatinib (Gleevec®). The trial showed that Inecalcitol inhibited CML stem cell proliferation, independently as well as synergistically with imatinib. Also, the combination of Inecalcitol and Imatinib could prolong CML remission or even cure the disease by eliminating the stem cells. The Company had commenced a clinical Phase II study in collaboration with FiLMC, the French cooperative group on CML. With encouraging preliminary results of Phase II clinical study and a very low study drop-out rate, the sample size of the pilot study has been reduced to 42 patients. The target for completion is H2 2018.

Hybrigenics has also received authorization and commenced a double-blind placebo-controlled clinical Phase II study of Inecalcitol in elderly or frail AML patients in the U.S. and France. The objective of the study is to focus on the elderly or frail AML patients who are unfit for standard chemotherapy and who can only receive monthly cycles of intravenous perfusions of decitabine. The primary endpoint will be overall survival. A total of 110 patients will be included in the study and it is designed to be sufficiently powered to evidence potential efficacy on mortality. The first patient has been enrolled in the U.S. and 14 patients were under treatment in France as of November 28, 2016. To finance these expenses, the Company has raised total of € 19.7 MM (€ 6.1 MM through a private placement in March 2014, € 4.6 MM from the Crede Capital Group in October 2014 and € 9.0 MM through a public offering in April 2015).

Hybrigenics also tied 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, the Company received its first milestone payment of € 0.33 MM demonstrating the Company's expertise in exploring the role of USPs during the drug discovery process. Till January 2016, the Company had reached the first preclinical milestone worth € 0.5 MM. The research collaboration, which started in 2011, focused on one USP especially relevant to oncology. This has now reached its objectives, triggering a €1.5 MM milestone payment to Hybrigenics. Servier will take charge of the continuation of the R&D program in oncology, while Hybrigenics will remain associated with its success, with a total of up to € 12 MM further payments linked to potential additional milestones until drug registration. Further, Hybrigenics will intensify its research to validate other USPs as innovative therapeutic targets and to discover new chemical series to efficiently inhibit them. Hybrigenics may also plan to pursue its research outside the partnered therapeutic areas in this field, such as inflammation and virology.

On January 26, 2015, the Company extended its partnership with Servier, validating its belief in 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$ 2.4 MM with American Life Sciences. As per the agreement, the yearly commitment had been increased from US$ 0.70 MM to US$ 0.79 MM. In October 2013, the Company acquired the genomics division of Imaxico 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 € 1.3 MM through private placement from Pradeyrol Development.

Hybrigenics' R&D pipeline includes the development of oral Inecalcitol in the treatment of CLL (Phase II - completed), CML (Phase II – ongoing), AML (Phase II – ongoing) and Prostate Cancer (Phase IIa - completed). The Company independently performs discovery through early clinical development and proposes to enter 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

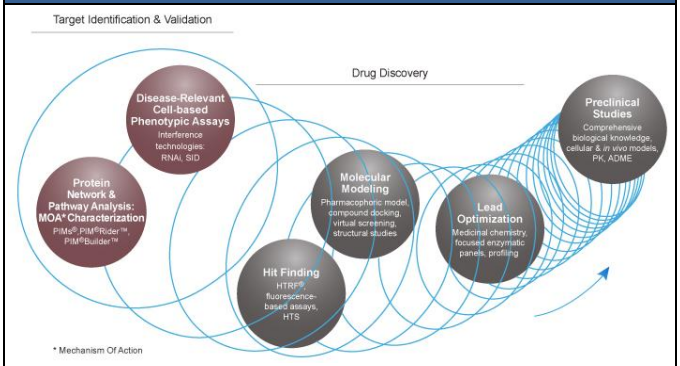
Sr. No.	Patent	Date of patent receipt	Patent Expiry Year	Patent Granting Authority	Comments
1	Therapeutic uses of high doses of Inecalcitol (doses higher than 1.5mg/day)	Filing in 2009: already granted in Europe	2030	European Patent Office	Per Patent Cooperation Treaty (PCT), the same patent application is still 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 1.5mg/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, U.S.	2031	European Patent Office and US Patent and Trademark Office	These patent applications have been granted in China and Europe and U.S. but are still under examination by the World Intellectual Property Organization under the PCT procedure, to get worldwide protection in the following countries.
4	Innovative formulations of Inecalcitol: tablets, new generation of soft gel capsules, and oral drinking solutions	Filing in 2010: already granted in Europe for tablets and new generation of soft gelatine capsules; in the U.S. for tablets	2031	European Patent Office and US Patent and Trademark 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 across 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 often conducted in partnership with larger pharmaceutical or biotechnology companies at various stages of research or development. Besides pursuing its internal drug discovery programs, Hybrigenics collaborates with pharmaceutical and biotechnology companies for joint research and product development. The 'Pharma' division constituted about 9.2% of the revenue of the group in 2015.

Exhibit 2: Drug Discovery and Development Process



Inecalcitol: Presently, Hybrigenics is undertaking development of Inecalcitol, a vitamin D analogue, for treatment of Prostate cancer, CLL, CML and AML. The Company has completed Phase II study for prostate cancer and CLL. It is conducting clinical phase II study with France for CML, and with France and U.S. for AML. After this, a Phase IIb/III registration trial to compare the efficacy of existing treatment of prostate cancer on overall survival with or without Inecalcitol will be conducted.

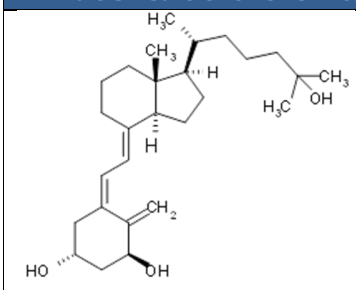
Ubiquitin Specific Proteases (USP): Hybrigenics undertakes investigation of USPs for the discovery and development of new cancer therapeutics. The Company has discovered innovative small molecule inhibitors of USPs showing potent anti-tumour activity in vivo. The Company has built a platform in the molecular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

2.2 Technology

2.2.1 Inecalcitol, a Vitamin D3 Analogue

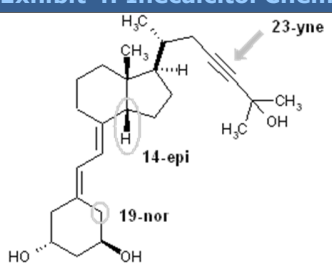
Inecalcitol is a synthetic chemical derivative of Calcitriol, the naturally active metabolite of vitamin D. Inecalcitol has been optimized to be more potent than Calcitriol and to play an active role in slowing down the growth of cancerous cells as well as hyper-proliferating normal cells, such as cells from skin affected by Psoriasis, or from benign (non-cancerous) hypertrophic prostate. Per the Company, Inecalcitol is about 10 times more anti-proliferative than Calcitriol and causes less than 100-fold lower calcium toxicity than calcitriol. 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 for preventing 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 3: Calcitriol Chemical Structure



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

Exhibit 4: Inecalcitol Chemical Structure



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

2.2.2 USP Program

Proteases play a key role in several 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. The pathway that regulates cellular protein turnover is implicated in the pathogenesis of many 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, USPs constitute one of the most favourable target classes due to their protease function being amenable to small molecule drug discovery.

2.3 Overview of Drug Candidates

Hybrigenics is involved in discovery and development of Inecalcitol for new treatments of proliferative 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 2023 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 for Inecalcitol, announced in September 2010, a total of 54 patients were enrolled to test 9 dose levels from 40 micrograms 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. 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, the difference between the two response rates was 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 in 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 made during 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 € 3.3 MM 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 13 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 administration 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.

Inecalcitol, a key drug for the treatment of CLL was designated with Orphan drug status in Europe, U.S. and Japan. 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 5 to 21 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 decrease in BLC and another patient showed BLC reduction after 4 and 5 months of treatment. In the case of next 10 patients (48%), the BLC increased at a regular exponential pace without any influence of treatment. Two patients experienced hypercalcaemic 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 Haematology, 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. Turhan, 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 started clinical phase II study of Inecalcitol in CML in collaboration with FiLMC. The study expected to enrol 54 CML patients within one year 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 continue until 1H 2017. The Company also expects to file an Orphan drug application by Q1 2017, if early clinical trial shows positive effects.

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)

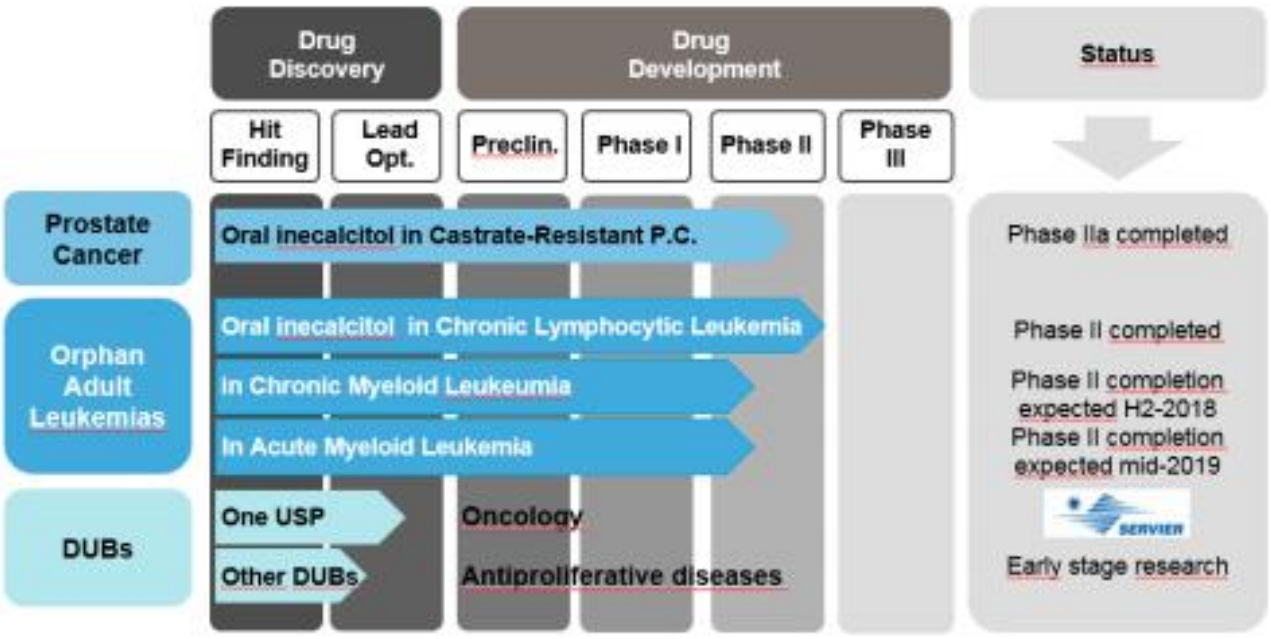
AML is a disorder wherein patients have many immature white blood cells in their bone marrow that are not capable of maturing properly. It is the most frequent leukemia, which accounts for 35% of all leukemia cases worldwide, with the survival rate of 25% (5-year survival rate). In March 2014, the Company announced the results of the research conducted by an 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 showed 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. It has been inferred that the 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) has prolonged survival.

The company has been granted authorization from France (IMPD OK) and U.S. (IND OK) for clinical Phase II study in 8 to 12 specialized centres by enrolling about 50 patients. This Phase II study of Inecalcitol is to be conducted in combination with either azacytidine or decitabine in older or frail AML patients, in France as well as in the U.S. The first patient has been enrolled in the United States and 14 patients were under treatment in France as of November 28, 2016. The Company has also received Orphan drug status for treatment of AML both in United States and Europe.

2.4 R&D Pipeline

Exhibit 5: R&D Pipeline



2.5 Company Premiums

- **Patented Drugs and Unique Technology:** Hybrigenics' core competency lies in its drug discovery capabilities and its worldwide proprietary rights for the use of Inecalcitol. The Company is researching the use of oral Inecalcitol for the treatment of diseases such as Prostate Cancer, CLL and AML (granted Orphan drug status). In addition, the Company is planning/undergoing clinical trials to pursue the use of Inecalcitol for 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 USPs and a license from Pasteur Institute to run the "ULTImate Y2H" screens. Recently, another patent has been granted to the company for new formulations including tablets, soft gel capsules and oral drinking solutions - these are more patient friendly forms of taking Inecalcitol.

- **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 asset. Currently, Intellectual Property on USP inhibitors include 56 granted patents protecting four chemical families 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, it has been announced that its first family including HBX 41,108 is to be commercialized by the Bio-Tech group of companies and is to be distributed by Fischer Scientific, under Hybrigenics' worldwide license as a reference pharmacological research tool.

- **Positive results of 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 6: 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 for 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 Hybrigenics' key drug, Inecalcitol, for CLL. The Orphan drug status would provide the Company several incentives such as:
  - Customary 10 years of marketing exclusivity for 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: As of December 31, 2017, Hybrigenics' retained activities cash was at € 7 MM as compared to € 8.5 MM on December 31, 2016. Despite the fall in cash and cash equivalents by 17.4%, the company has a positive cash position. The net cash flow from discontinued operations of genomic service provider, Helixio has been the most important structural change since the introduction of the mixed model R & D pharma and services in 2004. This lead to an increase in cash position by 62.3%, from € 0.2 MM in 2016 to € 0.3 MM in 2017.

- The constant scope cash position of the Company amounted to € 8.8 MM as of December 31, 2016. The Company recorded the strongest cash position at the end of 2015, since 2006. It successfully raised € 11.75 MM funding through two private placements (€ 6.1 MM from French and Swiss investors, € 4.6 MM from US-based CREDE Capital Group, and € 1.05 MM from equity line agreement with the American fund Yorkville Global Advisors). It also raised € 9.0 MM through public offering in April 2015.

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 was fees derived from services using Y2H technology. However, these funds were 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. The Company has not yet tied up with other companies for co-development of drugs; thereby, creating additional uncertainty in the cash flows. Also, Hybrigenics S.A. has sold its controlling stakes in Hybrigenics Services S.A.S., its subsidiary dedicated to scientific proteomic services. The Company changed its strategic perspective to refocusing on biopharmaceutical R&D, given (a) the success of the research collaboration with Servier in the field of USPs, (b) the launch of the Phase II clinical study of inecalcitol in AML both in France and the U.S., and (c) the encouraging results of the Phase II clinical study of inecalcitol in CML in France. Hybrigenics S.A. retains 20% of Hybrigenics Services' capital.
- **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. The existence of the Company's services subsidiary offseted the risk of heavy investments in Inecalcitol, as it invested steadily on expanding this division (through acquisitions and by launching the U.S. subsidiary) in all areas of life sciences. The presence of the services segment enabled the Company to diversify its business model and reduce the risk of loss on invested capital. However, the Company is now refocusing on biopharmaceutical R&D and has sold its controlling stakes in Hybrigenics Services S.A.S., the subsidiary dedicated to scientific proteomic services. Retained activities with Hybrigenics are the development of inecalcitol, the research on ubiquitin-specific proteases and the genomic scientific services performed by the Helixio branch.

- **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 lies in drug discovery and development. 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.
- **Legal Risks:** There are no legal risks associated with the Company, to the best of the author's knowledge.

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 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 € 4 B in 2014) in the field of DUBs. As per the agreement, Hybrigenics will identify and validate new targets among DUBs in these therapeutic areas and screen potential therapeutic agents which can 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 € 4 MM, which represents a research funding of € 0.75 MM per year since 2011 and includes the upfront amount the Company received before initiating the research in 2011. It is important to note that the Company received its first milestone payment of € 0.33 MM 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 € 9.5 MM or € 11.5 MM 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 accounted 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., to augment the revenue contribution from this region, which has a huge biomedical R&D market. This incorporated subsidiary represents the Company for R&D, regulatory and business development matters in the American terrain. Further, it helped 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 increased 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.

  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.

- **Strategic refocusing on biopharmaceutical R&D:** Hybrigenics S.A. has sold its controlling stakes in Hybrigenics Services S.A.S., its subsidiary dedicated to scientific proteomic services. The Company changed its strategic perspective to refocusing on biopharmaceutical R&D, given (a) the success of the research collaboration with Servier in the field of USPs, (b) the launch of the Phase II clinical study of inecalcitol in AML both in France and the U.S., and (c) the encouraging results of the Phase II clinical study of inecalcitol in CML in France. Hybrigenics S.A. retains 20% of Hybrigenics Services' capital. Retained activities with Hybrigenics are the development of inecalcitol, the research on ubiquitin-specific proteases and the genomic scientific services performed by the Helixio branch.

2.8 Shareholding Pattern

The total basic shares outstanding are 46.8 MM as on 20 September 2018.

Exhibit 7: Shareholding Pattern (As on September 20, 2018) [viii]

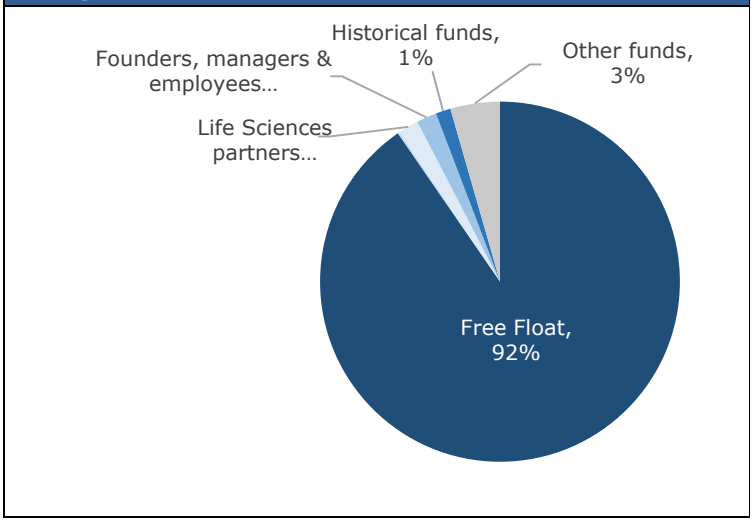


Exhibit 8: Shareholding Pattern [ix]

Shareholders	No. of Shares	% of total
Free Float	43,013,632	92%
Life Sciences partners	935,079	2%
Founders, managers & employees	935,079	2%
Historical funds	467,540	1%
Other funds	1,402,618	3%
Total Shares Outstanding	**46,753,948**	**100.0%**

2.9 Listing and Contact Details

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

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3. Key variable analysis [x]

3.1 Market share captured in terms of number of patients tapped

Hybrigenics is currently developing drugs for adult leukemias -CLL, AML and CML. They are studying the administration of oral Inecalcitol for CLL, AML and CML. The CLL drug program has completed the Phase II study while the drug program for both CML and AML are undergoing Phase 2 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 CLL, AML and CML patients in the key geographies (Company's target markets), i.e., U.S., and Europe.

3.1.1 Market Share: Percentage of patients tapped – CLL

Based on the assumption that the oral Inecalcitol drug for CLL will be launched in 2025, the market share captured by the Company post-launch is estimated to be as follows:

Exhibit 9: Market share: Percentage of patients tapped – CLL

%	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	0.13%	0.14%	0.15%	0.15%	0.35%	0.35%	0.39%	0.49%	0.57%	0.42%	0.37%	0.30%	0.25%
High estimate	0.15%	0.16%	0.17%	0.17%	0.37%	0.37%	0.41%	0.51%	0.59%	0.44%	0.39%	0.32%	0.27%

3.1.2 Market Share: Percentage of patients tapped – AML

Based on the assumption that the oral Inecalcitol drug for AML will be launched in 2023, the market share captured by the Company post-launch is estimated to be as follows:

Exhibit 10: Market share: Percentage of patients tapped – AML

%	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Low estimate	0.15%	0.19%	0.20%	0.23%	0.27%	0.30%	0.32%	0.33%	0.34%	0.35%	0.35%	0.34%	0.32%
High estimate	0.17%	0.21%	0.22%	0.25%	0.29%	0.32%	0.34%	0.35%	0.36%	0.37%	0.37%	0.36%	0.34%

Note-Assumption has been taken till 2037.

3.1.3 Market Share: Percentage of patients tapped – CML

Based on the assumption that the oral Inecalcitol drug for CML will be launched in 2024, the market share captured by the Company post-launch is estimated to be as follows:

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

%	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	0.15%	0.19%	0.20%	0.23%	0.27%	0.30%	0.32%	0.33%	0.34%	0.35%	0.35%	0.34%	0.32%	0.29%
High estimate	0.17%	0.21%	0.22%	0.25%	0.29%	0.32%	0.34%	0.35%	0.36%	0.37%	0.37%	0.36%	0.34%	0.31%

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 start of a partnership

- **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 rise once Hybrigenics' partners start generating revenue from sales

3.2.1 Revenue from Upfront and Milestone Payments – CLL

According to Arrowhead estimates, the expected deal value for CLL drug program lies between € 125 MM – € 135 MM. The upfront payments are expected to be in the range of € 27 MM in the low bracket and € 30 MM in the high bracket.

Exhibit 12: Revenue from Upfront and Milestone Payments – CLL

€ MM	2018E	2019E	2020E	2021E	2022E	2023E	2024E	Estimated Deal value (MM)
Low estimate	32	15	17	11	11	12	23	**€125**
High estimate	35	16	18	12	12	12	26	**€135**

3.2.2 Revenue from Upfront and Milestone Payments – AML

According to Arrowhead estimates, the expected deal value for AML drug program lies between € 125 MM – € 135 MM. The upfront payments are expected to be in the range of € 27 MM in the low bracket and € 30 MM in the high bracket.

Exhibit 13: Revenue from Upfront and Milestone Payments – AML

€ MM	2018E	2019E	2020E	2021E	2022E	Estimated Deal value (MM)
Low estimate	38	19	24	17	28	**€125**
High estimate	44	21	26	17	28	**€135**

3.2.3 Revenue from Upfront and Milestone Payments – CML

According to Arrowhead estimates, the expected deal value for CML drug program lies between € 125 MM – € 135 MM. The upfront payments are expected to be in the range of € 27 MM in the low bracket and € 30 MM in the high bracket.

Exhibit 14: Revenue from Upfront and Milestone Payments – CML

€ MM	2018E	2019E	2020E	2021E	2022E	2024E	Estimated Deal value (MM)
Low estimate	38	19	22	2	17	28	**€125**
High estimate	44	21	24	2	17	28	**€135**

3.3 Royalty Receipts

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

3.3.1 Royalty Receipts – CLL

The royalty payments are expected to commence in FY2025. Arrowhead expects the revenue to peak in 2033.

Exhibit 15: Royalty Receipts – CLL

€ MM	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	4.6	5.7	7.0	8.4	21.9	24.8	31.5	44.9	59.4	49.5	48.6	44.9	42.1
High estimate	6.4	7.8	9.6	11.3	27.7	31.5	39.7	56.1	73.7	62.2	61.5	57.5	54.6

3.3.2 Royalty Receipts – AML

The royalty payments are expected to commence in FY2023. Arrowhead expects the revenue to peak in 2034.

Exhibit 16: Royalty Receipts – AML

€ MM	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
Low estimate	8.9	11.8	13.8	16.9	21.3	25.3	28.8	31.8	35.1	38.4	40.9	42.0	41.3	40.2
High estimate	12.1	15.7	18.2	22.1	27.4	32.3	36.8	40.5	44.6	48.7	51.8	53.4	52.6	51.6

3.3.3 Royalty Receipts – CML

The royalty payments are expected to commence in FY2024. Arrowhead expects the revenue to peak in 2034.

Exhibit 17: Royalty Receipts – CML

€ MM	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	1.7	2.2	2.5	2.9	3.5	3.9	4.3	4.5	4.7	4.9	5.0	4.9	4.6	4.3
High estimate	2.4	3.0	3.3	3.8	4.5	5.0	5.4	5.7	6.0	6.2	6.3	6.2	5.8	5.5

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 – CLL

Exhibit 18: Probability of Occurrence (Success) – CLL

€ MM	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	Post 2026E
Low estimate	30%	45%	50%	60%	70%	75%	90%	90%	100%
High estimate	45%	50%	60%	70%	80%	90%	95%	100%	100%

3.4.2 Success Probability – AML

Exhibit 19: Probability of Occurrence (Success) – AML

€ MM	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	Post 2025E
Low estimate	50%	50%	60%	70%	80%	85%	90%	90%	100%
High estimate	50%	60%	70%	80%	85%	90%	100%	100%	100%

3.4.3 Success Probability – CML

Exhibit 20: Probability of Occurrence (Success) – CML

€ MM	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	Post 2025E
Low estimate	50%	50%	60%	70%	80%	85%	90%	90%	100%
High estimate	50%	65%	75%	80%	85%	90%	100%	100%	100%

4. News [xi]

- **Recruitment in Phase II International Trial of Inecalcitol in Acute Myeloid Leukemia (AML) closed:** On July 18, 2018 Hybrigenics announced that they have closed the recruitment of the clinical study Phase II International Trial of Inecalcitol in Acute Myeloid Leukemia (AML). A total of 115 patients recruited in 31 hospitals across France, United States, Spain, Germany and Belgium.

- **Hybrigenics released preclinical data:** The company proclaimed data from preclinical lead optimization studies of HBX 96,819, a USP8 inhibitor, which utilizes an innovative chemical modification switching inhibition from USP7 to USP8. In murine xenograft in vitro and in in vivo models, HBX 96,819 effectively killed human lung cancer cell lines, irrespective of their resistance to gefitinib.

- **Hybrigenics reaffirmed its eligibility for the PEA-PME scheme:** The company reaffirmed its eligibility for the PEA-PME scheme for 12 months forthcoming. Investors can continue to integrate Hybrigenics shares into PEA-PME accounts, device dedicated to investing in small and medium-sized companies.

- **Hybrigenics sold off Helixio:** The company is refocusing on R&D by selling off its genomics division, Helixio. Hybrigenics now have no stake in Helixio and both the companies are now completely independent.

- **Hybrigenics broad spectrum inhibitor of (USPs) shows antiviral activity against human adenoviruses:** The company announced the publication by a group of German researchers of the antiviral activity against human adenoviruses of an inhibitor of Ubiquitin- Specific Proteases (USPs) discovered and patented by Hybrigenics.

- **Hybrigenics announced full year 2017 results:** Hybrigenics released its accounts for full year 2017. The company registered no revenue in 2017 in comparison to € 1.4 MM of 2016. As of 31st December 2017, the cash position of Hybrigenics' retained activities was € 7.0 MM in 2017 vs. € 8.5 MM in 2016.

- **Hybrigenics H1 operating loss widens to € 3.5 MM euros:** Hybrigenics' 2017 half yearly operating result showed a loss of € 3.5 against a loss of € 2.5 in H1 2016. This increase was mainly due to the increase in R & D. Research and development costs were rising in line with the rise of the phase II clinical study in acute myeloid Leukemia. The commercial expenses exclusively related to the service activity remains stable.

- **Hybrigenics announced half year 2017 results:** Hybrigenics released its consolidated accounts for half year 2017. The turnover declined by around 21% from € 0.5 MM in 2016 to € 0.4 MM in 2017.

- **Hybrigenics' compound inhibits USP10 and shows activity in preclinical models of AML:** The company announced the publication of a scientific paper "Nature Chemical Biology" by a team of researchers led by Professor James D. Griffin. The publication has identified the ubiquitin-specific protease 10 (USP10) as a factor essential enzyme for tumour growth and survival of patients with AML with FLT3 and states that, the most effective compound in our screening, HBX 19.818, exercised effects antiproliferative impressive selective against cells [ed. LMA] positive for mutants FLT3. The study validates the importance of Ubiquitin-Specific Protease 10 (USP10) as a new target therapy for the potential treatment of Acute Myeloid Leukemia with FLT3 mutation. Hybrigenics occupies a pioneering position in the field of USPs research and already holds several patents covering various series of small molecule inhibitors of USPs

- **Strategic refocusing on biopharmaceutical R&D:** Hybrigenics S.A. has sold its controlling stakes in Hybrigenics Services S.A.S., its subsidiary dedicated to scientific proteomic services. The Company changed its strategic perspective to refocusing on biopharmaceutical R&D, given (a) the success of the research collaboration with Servier in the field of USPs, (b) the launch of the Phase II clinical study of inecalcitol in AML both in France and the U.S., and (c) the encouraging results of the Phase II clinical study of inecalcitol in CML in France. Hybrigenics S.A. retains 20% of Hybrigenics Services' capital. Hybrigenics' CEO, Remi Delansorne, said that the Company's past dual services and R&D business model is being simplified for a clearer perception of its new profile of pure biotechnology therapeutic player. Management buy-out of 75.8% of Hybrigenics Services' share capital is for a total amount of € 0.796 MM which includes down payment of € 0.196 MM and three earn-out payments for a maximum amount of € 0.200 MM each contingent to net result of Hybrigenics Services in 2018, 2019 and 2020.

- **Total constant scope turnover increased by 30%:** Hybrigenics' revenue of the constant scope (Hybrigenics Services + Helixio + Pharma R&D) reached a historical high level of € 6.1 MM in 2016, a 30% growth over 2015. This was mainly due to € 1.5 MM milestone payment received from Servier for the success of the research collaboration on one USP in oncology. Helixio business unit's scientific genomic services turnover growth of 67%, approximately by € 0.4 MM, also contributed to the growth of total revenue. Hybrigenics Services, which is in charge for scientific proteomic services and has been sold to its key managers, remained almost stable at € 3.6 MM in 2016, with 3% growth over € 3.5 MM in 2015. The new scope of the Company is Helixio + Pharma R&D.

- **Net Cash declined by half:** Cash position as of June 30, 2017 for Hybrigenics' retained activities was € 4.9 MM as compared to € 8.5 MM on December 31, 2016. The decline in cash mainly attributable to negative cash flow generated from operating activities. Also, company didn't raise any funds from financing over the period of time which lead the cash position to decline logically.

- **Hybrigenics presented new results at AACR 2017 on the specificity of inecalcitol in AML and MM:** Hybrigenics' research team documented the effects of inecalcitol on four AML and four MM human cell lines in vitro. Hybrigenics' CEO, Remi Delansorne, said that the results will support the ongoing clinical Phase II study of inecalcitol in AML and finding similar results on human MM cell lines will encourage to investigate the therapeutic role that inecalcitol could play in the new indication. Results of Phase II clinical study of inecalcitol in combination with decitabine in AML is expected in 1H 2019.

- **Encouraging preliminary results of the Phase II clinical study of inecalcitol in CML:** The ongoing, open-label Phase II study evaluates the efficacy of oral inecalcitol added to oral imatinib in CML patients with the objective to reach DMR within one year of treatment. The patients comprise people, who after at least two years of treatment with imatinib alone, have achieved MMR but not DMR. 21 patients have been enrolled to date out of which 12 remain under treatment and 9 have completed one year of treatment. At this intermediate stage of study, (a) 43% of the patients (6 out of 14) have shown further decrease in BCR-ABL from MMR at three months, and (b) 33% (3 out of 9) have demonstrated reduction in BCR-ABL beyond DMR, i.e. undetectable biomarker traces after one year of treatment. These results can be compared with two recently published independent reports which demonstrate a simple 7.5% yearly increase in the percentage of patients reaching DMR under imatinib alone. Based on these intermediate results and a very low study drop-out rate, the sample size of this pilot study has been reduced to 42 patients, with a target completion in H2 2018. Hybrigenics' Clinical Advisory Board has reviewed these preliminary observations and made suggestions to widen the scope of the potential clinical use of inecalcitol in CML. Results of Phase II clinical study of inecalcitol in combination with imatinib in CML expected in 2H 2018.

- **Hybrigenics granted its fifth family of patents on inhibitors of USP:** Hybrigenics has been granted patent in Europe, Japan and United States which protect a chemical series of specific reversible competitive inhibitors of USP7 until August 29, 2032. In total, Hybrigenics' intellectual property on USP inhibitors amounts to 72 granted and 22 pending patents protecting five chemical families and covers more than thirty countries.

- **Hybrigenics commenced Phase II clinical study of Inecalcitol in AML in the U.S.:** On January 11, 2016, Hybrigenics announced that it had received the authorization from the American FDA to perform a double-blind placebo-controlled clinical Phase II study of Inecalcitol in elderly or frail AML patients in the U.S. The company announced enrolment of first patient from U.S. in November and from France in September; there were 14 patients were under treatment in France as of November 28, 2016. The objective of the study is to focus on the elderly or frail AML patients who are unfit for standard chemotherapy and who can only receive monthly cycles of intravenous perfusions of decitabine (Dacogen®, Johnson & Johnson). In addition to this treatment, they will receive oral inecalcitol or placebo. The primary endpoint will be overall survival. The total number of 110 patients to be included in the study is designed to be sufficiently powered to evidence potential efficacy on mortality. Prof. J. Cortes, Chair of the AML and CML sections, Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, will be the principal investigator in the U.S.

- **Hybrigenics presented expanded in vitro results on Inecalcitol in multiple myeloma (MM) and AML:** On December 4, 2016 at the 58th Annual Meeting of the American Society of Hematology (ASH) in San Diego, U.S., the Company presented expanded in vitro results showing that Inecalcitol reproducibly stimulates the expression of the CD38 antigen at the surface of human MM or AML cell lines in culture. It has been confirmed that Inecalcitol increases the expression of CD38 at the surface of five MM cell lines in vitro; therefore, Inecalcitol could potentiate the clinical response of MM patients to a therapeutic anti-CD38 monoclonal antibody. It has also been confirmed

that Inecalcitol induces the expression of the CD38 antigen at the surface of four AML cell lines in vitro; thus, Inecalcitol could render AML patients sensitive to a therapeutic anti-CD38 monoclonal antibody.

- **Target of research collaboration with Servier on a USP relevant to oncology has been met:** The Company announced a new step in its R&D partnership with Servier in the field of USPs stating that the research collaboration, which started in 2011 has now reached its objectives, triggering a € 1.5 MM milestone payment to Hybrigenics. Servier will take charge of the continuation of this R&D program in oncology, while Hybrigenics will remain associated with its success, with a total of up to € 12 MM further payments linked to potential additional milestones until drug registration. Also, Hybrigenics will intensify its research to validate other USPs as innovative therapeutic targets and to discover new chemical series to efficiently inhibit them.

- **Hybrigenics' Inecalcitol receives key patent protection in the U.S. until 2031:** On April 04, 2016, Hybrigenics announced it had received from the USPTO the issue notification of two new different patents - one on the 14-epimerisation step in the chemical synthesis of Inecalcitol and the other on its convenient formulation as innovative tablets. A third patent on the therapeutic use of Inecalcitol at high doses had already been granted earlier in the U.S. These three American patents are all valid into 2031, with the earliest expiry on September 10, 2031.

- **Collaboration between Hybrigenics and the MD Anderson Cancer Center is nominated for the final round of the MedStartUp Awards 2016:** The Company announced the nomination of its collaboration with the University of Texas MD Anderson Cancer Center to the final round of the MedStartUp Awards, which took place in New York on October 27, 2016, in the "Best Collaboration with Academia Leading to a Breakthrough Solution" category. The outcome of the collaboration between Hybrigenics and the MD Anderson Cancer Center is the design and the implementation of a Phase II clinical trial of daily oral Inecalcitol in elderly or frail AML patients who are unfit for standard chemotherapy and who can only receive monthly cycles of intravenous perfusions of decitabine (Dacogen®, Johnson & Johnson).

- **Hybrigenics set up an international Clinical Advisory Board:** On November 16, 2015, Hybrigenics announced the first meeting of its newly assembled Clinical Advisory Board (CAB). The meeting had taken place on November 10, 2015 at its headquarters in Paris. Hybrigenics' CAB comprises three American and two French clinical experts in hematologic oncology namely, Prof. J. Cortes, Chair of the AML and CML sections at Department of Leukemia, University of Texas MD Anderson Cancer Center in Houston; Prof. O. Hermine, Chair of the Department of Hematology at Necker Hospital in Paris; Prof. M. Mauro, Leader of the Myeloproliferative Diseases Program at Memorial Sloan-Kettering Cancer Center in New York; and Prof. A. Turhan, Chair of the Department of Hematology at Kremlin-Bicetre Hospital in France. The company is in phase II clinical trial of oral inecalcitol in elderly or frail AML patients. Prof. O. Hermine will lead this study in Europe, while Prof. J. Cortes will be the principal investigator in the U.S.

- **Inecalcitol gets Orphan Drug designation for the treatment of AML in the U.S.:** On August 10, 2015, Hybrigenics announced that American Food and Drug Administration designated Inecalcitol for the treatment of AML as Orphan drug in the U.S. This favorable decision is based on in vitro and in vivo preclinical evidence showing the synergy between inecalcitol and azacytidine or decitabine to inhibit the growth of human AML cell lines in vitro and, in vivo, to prolong the survival of mice in two different experimental models of AML. The molecular basis of their synergy with inecalcitol, a vitamin D receptor agonist, has been elucidated: azacytidine or decitabine "unmask" the gene coding for vitamin D receptors. Consequently, more vitamin D receptors are expressed and available to be activated by inecalcitol, resulting in an improved efficacy to limit leukemia progression over the hypo-methylating agents alone.

- **Hybrigenics raises €9 MM from investors:** On April 7, 2015, Hybrigenics announced that it has successfully completed its capital increase program and has raised €9 MM from this offering. Of the total amount, the Company raised €6.5 MM by issuing about 4.6 MM shares at a price of €1.41 per share. The remaining €2.5 MM was raised through transaction reserved for subscribers under the TEPA law. The funds are intended to be used to finance the U.S. based Phase II study to evaluate the potential of inecalcitol in elderly or frail AML patients, in combination with azacytidine (Vidaza®, Celgene) and decitabine (Dacogen®, Janssen-Cilag, Eisai). The Company launched the study in France in September 2016 and in the US in November 2016.

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.

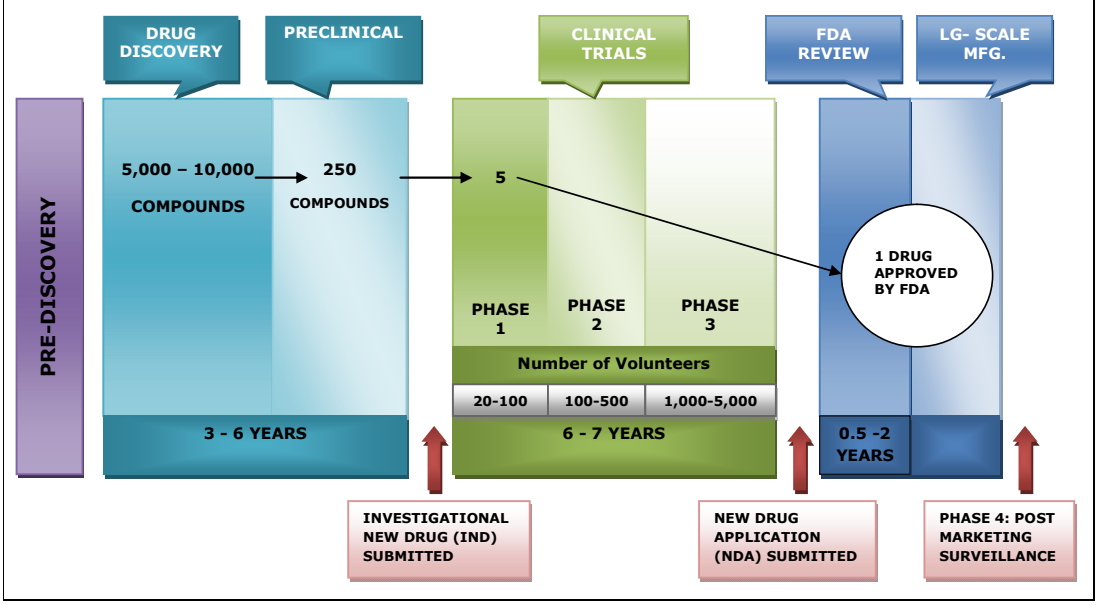
Exhibit 21: Management and Governance

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 possesses a broad experience in clinical development in oncology basis his earlier work experience 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, at the position of Manager, Business Planning & Performance. • He has served as Financial Director of Hybrigenics SA since June 2008.	• DESCF Accounting degree

6. Technologies and Markets

Drug Discovery and Development Process [xiii]

Exhibit 22: 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$ 800 MM to US$ 1 B per molecule. [xiv]

6.1 Drug Discovery Process

6.1.1 Pre-discovery Stage

Exhibit 23: 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 disease. They select the target that 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 must 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 the 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 results. 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 requires 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. At 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 about 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$ 0.1 MM-US$ 1 MM.
FDA approval is not required prior to the beginning of phase II. This stage involves 100-500 patient volunteers and takes from six months to up to three years. At 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$ 10 MM-US$ 100 MM.
FDA consultation is required prior to the beginning of phase III. Phase III trials confirm the effectiveness and safety of the drugs. About 1,000 – 5,000 patient volunteers are tested during this stage. Phase III trials are the most expensive and the longest. Cost: US$ 10 MM-US$ 500 MM.

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. If approved, this 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. Few 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. Post this new regulation, Takeda's drug 'Actos' was the first to be removed from the market. In addition, visits by sales representatives are also being restricted and 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 should continuously monitor the periodic reports as larger number of people start using it. Companies must continue research to evaluate the long-term safety of the drug.

6.3 Global Pharmaceutical Market

Per IMS Health report, the global pharmaceutical industry has reached US$ 1 T by 2014 and is expected to grow at a CAGR of 4.7% to reach US$ 1.3 T in 2018 led by US and Pharmerging markets (term used for most promising emerging markets), which would constitute 60% of sales and 80% of sales growth as per expectations.

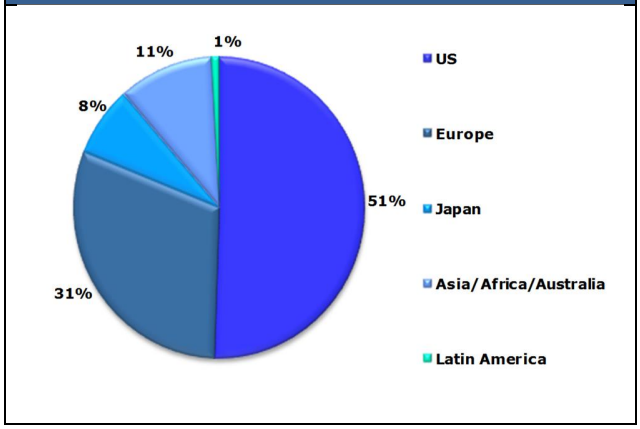
The global pharmaceutical market is dominated by the U.S., which accounted for about 40% of global market in 2014, followed by Europe with 24%, Asia/Africa/Australia together with 20% share and Latin America with 7%. This geographic distribution of medicine spending is forecasted to grow in 2014-2019, with U.S. growing by 2.7-5.7%, Europe by 1.3-4.3%, Asia/Africa/Australia together by over 6.9-9.9% and Latin America by 4.8-7.8%. Patent expirations and limits on drug spending could weigh down the growth of drug sales in developed countries. The growth is expected to rise by more than 50% in next five years in Pharmerging economies, which account for more than 25% of global spending on medicines. This will be led by China, whose spending is expected to reach about US$ 155-185 B by 2018.

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). [xix] Rising cost pressure on healthcare has resulted in an increase in generic pharmaceutical usage as generic drugs cost 80% less than their original equivalents.[xx]

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. [xxi]

Exhibit 24: Global Biopharmaceutical Market Share by Region [xxii]



The biopharmaceuticals market has a strong growth potential and is expected to have a bright future. Per the Market Research report from Industry Experts, biopharmaceutical products revenue contributed 10% to the total pharmaceutical industry revenue in 2006 which was expected to grow to around 15% in 2015. [xxiii]

Per Global Market Study on Biopharmaceuticals, in 2014, the global biopharmaceuticals market was valued at US$ 162 B, which is expected to grow at a CAGR of 9.4% over the period 2014-2020 to reach US$ 278 B by 2020. [xxiv]

6.4 Market Trends

6.4.1 Global R&D Investments recover gradually [xxv] [xxvi]

R&D is the most important aspect of the pharmaceutical industry. Innovation and discovery of new targets and drug compounds define 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 US$ 160 B in 2020 at a CAGR of 2.4% from 2013 to 2020, as per World Preview report 2014 from market intelligence firm, Evaluate Ltd. [xxvii] According to the report, the pharmaceutical industry is expected to gradually recover from the adverse effects of the patent cliff in the U.S. 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 for expansion of the industry.

Per the Pharmaceutical R&D Fact book compiled by Thomson Reuters unit CMR International August 2015, the number of new molecular entities (NME) launched globally in 2014 reached 46, the highest in over a decade v/s 29 in 2013[xxviii]. 67% of overall launches were of speciality drugs for the treatment of diseases such as cancer, HCV and eye disorders, while one-third of total launches were for rare indications. Also, out of 46, eleven were indicated within oncology, of which seven received orphan status.

R&D productivity has seen years of decline in biopharmaceutical industry, reaching its bottom in 2008. But fortunes have turned and 2014 was the year of new drug w approvals by the USFDA, with 53 new therapeutic drugs (NTDs) approvals, the highest in last two decades totalling to US$ 48 B in value, which is above the 25-year average of US$ 36 B per year.

Exhibit 25: FDA Drug Approvals and Peak Sales, 1990-2014 [xxix]

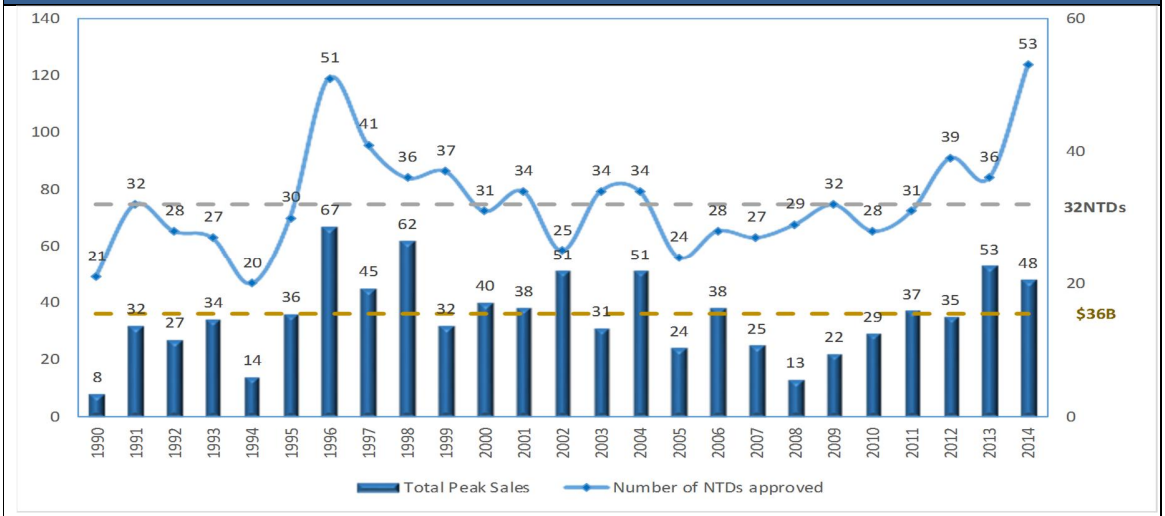
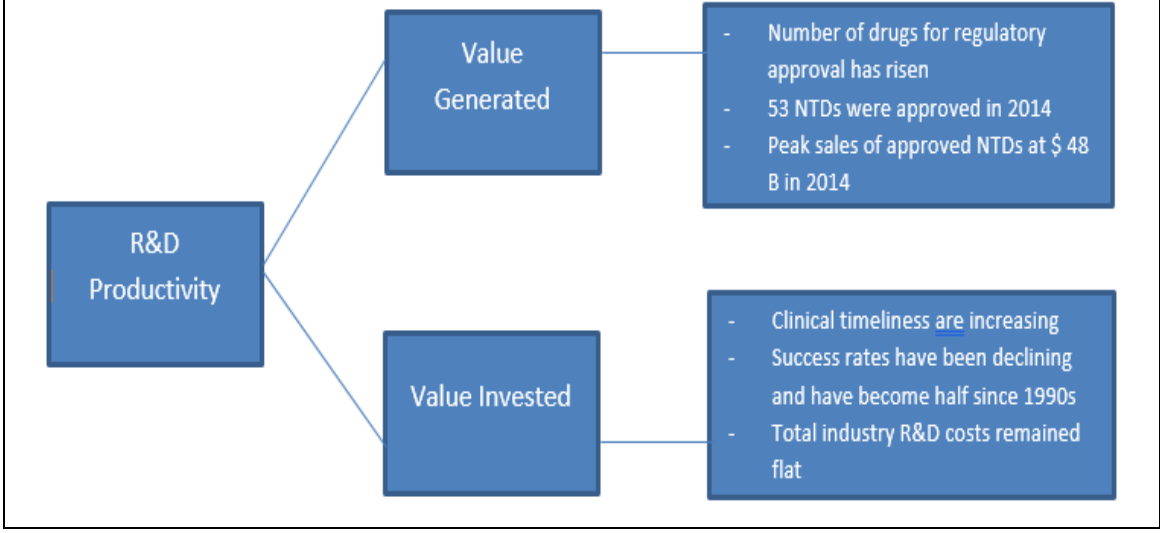


Exhibit 26: R&D Productivity stable – BCG Analysis [xxx]



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

The new drug discovery and development process is lengthy (average 15 years) and very expensive (average cost US$ 800 MM to US$ 1 B per drug) and manufacturing companies must make large R&D investments over this long period. It is difficult for large pharmaceutical companies to sustain such high internal R&D cost. Because 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 impact the sales directly and there could be price erosion up to 70% within months. [xxxiii] Given the dearth of new products and increasing competition in the market from generic versions of branded drugs, pharmaceutical companies are increasingly moving toward 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 partnerships agreements to license developmental drugs with biotechnology companies that have novel therapeutic drugs in development. Such partnership agreements give the pharmaceutical companies access to innovative new technologies, promising compounds as well as allow them to 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 can generate 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 US$ 215 B by 2020 from US$ 130.65 B in 2015 representing CAGR of about 8.7%. Within the outsourcing industry, the market value of Contract Research Outsourcing currently is estimated to be about US$ 114 B in 2015 and is projected to grow at a compound annual growth rate of 10.28% over the forecast period to reach US$ 205 B by 2021[xxxiv]

6.5 Trends in Prostate Cancer and Leukemia

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 are 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. [xxxv] Per 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 and this is expected to increase by 43% by 2020. [xxxvi]

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

Few 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).

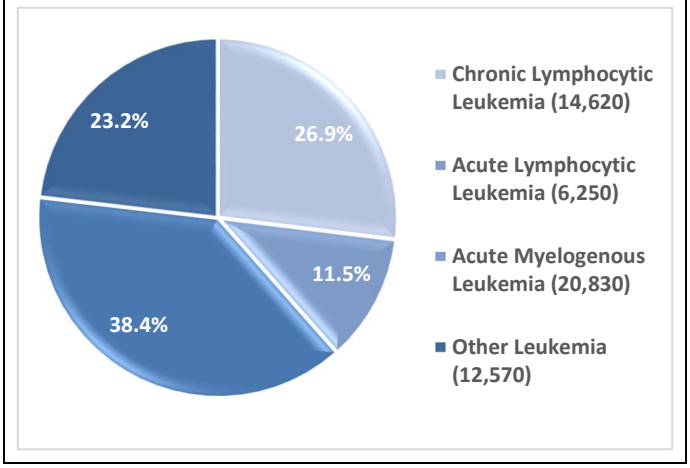
6.5.2 Leukemia

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. In 2015-2020, the Leukemia therapeutics market is expected to grow at a CAGR of 3.8% to reach US$ 11.3 B 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.[xxxviii]

Per the report published by American Leukemia and Lymphoma Society, in 2015, new cases of Leukemia are expected to be around 54,270 in the U.S.[xxxix]

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 2015, an estimated 327,520 number of patients were either living with ALL, AML, ALL or CML or were in remission from Leukemia. [xli]

Exhibit 27: Total Estimated Number of New Leukemia Cases in the U.S. – 2015 [xl]



CLL is a type of Leukemia, which is expected to account for about 27% of all leukemic patients in the U.S. in 2015.[xlii] 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 14,620 in the U.S. (American Leukemia Lymphoma Society, Facts 2014-15), 18,500 in Europe and 110,000 worldwide (Globocan 2012). [xliii] It has been found that 90% of the patients affected by CLL are middle aged and the probability increases in the 50+ age bracket. The CLL market is expected to grow at a CAGR of 13.4% from 2015-2020.

AML is expected to witness the highest number of new cases in 2015, accounting for about 38% of all leukemic patients.[xliv] Per American Leukemia Lymphoma Society, Facts 2014-15, annual estimates of newly diagnosed AML cases amounted to 20,830 in the U.S. and 22,500 in Europe as per RARECARE Working Group, 2012. Furthermore, per Globocan, 120,000 cases were recorded worldwide.[xlv]

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.[xlvi]

Per the report 'Facts & Figures' published by American Leukemia and Lymphoma Society, in all, there were approximately 3.3 MM patients living in the U.S. with Acute Lymphoblastic Leukemia (ALL), AML, CLL and CML.[xlvii]

According to 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 about US$ 3.9 B and US$ 3.6 B respectively). [xlviii]

Exhibit 28: The Four Major Types of Leukaemia: Acute or Chronic and Lymphoid or Myeloid [xlix]

Type of Leukemia	Lymphoid	Myeloid
Chronic	**Chronic Lymphocytic Leukemia** 32% annual incidence 19% deaths from leukemia Most frequent > 50 years 5-year survival rate = 85%	**Chronic Myeloid Leukemia** 14% annual incidence 4% deaths from leukemia Most frequent > 65 years 5-year survival rate = 63%
Acute	**Acute Lymphoblastic Leukemia** 11% annual incidence 6% deaths from leukemia Most frequent < 20 years 5-year survival rate = 70%	**Acute Myeloid Leukemia** 33% annual incidence 43% deaths from leukemia Most frequent > 50 years 5-year survival rate = 26%

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 more than US$ 100 MM, were entered during the Q3 2014. Of these, nine could potentially generate US$ 0.5 B or more in revenue for their primary collaborators. [l]

6.7 French Pharmaceutical Industry [li] [lii]

Per GlobalData, the French Pharmaceutical market is expected to grow at a very slow pace, i.e., CAGR of 0.7% to US$ 48.2 B in 2020 from US$ 46.2 B in 2014 owing to the growing focus on generic drugs. Shift to increased usage of generic medicine is 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. [liii] [liv]

In comparison with European countries such as UK and Germany, France is considered to be 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. Regarding 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:

- 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 these 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.

Shift in preference for generic drugs had affected the France Pharmaceutical market. But, 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.

7. Valuation

The Fair Market Value for all Hybrigenics shares stands between € 93 MM and € 124 MM as of September 20, 2018. The Fair Market Value for one of Hybrigenics' publicly traded regular shares stands between € 1.98 and € 2.66 as of September 20, 2018. The valuation approach followed is the Discounted Cash Flow method.

7.1 Discounted Cash Flow Method

Valuation	
WACC	
Risk-free rate	0.70%[lv]
Beta	0.97[lvi]
Market Return	9.8%[lvii]
Additional Risk Premium	9.7%
Cost of Equity	18.91%
Cost of Debt	2.3%
Terminal Growth Rate	0.5%
WACC (Discount Rate)	18.74%

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		

Exhibit 29: Year Ending - December	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
FCFF (High)*								
Net cash from operating activities	10,653	22,543	14,134	1,255	(7,783)	5,310	16,719	17,838
Capital Expenditure	(100)	(100)	(500)	(500)	(500)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	10,553	22,443	13,634	755	(8,283)	4,810	16,219	17,338
Discount factor	0.95	0.80	0.68	0.57	0.48	0.40	0.34	0.29
Present Value of FCFF	10,058	18,015	9,216	430	(3,971)	1,942	5,515	4,965
FCFF (Low)*								
Net cash from operating activities	8,849	17,386	8,685	(2,394)	(9,734)	3,116	12,848	12,970
Capital Expenditure	(100)	(100)	(500)	(500)	(500)	(500)	(500)	(500)
Net Debt Addition	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	8,749	17,286	8,185	(2,894)	(10,234)	2,616	12,348	12,470
Discount factor	0.95	0.80	0.68	0.57	0.48	0.40	0.34	0.29
Present Value of FCFF	8,339	13,875	5,533	(1,648)	(4,907)	1,056	4,199	3,571

** In the model, the valuation is continued to the year 2037, from which point the terminal value is established. For all data refer to the Appendix section 8*

Arrowhead Fair Value Bracket	High	Low	
Terminal Value (TV)	3,78,085	2,99,017	
Present Value of TV	23,075	18,249	
Present value of FCF	96,291	69,589	
Present Value of FCF + TV	1,19,366	87,838	
Net Debt	(4,815)	(4,815)	lviii
Equity Value Bracket	**1,24,181**	**92,653**	
Shares on issue ('000)	46,754	46,754	lix
Fair Share Value Bracket (€)	**2.66**	**1.98**	
Current Market price (€)	0.45	0.45	lx
Current Market Cap. (€) MM	21	21	
Target Market Cap. Bracket (€) MM	124	93	

Approach for DCF Valuation

Time Horizon: The Arrowhead fair valuation for Hybrigenics is based on the Discounted Cash Flow (DCF) method. The time chosen for the valuation is 228 months (2018E-2037E).

Terminal Value: Terminal Value is estimated to depend on a terminal growth rate of 0.5%, 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– CLL

Exhibit 30: Market share: Percentage of patients tapped – CLL

%	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	0.13%	0.14%	0.15%	0.15%	0.35%	0.35%	0.39%	0.49%	0.57%	0.42%	0.37%	0.30%	0.25%
High estimate	0.15%	0.16%	0.17%	0.17%	0.37%	0.37%	0.41%	0.51%	0.59%	0.44%	0.39%	0.32%	0.27%

Market Share: Percentage of patients tapped– AML

Exhibit 31: Market share: Percentage of patients tapped – AML

%	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
Low estimate	0.15%	0.19%	0.20%	0.23%	0.27%	0.30%	0.32%	0.33%	0.34%	0.35%	0.35%	0.34%	0.32%
High estimate	0.17%	0.21%	0.22%	0.25%	0.29%	0.32%	0.34%	0.35%	0.36%	0.37%	0.37%	0.36%	0.34%

Note-Assumption has been taken till 2037

Market Share: Percentage of patients tapped– CML

Exhibit 32: Royalty Receipts – CML

€ MM	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Low estimate	1.7	2.2	2.5	2.9	3.5	3.9	4.3	4.5	4.7	4.9	5.0	4.9	4.6	4.3
High estimate	2.4	3.0	3.3	3.8	4.5	5.0	5.4	5.7	6.0	6.2	6.3	6.2	5.8	5.5

Revenue from Upfront and Milestone Receipts – CLL

Exhibit 33: Revenue from Upfront and Milestone Payments – CLL

€ MM	2018E	2019E	2020E	2021E	2022E	2023E	2024E	Estimated Deal value (MM)
Low estimate	32	15	17	11	11	12	23	**€125**
High estimate	35	16	18	12	12	12	26	**€135**

Revenue from Upfront and Milestone Receipts – AML

Exhibit 34: Revenue from Upfront and Milestone Payments – AML

€ MM	2018E	2019E	2020E	2021E	2022E	Estimated Deal value (MM)
Low estimate	38	19	24	17	28	**€125**
High estimate	44	21	26	17	28	**€135**

Revenue from Upfront and Milestone Receipts – CML

Exhibit 35: Revenue from Upfront and Milestone Payments – CML							
€ MM	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2024E**	**Estimated Deal value (MM)**
Low estimate	38	19	22	2	17	28	**€125**
High estimate	44	21	24	2	17	28	**€135**

Royalty Receipts – CLL

Exhibit 36: Royalty Receipts – CLL													
€ MM	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**	**2034E**	**2035E**	**2036E**	**2037E**
Low estimate	4.6	5.7	7.0	8.4	21.9	24.8	31.5	44.9	59.4	49.5	48.6	44.9	42.1
High estimate	6.4	7.8	9.6	11.3	27.7	31.5	39.7	56.1	73.7	62.2	61.5	57.5	54.6

Royalty Receipts – AML

Exhibit 37: Royalty Receipts – AML														
€ MM	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**	**2034E**	**2035E**	**2036E**
Low estimate	8.9	11.8	13.8	16.9	21.3	25.3	28.8	31.8	35.1	38.4	40.9	42.0	41.3	40.2
High estimate	12.1	15.7	18.2	22.1	27.4	32.3	36.8	40.5	44.6	48.7	51.8	53.4	52.6	51.6

Note – Assumption has been taken till 2037

Royalty Receipts – CML

Exhibit 38: Royalty Receipts – CML														
€ MM	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**	**2034E**	**2035E**	**2036E**	**2037E**
Low estimate	1.7	2.2	2.5	2.9	3.5	3.9	4.3	4.5	4.7	4.9	5.0	4.9	4.6	4.3
High estimate	2.4	3.0	3.3	3.8	4.5	5.0	5.4	5.7	6.0	6.2	6.3	6.2	5.8	5.5

Success Probability – CLL

Exhibit 39: Probability of Occurrence (Success) – CLL									
€ MM	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**Post 2026E**
Low estimate	30%	45%	50%	60%	70%	75%	90%	90%	100%
High estimate	45%	50%	60%	70%	80%	90%	95%	100%	100%

Success Probability – AML

Exhibit 40: Probability of Occurrence (Success) – AML									
€ MM	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**Post 2025E**
Low estimate	50%	50%	60%	70%	80%	85%	90%	90%	100%
High estimate	50%	60%	70%	80%	85%	90%	100%	100%	100%

Success Probability – CML

Exhibit 41: Probability of Occurrence (Success) – CML									
€ MM	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**Post 2025E**
Low estimate	50%	50%	60%	70%	80%	85%	90%	90%	100%
High estimate	50%	65%	75%	80%	85%	90%	100%	100%	100%

Note: Refer the Key Variable Section 3, for more details.

7.2 NPV Method Based on Peak Sales

Arrowhead has done an NPV valuation of Hybrigenics based on 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	2018
Discount Rate	18.7% [lxi]
Shares outstanding ('000)	46,754
Pharmaceutical Industry – PE (x)	13.00x [lxii]

Exhibit 42: NPV Based on Peak Sales

Drug Name	Indication	Current Status	Estimated launch	Years to Launch	Years to peak	Success rate		Peak Royalty - € '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	CLL	Phase 2	2025	7	8	28%	31%	31,452	39,677	89,714	96,714	33,926	42,281	21%	23%	1,803	2,461
Inecalcitol	AML	Phase 2	2023	5	11	28%	31%	35,063	44,551	97,000	1,07,000	36,978	46,981	21%	23%	1,174	1,633
Inecalcitol	CML	Phase 2	2024	6	10	28%	31%	4,272	5,447	1,25,000	1,35,000	36,196	43,539	21%	23%	1,364	1,797

	Low	High
Fair value (Intrinsic) (€)	**1.21**	**1.64**

Sensitivity Table - High

		11.0	12.0	13.0	14.0	15.0
Discount Rate (%)	**16.7%**	1.63	1.78	1.92	2.07	2.22
	17.7%	1.50	1.64	1.77	1.91	2.05
	18.7%	1.39	1.51	**1.64**	1.76	1.89
	19.7%	1.28	1.40	1.51	1.63	1.75
	20.7%	1.18	1.29	1.40	1.51	1.61

Sensitivity Table - Low

		11.0	12.0	13.0	14.0	15.0
Discount Rate (%)	**16.7%**	1.20	1.31	1.42	1.53	1.64
	17.7%	1.11	1.21	1.31	1.41	1.51
	18.7%	1.02	1.11	**1.21**	1.30	1.39
	19.7%	0.94	1.03	1.12	1.20	1.29
	20.7%	0.87	0.95	1.03	1.11	1.19

7.3 Project NPV

Arrowhead has calculated the NPV for each of the three 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 CLL Drug Program

Exhibit 43: NPV Calculations (€ '000)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Revenue - High	35,143	16,143	18,143	12,143	12,143	12,143	26,143	6,386	7,834	9,572
Cost and Expenses	1,344	2,007	8,335	13,549	16,525	9,789	3,415	2,085	2,397	2,326
EBIT	33,799	14,136	9,808	(1,406)	(4,383)	2,354	22,728	4,301	5,437	7,246
Success Rate	0%	45%	50%	60%	70%	80%	90%	95%	100%	100%
Risk Adjusted Cash flow	(1,344)	5,258	736	(6,263)	(8,025)	(75)	20,113	3,982	5,437	7,246
Year	0.3	1.3	2.3	3.3	4.3	5.3	6.3	7.3	8.3	9.3
Discount factor	0.95	0.80	0.68	0.57	0.48	0.40	0.34	0.29	0.24	0.20
Present Value	(1,281)	4,220	498	(3,566)	(3,848)	(30)	6,840	1,140	1,311	1,472

NPV Calculations (€ '000)	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue - High	11,340	27,723	31,507	39,677	56,091	73,745	62,193	61,478	57,497	54,588
Cost and Expenses	2,783	3,516	3,427	2,837	2,979	3,420	2,899	2,669	2,285	1,946
EBIT	8,557	24,207	28,079	36,840	53,111	70,325	59,294	58,809	55,212	52,643
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	8,557	24,207	28,079	36,840	53,111	70,325	59,294	58,809	55,212	52,643
Year	10	11	12	13	14	15	16	17	18	19
Discount factor	0.17	0.14	0.12	0.10	0.09	0.07	0.06	0.05	0.04	0.04
Present Value	1,464	3,487	3,407	3,764	4,570	5,096	3,619	3,023	2,390	1,919
Net Present value of cash flow (rNPV)	**39,496**									

7.3.2 AML Drug Program

Exhibit 44: NPV Calculations (€ '000)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Revenue - High	44,000	20,500	25,500	17,000	28,000	12,145	15,667	18,165	22,082	27,402
Cost and Expenses	1,344	2,007	8,335	13,549	16,525	9,789	3,415	2,085	2,397	2,326
EBIT	42,656	18,493	17,165	3,451	11,475	2,356	12,252	16,080	19,685	25,076
Success Rate	50%	60%	70%	80%	85%	90%	100%	100%	100%	100%
Risk Adjusted Cash flow	20,656	10,293	9,515	51	7,275	1,141	12,252	16,080	19,685	25,076
Year	0	1	2	3	4	5	6	7	8	9
Discount factor	0.95	0.80	0.68	0.57	0.48	0.40	0.34	0.29	0.24	0.20
Present Value	19,688	8,262	6,432	29	3,488	461	4,166	4,605	4,748	5,093

NPV Calculations (€'000)	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue - High	32,347	36,766	40,488	44,551	48,741	51,832	53,416	52,648	51,602	51,130
Cost and Expenses	2,783	3,516	3,427	2,837	2,979	3,420	2,899	2,669	2,285	1,946
EBIT	29,563	33,250	37,061	41,714	45,762	48,412	50,517	49,979	49,317	49,184
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	29,563	33,250	37,061	41,714	45,762	48,412	50,517	49,979	49,317	49,184
Year	10	11	12	13	14	15	16	17	18	19
Discount factor	0.17	0.14	0.12	0.10	0.09	0.07	0.06	0.05	0.04	0.04
Present Value	5,057	4,790	4,496	4,262	3,938	3,508	3,083	2,569	2,135	1,793
Net Present value of cash flow (rNPV)	**92,605**									

7.3.3 CML Drug Program

Exhibit 45: NPV Calculations (€ '000)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Revenue – High	44,000	20,500	23,500	2,000	17,000	28,000	2,377	2,953	3,263	3,780
Cost and Expenses	1,344	2,007	8,335	13,549	16,525	9,789	3,415	2,085	2,397	2,326
EBIT	42,656	18,493	15,165	(11,549)	475	18,211	(1,038)	868	866	1,454
Success Rate	50%	65%	75%	80%	85%	90%	100%	100%	100%	100%
Risk Adjusted Cash flow	20,656	11,318	9,290	(11,949)	(2,075)	15,411	(1,038)	868	866	1,454
Year	0	1	2	3	4	5	6	7	8	9
Discount factor	0.95	0.80	0.68	0.57	0.48	0.40	0.34	0.29	0.24	0.20
Present Value	19,688	9,085	6,280	(6,803)	(995)	6,223	(353)	249	209	295

NPV Calculations (€'000)	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E
Revenue - High	4,470	5,029	5,447	5,716	5,994	6,249	6,333	6,220	5,842	5,457
Cost and Expenses	2,783	3,516	3,427	2,837	2,979	3,420	2,899	2,669	2,285	1,946
EBIT	**1,687**	**1,513**	**2,020**	**2,879**	**3,015**	**2,829**	**3,434**	**3,551**	**3,557**	**3,511**
Success Rate	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Risk Adjusted Cash flow	1,687	1,513	2,020	2,879	3,015	2,829	3,434	3,551	3,557	3,511
Year	10	11	12	13	14	15	16	17	18	19
Discount factor	0.17	0.14	0.12	0.10	0.09	0.07	0.06	0.05	0.04	0.04
Present Value	289	218	245	294	259	205	210	183	154	128
Net Present value of cash flow (rNPV)	**36,063**									

See important disclosures on page 42 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 41 of this report.

8. Appendix

Hybrigenics' Balance Sheet Forecast – High Estimates

Exhibit 46: Consolidated Balance Sheet € '000	all figures in '000 €, unless stated differently						*High Bracket estimates*				
Year Ending December 31	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total current assets	43,771	59,787	75,127	58,688	55,011	57,100	68,277	76,767	89,948	1,07,636	1,29,596
Total Non-current assets	3,729	6,211	9,350	12,744	16,393	20,298	24,457	28,871	33,539	38,460	43,636
TOTAL ASSETS	**47,500**	**65,998**	**84,477**	**71,432**	**71,404**	**77,398**	**92,734**	**1,05,638**	**1,23,486**	**1,46,097**	**1,73,232**
Total current Liabilities	3,192	3,755	9,077	14,060	16,708	10,714	5,042	3,858	4,235	4,169	4,594
Total Non-Current Liabilities	306	258	306	306	306	306	306	306	306	306	306
TOTAL LIABILITIES	**3,498**	**4,012**	**9,383**	**14,366**	**17,014**	**11,020**	**5,348**	**4,164**	**4,541**	**4,475**	**4,900**
Total Shareholder's Equity	44,002	61,986	75,093	57,066	54,390	66,378	87,386	1,01,474	1,18,946	1,41,622	1,68,332
TOTAL LIABILITIES & EQUITY	**47,500**	**65,998**	**84,477**	**71,432**	**71,404**	**77,398**	**92,734**	**1,05,638**	**1,23,486**	**1,46,097**	**1,73,232**

Hybrigenics' Balance Sheet Forecast – Low Estimates

Exhibit 47: Consolidated Balance Sheet € '000	all figures in '000 €, unless stated differently						*Low Bracket estimates*				
Year Ending December 31	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total current assets	39,770	49,222	59,119	40,390	33,597	33,833	38,996	43,804	52,934	65,902	82,245
Total Non-current assets	3,729	6,211	9,350	12,744	16,393	20,298	24,457	28,871	33,539	38,460	43,636
TOTAL ASSETS	**43,500**	**55,433**	**68,469**	**53,134**	**49,990**	**54,131**	**63,453**	**72,675**	**86,473**	**1,04,363**	**1,25,881**
Total current Liabilities	3,192	3,755	8,258	13,847	16,398	10,073	3,943	3,057	3,432	3,413	3,719
Total Non-Current Liabilities	306	258	306	306	306	306	306	306	306	306	306
TOTAL LIABILITIES	**3,498**	**4,012**	**8,564**	**14,153**	**16,704**	**10,379**	**4,249**	**3,363**	**3,738**	**3,719**	**4,025**
Total Shareholder's Equity	40,002	51,421	59,905	38,981	33,286	43,752	59,204	69,312	82,735	1,00,644	1,21,857
TOTAL LIABILITIES & EQUITY	**43,500**	**55,433**	**68,469**	**53,134**	**49,990**	**54,131**	**63,453**	**72,675**	**86,473**	**1,04,363**	**1,25,881**

FCFF Calculation (2026E-2035E) – Continued from page 32

Exhibit 48: Year Ending – December (€ '000)	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
FCFF (High)										
Net cash from operating activities	16,045	19,888	24,459	32,765	43,212	49,656	61,283	74,654	78,205	75,191
Capital Expenditure	(500)	(500)	(500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	15,545	19,388	23,959	30,265	40,712	47,156	58,783	72,154	75,705	72,691
Discount factor	0.24	0.20	0.17	0.14	0.12	0.10	0.09	0.07	0.06	0.05
Present Value of FCFF	3,749	3,938	4,098	4,360	4,939	4,818	5,058	5,229	4,620	3,736
FCFF (Low)										
Net cash from operating activities	11,872	15,481	19,343	26,209	34,750	40,036	49,589	60,638	63,426	60,677
Capital Expenditure	(500)	(500)	(500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)
Net Debt Addition	-	-	-	-	-	-	-	-	-	-
Free Cash Flow to Firm	11,372	14,981	18,843	23,709	32,250	37,536	47,089	58,138	60,926	58,177
Discount factor	0.24	0.20	0.17	0.14	0.12	0.10	0.09	0.07	0.06	0.05
Present Value of FCFF	2,743	3,043	3,223	3,416	3,913	3,835	4,052	4,213	3,718	2,990

Exhibit 49: Year Ending – December (€ '000)	2036E	2037E
FCFF (High)		
Net cash from operating activities	73,444	71,123
Capital Expenditure	(2,500)	(2,500)
Net Debt Addition	-	-
Free Cash Flow to Firm	70,944	68,623
Discount factor	0.04	0.04
Present Value of FCFF	3,071	2,502
FCFF (Low)		
Net cash from operating activities	58,977	56,772
Capital Expenditure	(2,500)	(2,500)
Net Debt Addition	-	-
Free Cash Flow to Firm	56,477	54,272
Discount factor	0.04	0.04
Present Value of FCFF	2,445	1,978

9. Analyst Certifications and Important Disclosures

Analyst certifications

I, Parvati Rai, certify that all 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.

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

Important disclosures

Arrowhead Business and Investment Decisions, LLC received fees in 2012, 2013, 2014, 2015, 2016 and 2017 and will receive fees in 2018 from Hybrigenics SA for researching and drafting this report and for a series of other services to Hybrigenics including distribution of this report and networking services. Neither Arrowhead BID nor any of its principals or employees own any long or short positions in Hybrigenics. Arrowhead BID's principals intend to seek a mandate for investment banking services from Hybrigenics and expect to receive compensation for investment banking activities for Hybrigenics in 2018 or 2019.

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

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

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

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

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

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

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10. Notes and References

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[lix] Shares as on November 30, 2017
[lx] Source: Bloomberg, December 18, 2017
[lxi] Source: WACC calculation Shown on Page 31
[lxii] Source: Arrowhead estimates