DolutePharm Industries +

Economics Report

Dolutegravir Production

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Nomenclature		
Symbol	Definition	Unit
AIDS	Acquired Immunodeficiency Syndrome	-
ART	Antiretroviral Therapy	-
API	Active Pharmaceutical Ingredient	-
BMGF	Bill and Melinda Gates Foundation	-
CAGR	Compound Annual Growth Rate	%
CAPEX	Capital Expenditure	USD
CEPCI	Chemical Engineering Plant Cost Index	-
CHAI	Clinton Health Access Initiative	-
D/E	Debt to Equity Ratio	-
D	Amount of Debt	USD
DMA	Dimethylamine	-
DMF	Drug Master File	-
DPI	DolutePharm Industries	-
DTG	Dolutegravir	-
EBITDA	Earnings Before Interest, Tax, Depreciation and Amortization.	-
FDA	Federal Drug Agency	-
GMP	Good Manufacturing Practice	-
HIV	Human Immunodeficiency Virus	-
INI	Integrase Inhibitors	-
IRR	Initial Rate of Return	%
ISBL	Inside Batter Limits	USD
KIZAD	Khalifa Industrial Zone	-
LF	Location Factor	-
LLE	Liquid-Liquid Extraction	-
MF	Material Factor	-
MOIC	Multiple on Invested Capital	-
NPV	Net Present Value	USD
OSBL	Outside Battery Limits	USD
P	Preferred Stock	-
PFR	Plug Flow Reactor	-
PPP	Public Private Partnership	-
S	Sizing Parameter	-
SEZ	Special Economic Zone	-
UAE	United Arab Emirates	-
WACC	Weighted Average Cost of Capital	%
WHO	World Health Organisation	-
β	Systemic risk of an asset.	-
CF_n	Cash flow in year n	USD
F	Lang Factor	-
i	Interest rate	%
K_e	Cost of Equity	%
r_f	Risk free rate	%
r_m	Return of the market	%
K_d	Cost of Debt	%
K_p	Cost of Preferred Stock	%

1. Introduction

Human Immunodeficiency Virus type-1 (HIV-1) remains a severe threat to public health. It was estimated at the end of 2021 that over 38 million people are living with HIV globally [1]. **Figure 1** shows the global profile of HIV cases and deaths. The number of deaths and new infections have declined over time despite an increase in number of people living with HIV. This is due to increased understanding and education on the virus. As of 2021, 85% of persons living with HIV globally were aware of their status. Furthermore, 75% of persons living with HIV were receiving access to HIV treatment and 68% had achieved viral suppression [2]. Viral suppression is responsible for this decline in new infections and deaths and is a result of significant advancements in Antiretroviral Therapy (ART) for HIV treatment [3]. There are six main classes of ARTs, treatment of HIV will typically involve a combination of these classes. They include Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), Integrase Inhibitors (INIs), Entry Inhibitors (EIs), Protease Inhibitors (PIs) and Booster Drugs (BD) [4].

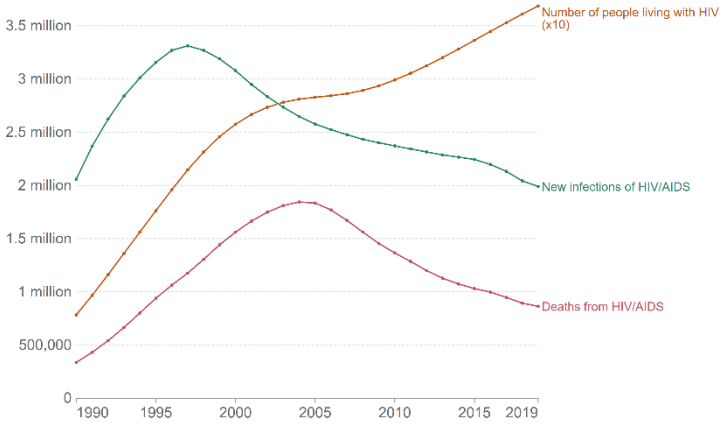

Figure 1. HIV-related deaths and new cases are declining, but there is still a linear growth trend of people living with HIV *[39]*.

Integrase Inhibitors are amongst the most widely used class of ARTs used in several combination therapies [5]. Among the wide variety of integrase inhibitors available, dolutegravir (DTG) has stellar properties in terms of its high genetic barrier to resistance and potent antiviral activity [6]. However, complicated synthesis steps and expensive high-performance liquid chromatography separations are involved for its preparation in the medicinal chemistry stage, which exerts conceivable difficulty for large-scale synthesis [7] [8]. DolutePharm Industries has designed a process to synthesise DTG at a large scale. The plant will be sited in the UAE and the manufactured Active Pharmaceutical Ingredient (API) will be distributed through Hawkes Industries.

2. Business Strategy

2.1. Market Assessment

The HIV drugs market is characterised by its large volume and steady, but decelerating growth rate. A 2021 estimate valued the global market at 30.46B USD , with an expected value of 45.58B USD by 2028. This corresponds to a Compound Annual Growth Rate (CAGR) of 5.9% [9]; a similar value to that of the wider pharmaceutical industry's at 5.39% [10]. This is however significantly lower than that of DTG which stands at 7.9% for 2022-2030 [11]. Tivicay, the branded version of DTG generated 1.98bn USD in sales in 2015 [12]. As this brand version accounted for 72% of market share, the total global market value of DTG in 2015 thus stood at 2.75bn USD [13]. Applying the 7.9% CAGR, the 2022 market value is estimated at 5.1B USD. This is due to DTG's superior efficacy, independence of action and safety profile, all of which are factors which led to it being named as the World Health Organisation's (WHO's) chosen first- and second-line treatment of choice [14], the results of which are illustrated in **Figure 2**. The open market value of DTG is expected to decrease as market share

increases. However, it is difficult to determine whether price suppression due to economies of scale would impact this more than price inflation due to a DTG monopoly of the integrase market.

Figure *2*. Share of different drugs as first-line (left) and second line (right) treatment *[15]*.

Currently, a majority of the market share is divided between ViiV Healthcare (Owned by GSK, Pfizer Inc and Shionogi & Co.), Shanghai Desano, Aurobindo Pharma, Laurus Labs, and Adcock Ingram. Whilst data is unavailable on the market share of these players, ViiV is the sole licensed manufacturer in the USA, whilst the CEO of Mylan (now owned by Viatris) stated in 2016 that "50% of people living with HIV/AIDS worldwide who are receiving treatment depend on a Mylan product" [16].

As stated in (**Economics Section 1**) DTG belongs to a class of ARTs known as Integrase Inhibitors (INI). **Figure 3** shows that INIs represent 25% of the HIV drug market, despite DTG's standing as the WHO's recommended treatment. This indicates a strong likelihood of a straightforward path to market entry. To maximise the likelihood of effective market penetration, South Africa, India, and Uganda were targeted as the primary sales countries for Dolutegravir. These countries represent the largest markets and are high-priority countries in the Public Private Partnership (PPP) established with the Bill and Melinda Gates Foundation (BMGF), UN agencies, and Local Government agencies. The PPP guarantees minimum sales prices and ensures that Dolutegravir will be supplied to the nations that need it the most, as, in these nations, researchers found that more than 10% of HIV patients starting ARV treatment had a strain of HIV which was resistant to the most widely used medications [17]. DPI's partaking in the PPP will provide good targets for the "Social" and "Governance" of ESG and will be advantageous for sustainable financing options. Additionally, 95% of children living with HIV in Western and Central Europe and North America are already on antiretroviral medication, creating market barriers that are much higher in those regions [18]. The UAE's existing free trade agreement with South Africa and other African nations further bolstered the PPP [19]. Focusing on these markets allows for tremendous growth potential, and the guaranteed sales through the PPP provide a strong foundation for success. Furthermore, approval by a foreign governing body for Good Manufacturing Practice (GMP) is sufficient for automatic approval within the target markets. Thus, only one DMF is required for submission to the FDA.

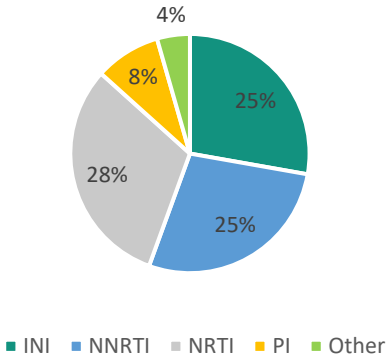

Figure 3. 2015 Sales by class, total 24.23B USD *[12]*

The greatest risk for the DTG market is the emergence of newer, more effective treatments which will be able to replace it as the recommended option. However, given UNAIDS' plans to end the AIDS

epidemic by 2030 [20], there may already be a reduction in research and development for a DTG substitute. Other risks, such as new adverse effects or regulation, are relatively minor. These are covered in greater detail in **Economics Section 2.7.**

2.2. Patent and Patent Expiry

The patent for DTG is due to expire in 2026. This typically results in decreased profit margins for a firm as a result of market saturation. In typical situations, this results in a decrease in margins and a slight increase in volume as smaller manufacturers begin manufacturing generic versions of the drug, saturating the market, and decreasing manufacturer bargaining power. Since the DTG market is characterised by a few large manufacturers (possibly due to the complexity of production), listed above, there may not be as many generic manufacturers who flood the market once the patent expires. Additionally, DPI's product is set at a highly competitive price point, being priced to allow a 75 USD per person per year cost, as opposed to the average developed market value of 2,458 USD [21]. Thus, it is unlikely that patent expiry will result in a decrease in sales as the current price is likely to be competitive with the generics that are introduced into the market.

DPI's plant is due to begin operation a year before the expiry of the DTG patent and 6 years before the expiry of the process patent, in 2025. Initial negotiations with Hawkes Industries resulted in a royalty rate of 20% of revenue for unlimited production and use of both patents. This rate was reduced to 17.2% [22] through a PPP with the Clinton Health Access Initiative and ViiV, which allows for royalty-free selling of the drug to children living with HIV in developing nations. This reduction is proportional to the share of the Dolutegravir market that is comprised of children.

2.3. Production rates and Product portfolio

Dolutegravir is the primary product of this process. The production rate has been specified at 88 tonnes per annum. This was selected based on market analysis and DPIs target market share.
As stated in **Economics Section 2.1**, limited major players exist within this market. Laurus labs, a manufacturer with the sixth largest market share, occupies just 8.8% of the market. Therefore, based on DPI's relatively cheap price point, limited barriers to entry in the target market, and the start-up nature of the firm, a conservative estimate of 6.1% maximum market capture was decided. Based on the market size, this would be equivalent to an annual DTG revenue of 352M USD, which corresponds to a production rate of 88 tonnes per annum.
Dimethylamine (DMA) is the secondary product of this process. It is widely used within the chemical industry as a methylating agent and solvent. The DMA market currently stands at 231.9M USD with a CAGR of 2.2% [23]. This is a significantly less attractive market, however, the decision to sell it was made based on its high purity recovery. Additionally, given that (petro)chemicals account for 13% of all UAE exports, there is the potential to sell these locally due to the UAE's strong chemicals industry [24].

2.4. Points of differentiation

There has long been a wide push within the pharmaceutical industry for continuous manufacturing. This is due to it allowing for greater control and being faster through the elimination of hold times [25]. Attention was bolstered by the covid-19 pandemic as it highlighted the need for stronger supply chains. However, despite this push, the current technological landscape, funding, and regulatory issues have resulted in a very gradual adoption of continuous manufacturing [26].
The novel continuous process proposed thus places DPI in a position to lead these new developments within the pharmaceutical innovation space. Moreover, continuous manufacturing also offers the advantage of adaptability. As a consequence of this, DPI will be able to respond more

nimbly to market changes [27]. Additionally, the by-product also has a growing market which DPI is primed to penetrate. These factors will all serve to protect DPI in the event of low demand of Dolutegravir or high market saturation upon patent expiry.

2.5. Plant Location

Following a TOPSIS analysis detailed in **Synthesis Appendix A.2**, the United Arab Emirates (UAE) was selected as the location for this chemical plant due to its favourable business environment. This includes its combination of low taxes, moderate utility prices, high talent competitiveness, regional stability and a low weighted average distance to the target market. The UAE's healthcare sector is also expected to grow at a CAGR of over 7% from 2021 to 2027 [28], beating the global prediction of 5.6% [29] and offering a competitive advantage for any future projects after DTG production ceases.

Established in 2012, the Khalifa Industrial Zone (KIZAD) has been widely recognised as a thriving industrial Special Economic Zones (SEZ) and is ranked as a top 10 industrial zone by the Financial Times [30]. This is where the facility will be sited. It offers the advantage of being situated close to the state-of-the-art Khalifa deep port, allowing easy access to global markets, and serving as a multi-modal transport hub. Additionally, KIZAD is nearly equidistant from central Abu Dhabi and Dubai, providing ample opportunity for business growth and talent attraction. Quantifiable benefits include 100% foreign ownership, 0% customs duty, and 0% corporate and income tax [31].

2.6. Pricing Strategy

The price for DTG was decided using judgements from DPIs PPP with the BMGF and Clinton Health Access Initiative (CHAI), and a WHO-approved framework for the estimation of a generic drug price from the cost of the API [32]. As the final drug price is known, the API cost can be back calculated, adjusting for inflation by applying an aggregate 30% inflation multiple from the date of announcement of the PPP to today. The framework used is set out in **Appendix 11.1**.

A final price of 4000 USD per kilogram was achieved through a combination of this method and negotiation with Hawkes Industries.

2.7. Market Environment Analysis

2.7.1. Porters Five Forces

Porter's Five Forces is a framework used to assess the competitiveness of a business environment by quantifying the risk associated with each force, with a score of 1 representing a low threat and a score of 5 representing a high threat to the firm's business. Although this framework provides a useful analysis of the five forces of competitive pressure, it has the limitation of being static and not accounting for future changes, such as the bargaining power of buyers, which may change over time. However, it is vital to understand an industry’s competitive landscape, as it will allow DPI to identify key progress indicators, assess supplier and buyer trends, and evaluate goals and performance.

THREAT OF NEW ENTRANTS - Medium

The Dolutegravir industry is subject to strict regulations by regulatory authorities, which act as a significant barrier to entry for new players. These regulations are in place to ensure that the drug is safe and effective for patients. In addition to regulatory barriers, there are also high fixed costs associated with manufacturing Dolutegravir. The production of the drug requires specialized equipment, and the costs associated with maintaining these facilities can be significant. As a result, companies that are interested in manufacturing Dolutegravir must make a substantial investment in capital expenditures before they can begin production.

However, the threat of new entrants to the Dolutegravir industry is still moderate due to the potential for generic versions of the drug. This is expected to happen once the patent expires in

2026. In addition, the low switching costs for patients who are using Dolutegravir can make it easier for new entrants to enter the market, as patients are not tied to a particular manufacturer. This can reduce the market share of established manufacturers.

Table 1. Threat of New Entrants.

Capital Requirements	Customer Switching Cost	Economies of Scale	IP Coverage	Incumbency Advantages
4	1	3	4	1

THREAT OF SUBSTITUTES - Low

The threat of substitutes for Dolutegravir is low due to the limited availability of effective alternatives for HIV treatment. Although there are other drugs available for HIV treatment, Dolutegravir's effectiveness, safety profile, and ease of use have made it the WHO's recommended first and second-line treatment for prevention and sustainment of HIV/AIDs cases in all populations [14]. This is advantageous, as DPI's PPP with the Bill and Melinda Gates Foundation to supply Dolutegravir is guided by WHO and UNAIDS guidelines.

Table 2. Threat of New Substitutes.

# Of Substitutes	Substitute Quality	Substitute Price	Cost of Switching
3	1	3	1

BARGAINING POWER OF SUPPLIERS – Medium to High

The bargaining power of suppliers in the Dolutegravir industry is high due to several factors. Firstly, the concentration of suppliers is a key factor, as the industry is reliant on a limited number of suppliers for specialised raw materials. This concentration can give suppliers significant leverage in dictating prices and terms of supply. Another important factor that increases the bargaining power of suppliers is the high switching costs for manufacturers. Switching suppliers can be costly, both in terms of time and resources, and may even require new regulatory approval for the drug. Suppliers may be aware of this and use it to their advantage when negotiating with manufacturers.

Table 3. Bargaining Power of Suppliers.

# Of Suppliers	Switching Cost	Supplier Concentration	Quality Importance
3	1	2	5

BARGAINING POWER OF BUYERS – High

The Dolutegravir industry is dominated by large purchasers such as government organizations and non-profit organizations, who purchase the drug in large volumes. This gives them significant bargaining power as they have the ability to negotiate lower prices from manufacturers. Furthermore, these organizations are often operating in resource-constrained environments, and therefore require access to the drug at affordable prices for long-term contracts. Finally, since DTG is subject to strict regulations, there is little differentiability between each API manufacturer's DTG product. Particularly in DPI's scenario, the buyer concentration is also very high due to the PPP.

Table 4. Bargaining Power of Buyers.

Buyer Concentration	Information Available to Buyer	Switching Cost	Buyer Loyalty
4	3	1	3

Competitive Rivalry – Medium

The industry is characterized by several established pharmaceutical companies, each with their own version of the drug, which creates competition among the players. The existence of patent protection for the drug in some countries also limits competition from generics, making it harder

for new entrants to break into the market. However, this situation is likely to change over time as patent protections expire, which will lead to the entry of generics and increased competition.
In addition to these factors, the potential for emerging markets to enter the space is another factor that could increase competition. Emerging markets have lower costs of production, which allows them to sell the drug at lower prices, thereby putting pressure on established players to lower their prices as well. This competition can lead to reduced profit margins for companies operating in the industry.

Table 5. Competitive Rivalry.

# Of Competitors	Differences in Products	Customer Loyalty	Exit Barriers
3	2	4	3

2.7.2. PESTEL Analysis

A PESTEL analysis was conducted to assess the risks and effects of macroenvironmental factors which may impact DPI. The results of which are summarised in **Table 6** represents the degree of likelihood of a risk and S represents the severity of the consequences if these risks were to be actualised.

Table 6. PESTEL Analysis.

Political		
Risk Event	Effect	Risk
Carbon tax imposed on pharmaceutical industry	A carbon tax such as those in effect in power, construction or similar industries would increase OPEX, reducing profit and economic performance. Alternatively, it could also result in a higher initial capital investment as measures are built in to reduce emissions.	L: Medium S: Medium
Nullification of KIZAD	The chosen location is a special Economic zone which offers advantages such as 0% import, corporate and income tax. If this is no longer the case, it would also result in reduced profits and economic performance.	L: Low S: Medium
Economical		
Risk Event	Effect	Risk
Increase in loan interest rates	A portion of the TCI will be funded through debt. If loan interest payments are increased so is OPEX. Consequently, net profit is reduced.	L: Medium S: Low
Increase in Foreign Exchange rates	All feedstock for the process is imported. If exchange rates are increased, then so will raw material costs. This would result in a lower profit margin for the process.	L: Medium S: Low
Economic recession	A recession similar to the one caused by the Covid-19 pandemic would result in supply chain disruptions. This would hinder production and impact revenue streams. Utilities costs would likely also increase which would reduce profits.	L: Medium S: High
Social		
Change in attitudes towards imported products	Consumers within the chosen target markets (India, South-Africa, and Uganda) could lose confidence in drugs not produced locally. India in particular could see this happen as a good number of HIV drug manufacturers are	L: Low S: Low

	sited there. This would result in reduced market penetration.	
Education & lifestyle change	The target markets are becoming developed nations. This is likely to result in people living healthier lifestyles and gaining more awareness on HIV. This would reduce market demand.	L: Low S: Low
Changes in attitudes towards generics	Consumers could lose confidence in drugs produced by smaller brands reducing market penetration.	L: Low S: Low
Technological		
Alternative & improved synthesis routes discovered	If a new more efficient manufacturing process is discovered which significantly reduces operating costs, this would result in a lower selling price. This would result in the market being composed primarily of these new players reducing DPI's market share. This is a risk that would be exacerbated by the expiry of the patent.	L: Medium S: Medium
Domination of different drug classes.	DTG is an integrase inhibitor. A scientific breakthrough could result in discovery of a new class of drugs that takes away market share from Integrase inhibitors. This would reduce DTG's market size and consequently DPI's revenue	L: Medium S: High
Environmental		
Pollution limits reduced	Reduced pollution limits would increase waste processing costs. This would impact DPI's profits	L: Medium S: Low
New bans or regulations	If new regulations are placed on certain materials, new and potentially more expensive replacements would have to be sourced.	L: Low M: Medium
Presence of toxic substances in product	If toxic substances are discovered in product by consumers this would adversely affect DPI's reputation.	L: Low M: Medium
Legal		
Changes to employee rights	Stricter laws being implemented with regards to workers' rights in the UAE would likely increase labour and overhead operating costs.	L: Low S: Low

2.7.3. SWOT Analysis

Table 7. SWOT Analysis.

Strength	Weaknesses
• Continuous nature of the process leads to reduced costs and more efficient process. • Public-Private Partnership allows for easy market entry.	• As DPI is a generics manufacturer, the firm currently has no brand identity which could negatively impact market penetration. • The Initial Capital Investment of the process is quite high. • Specialty feedstock is largely required for the process. This could result in supply chain issues.

Opportunities	Threats
• Easy reconfiguration of plants for production of other pharmaceuticals. • Government Schemes to improve healthcare access will boost market penetration.	• Patent Expiry would result in market saturation. • New regulations could increase operating costs.

2.8. Business Timeline and Turndown scenarios

DPI has proposed a 10-year lifespan for this plant marking the key dates is shown below.
Early 2023: Business is registered, Capital structure and plant design finalised.
Late 2023: Construction of plant begins.
2024: Safety test conducted. Plant ready to begin operation.
2025: Plant begins operation at 60% capacity
2026: Plant operates at full capacity.
2031: re-evaluation of process and business strategy to identify potential by-products as patents expire.
2034: Decommissioning of plant at end of its lifetime

3. Key Assumptions and Decisions

3.1. Key Assumptions

A set of key assumptions used in the estimation of costs and conducting financial analysis are listed below.

- All prices and costs have been agreed with Hawkes Industries
- The 2023 agreed contract price of labour, materials and waste treatment increase every year based on the past average 10-year inflation rate in UAE of 1.81% [33].
- The operating lifetime of the plant is 10 years commencing from 2025 following the completion of construction.
- The CAPEX is based on 2023 prices whereas OPEX is calculated based on 2025 prices.
- By-product prices increase at the same rate as the 10 year UAE inflation rate. DTG price and waste treatment price per tonne will however remain the same.
- Project costs will be paid entirely in 2023, with interest payments commencing from 2025.
- Depreciation is calculated using straight-line depreciation from beginning of plant operation with a salvage value of 15% of the initial capital investment.
- Equity investors will be reimbursed as followed:
    - The projected final value of their stake will be calculated over the investment term and projected growth using the CAPM.
    - They will be paid this final value in annual instalments over the plant life, effect from the first full year of operation.

3.2. Key decisions motivated by Economics.

Economic factors were considered as key decision metrics at several stages to guide DPI's operation. Economic potential was a key criterion in the MCDM for selection of the synthesis route. This is detailed in **Syntheses Section 2.6**. Upon selection of this an assessment of the current market landscape and the share which could be reasonably captured then prompted the selection of the plants target capacity. In addition to this, economic factors also resulted in the adoption of a heat integration system. The utilisation of this resulted in the complete elimination of the associated

cooling and heating operating costs. This is because of the heaters and coolers requiring either cooling water, steam, electricity, natural gas, or refrigerant. Ultimately, as a result of the extreme profitability of the process strict economic constraints were not placed on the process to allow for design innovation.

4. Capital Costs

4.1. Cost Estimation Methods

The Towler & Sinnott correlation (T&S) was used to estimate the purchased equipment cost (PCE) [34]. This was selected due to its applicability to a wide range of units and additional costs such as piping and site development. A correlation was used as purchase costs of most units are not readily publicly available. The correlation is shown in **Equation 1.**

$$C_e = (a + bS^n) * LF * MF * TF \quad (1)$$

C_e refers to the purchased equipment cost on a US Gulf Coast basis as of January 2007, S refers to the sizing parameter with defined upper and lower validity limits, a, b, and n are cost constants specific to each unit type. Estimation of the total CAPEX requires adjustment based on multiple factors (location (LF), material (MF), installation and inflation (TF)). These factors can be found in **Appendix 11.2**. Due to the relatively small capacity of the process, several of the units have size parameter values that fall below the lower bound for which the correlation is valid. Where this occurred the cost at the lower bound of the range of validity was used as it was assumed to still be a good estimate. This assumption is made on the basis that marginal cost decreases as size decreases.

PCEs were also estimated using the Matche Plant Equipment Cost Website where possible. This offers order of magnitude estimates for plant equipment using a database of historical prices. An average of both estimates was then used as the final PCE to improve accuracy.

4.2. Purchases Equipment Costs

4.2.1. Reactors

Seven reactors are used in the main process. The reactors associated with waste treatment are covered in **Economics section 4.2.7**. Reactors 1 to 7 are plug flow reactors. The PCEs of the PFRs were estimated by costing the shells as horizontal pressure vessels with cost of specific internals added. Example of these internals is the small tubes and static mixer within reactor R-6 which are added to improve reactor performance. These internals are modelled as structured packings. The material of the shells and internals is stainless steel. The cost of the reactors is shown in **Table 8**.

Table 8. Reactors.

Reactor Type	Number of this type	Total Cost (USD)
PFR	7	280737

4.2.2. Separation Units

A wide range of separation units are utilised in the process. These include distillation columns, extractors, crystallisers, filters, driers, and flash vessels. Costing of the distillation columns, similar to the reactors was done by modelling the units as pressure vessels with specific internals added. For the columns, this was random super intalox packing. Further adding to the costs of these units are the external modifications applied to its costing. For example, distillation columns include a reboiler and condenser. The summary of these costs is shown in **Table 9**.

Table 9. Reactors.

Separator Type	Number of this type	Total Cost (USD)
Distillation Column	8	559547

LLE	3	60692
Flash Vessel	1	504616
Crystalliser	3	1080210
Filter	3	1142943
Drier	3	150659

4.2.3. Heat Exchangers

Shell and tube heat exchangers were primarily utilised in the process. The alternative exchanger type utilised was the double pipe heat exchanger. These are used for low flowrates. The costs for these are shown in **Table 10**.

Table 10. Heat Exchangers.

Exchanger Type	Number of this type	Total Cost (USD)
Double Pipe	8	146427
Shell and Tube	16	4994703

4.2.4. Storage tanks and bins

Thirteen storage tanks and five bins are used in this process. These were sized based on the volume required for a month of storage of each unit's respective material. Buffer tanks were also utilised for process control. These were however not included in the PCE and instead assumed to be accounted for by the instrumentation factor for the ISBL cost. This assumption was made because of the very small volumes of the buffer tanks. All tanks and bins are cone roof tanks made of stainless stell. Summary costs are shown in **Table 11**.

Table 11. Storage tanks and bins.

Tank Type	Number of this type	Total Cost (USD)
Storage tank	15	1500632
Bins	3	198899

4.2.5. Heat Exchangers

The conveyor belts were used to transport solid materials. Half meter wide conveyor belts were used as they are cheaper while still being able to meet process demands. There are five utilised in the process. All pumps used are single stage centrifugal pumps. This was selected as the pumps are only required to drive flow and not induce significant pressure changes.

Table 12. Pumps and Conveyor Belts.

Pump/Belt Type	Number of this type	Total Cost (USD)
Single Stage Centrifugal Pumps	7	101519
0.5m wide Belts	5	386733

4.2.6. Mixers and Splitters

Several types of mixers were used in the process. The costs of which are summarised in **Table 13**. It was assumed that splitters, rather than being a singular unit were instead a branching pipe. As such the costing of the splitters is incorporated into the piping factor for the ISBL cost.

Table 13. Mixers and Splitters.

Mixer Type	Number of this type	Total Cost (USD)
Liquid-liquid (static) mixer	10	35174
Solid-liquid (propeller) mixer	4	119029

4.2.7. Waste Treatment

This plant requires a waste treatment facility. This will include seven reactors and 19.05m of ducting (the cost of which is accounted for by the piping factor). The summary of the waste treatment units is shown in **Table 14**.

Table 14. Waste Treatment.

Waste treatment unit	Number of this type	Total Cost (USD)
Reactor	5	2971621
Filters	5	1751235
Incinerators	2	4515348

4.2.8. Utility Generation units

A boiler, cooling tower and refrigeration system are required for the plants heat integration system, the costs of which are shown in **Table 15**.

Table 15. Waste Treatment.

Utility Generation Unit	Number of this type	Total Cost (USD)
Boiler	1	2971621
Refrigeration System	1	1751235
Cooling Tower	1	4515348

4.2.9. Total PCE

The total purchased equipment cost was 21.1M USD. The largest contributors to this being the waste treatment system (8.68M USD), heat exchangers (5.14M USD) and separations system (3.52M USD) [34].

4.3. ISBL Costs

ISBL costs refers to all costs associated with the construction of the plant. This is inclusive of the total purchased equipment cost. This is estimated by correcting the total PCE by an adjustment factor (F). There are three methods for obtaining this adjustment factor. An overall value of 3.63 (Lang Factor) for fluid-solid processing may be utilised according to **Equation 2**.

$$C = F \sum C_e \tag{2}$$

Alternatively, Hand proposed that accuracy could be improved by using individual Hand factors for each process unit and then summing these products according to **Equation 3**. These factors are shown in **Appendix 11.3**.

$$C = F_{distillation\ columns} \sum C_{e,distillation\ columns} + F_{pumps} \sum C_{e,pumps} \tag{3}$$

The final method involves using detailed factorials according to the **Equation 4**. Here $C_{e,i,CS}$ refers to the PCE of a unit in Carbon Steel. Values and meanings of the factorials are shown in **Appendix 11.4**.

$$C = \sum_{i=1}^{i=M} C_{e,i,CS}\left[\left(1 + f_p\right)f_m + \left(f_{er} + f_{el} + f_i + f_c + f_s + f_l\right)\right] \tag{4}$$

In some instances, the C_e value is already obtained for the unit in its required alloy form (e.g., 316 stainless steel). In this case a modified version of **Equation 4** is used shown in **Equation 5**. Here $C_{e,i,A}$ refers to the PCE of a unit in its required alloy.

$$C = \sum_{i=1}^{i=M} C_{e,i,A}\left[\left(1 + f_p\right) + \left(f_{er} + f_{el} + f_i + f_c + f_s + f_l\right)/f_m\right] \tag{5}$$

The ISBL cost of all three methods is shown in table 16. Accuracy of the ISBL estimate is important as further economic analysis is based on it. The detailed factorial estimate of the ISBL cost was thus selected due to its greater accuracy [34].

Table 16. ISBL Estimates.

ISBL Estimation Method	ISBL Estimate (USD)
Lang Method	76690250
Hand Method	59480580
Detailed Factorial Method	61430207

4.4. Additional Capital Costs

Table 17. Additional Capital Costs.

Category	Description	Cost (USD)
Working Capital	This comprises the cost associated with the stockpiling of materials and other consumables (solvents & catalysts) necessary for plant operation. It is estimated at 25% of ISBL.	15357552
OSBL	This includes all offsite investments required for the plant and is estimated as 40% of ISBL [34].	24572083
Design and Engineering	This includes the cost of detailed design, contractors, and other associated costs of this nature. It is estimated as 25% of the ISBL and OSBL costs [34].	21500574
Contingency	These include costs added to the budget to account for minor changes in project design and/or scope. It is estimated as 10% of the ISBL and OSBL costs [34].	8600229
Land	An 44711m^2 plot of land in the Khalifa Industrial Zone in Abu Dhabi, UAE has been selected as the plant's location. This land is priced at USD86/m^2 [35]. This has increased in recent years as the introduction of general corporate taxes has pushed business migration to SEZs in the UAE.	3845146
Hiring and Training	Hiring and training of onsite personnel is estimated to cost 25% of labour costs [34].	370373
Heat Integration Utilities	The heat Integration system requires a one-time purchase of water and refrigerant that is recycled through the system.	37636

5. Operating Costs

5.1. Variable Costs

5.1.1. Raw Materials

Table 18 shows the raw material prices and quantities that have been agreed with Hawkes Industries. The price contract can be found in **Supporting document section 9.1**. Prices of this are estimated to rise by 1.81% each year in line with inflation rates in UAE.

Table 18. Raw Materials Costs

Raw Material	Unit Price (USD/kg)	Cost (USD/annum)
Reactants		
Amino Acetaldehyde Dimethyl Acetal	7.036	1421272
Dimethyl Oxalate	0.980	646800
(R)-3-Aminobutan-1-ol	0.823	56787

Difluoro Benzylamine	0.823	139910
Methyl 4-Methoxyacetoacetate	3.428	658176
Lithium Bromide	2.198	59346
Dimethylformamide Dimethyl Acetal (DMF-DMA)	6.227	1463345
Catalysts		
Sodium Methoxide	0.540	189000
p-Toluenesulfonic acid monohydrate	0.812	75516
Acetic acid	0.574	15498
Solvents		
Toluene	0.180	60480
Acetonitrile	1.889	7971580
Methanol	0.428	390336
Citric acid	0.387	35991
Tetrahydrofuran	1.886	2868606
Dichloromethane	0.275	747175
Waste Disposal		
Chlorine Dioxide	0.728	24518

5.1.2. Utilities

Utility costs, the prices of which have been agreed with Hawkes Industries and are shown in **Table 19**. The steam and cooling water flowrates are excluded as the utility cost associated with them has been eliminated by the heat integration system. It was also decided that gas would not be utilised in the process due to environmental considerations. The electricity requirement was estimated by summing the power requirements of all units utilising electricity.

Table 19. Utilities costs

Utility	Unit Price	Annual Consumption	Cost (USD)
Electricity	0.1 USD/kWh	33044088	3304408.8

5.1.3. Additional Variable Costs

Table 20. Additional Variable Costs

Utility	Description	Unit Price	Cost (USD)
Waste Disposal	This is inclusive of all operating costs associated with the treatment of effluent streams.	21.52 per tonne of waste	1874296
Miscellaneous	This accounts for minor costs which have been unaccounted for. It is estimated as 10% of the ISBL costs	N/A	13571380
Silicon Oil	This is required for reactor jacketing and is changed during bi-annual maintenance periods	1.72 USD per kg	4199

5.2. Fixed Costs

5.2.1. Labour Costs

The plant has been designed to operate continuously. This means it will operate for 24 hours daily. Therefore, according to the recommendation by T&S, three eight-hour shifts are required for plant

operation. The shifts teams will consist of four plant operators instead of the standard three due to the process involving solids handling. A process engineer and a quality assurance engineer will also be required per shift. Five shift teams will be hired to allow for process flexibility. A management team of five shift foremen (one per shift team), two deputy plant managers, and a plant manager will also be required. This is below the typical recommendation, however as this is a smaller plant with only one product in its portfolio, the size of the management team should reflect that. Four office administrators will also be hired [34].

Table 21. Labour Costs

Position	Total	Salary (USD/annum)	Total Salary (USD/annum)
Plant Operator	20	26880	537600
Process Engineer	5	52710	263550
Quality Assurance Engineer	5	45090	225450
Foreman	5	43392	216960
Deputy Plant Manager	2	47850	95700
Plant Manager	1	62910	62910
Administrative staff	4	19830	79320

5.2.2. Additional Fixed Costs

Table 22. Additional Fixed Operating Costs

Category	Description	Cost (USD)
Maintenance costs	This is estimated as 5% of ISBL investment as this plant requires solids handling which will typically result in more maintenance [34].	6785690
Laboratory Costs	This includes all offsite investments required for the plant and is estimated as 20% of operating labour costs [34].	296298
Supervision	This is estimated to be 25% of operating labour costs [34].	370373
Salary Overheads	These include costs to cover benefits such as payroll taxes, health insurance etc. This is estimated as 60% of operating labour costs [34].	888894
Plant Overheads	This is inclusive of costs to cover corporate overhead functions such as Human resources, Information Technology, Legal, Sales, Marketing etc. It is estimated as 65% of total labour (operating labour, supervision, and salary overhead) and maintenance costs [34].	1974085
Licensing	This has been negotiated with Hawkes Industries as 17.2% of revenue of the sale of all products up until patent expiry [34].	36326400 (2025) 60544000 (2026-2031)
Depreciation	The plant has a lifetime of 10 years. A straight-line depreciation method was used with a salvageable value equal to the 15% of the initial capital investment.	9900256
Capital Charges	This refers to interest payments on all debt and loans in initial capital investment. This does not include expected returns on equity capital.	4070288.954
Insurance	This is estimated as 1% of ISBL [34].	1357138

6. Financial Strategy

6.1. Capital Structure

Capital structure refers to the mix of debt and equity financing that a company uses to fund its operations and growth, represented as a D/E ratio. It is a crucial aspect of financial management as it has significant implications for the risk and return of the company's investments, as well as the cost of capital.

The type and amount of financing a company uses can affect the cost of capital and the level of risk associated with the investment. For example, a company that relies heavily on debt financing may have higher interest payments and be more vulnerable to financial distress if it experiences a downturn. On the other hand, it has the chance to amplify returns on investment through using leverage. Similarly, a company that has a more conservative capital structure with a higher proportion of equity financing may have a lower cost of capital and be more resilient in tough economic conditions. However, this comes with higher profit sharing with other equity investors and lower potential to reinvest profits into the business. A decision on DPI's cost of debt and equity was made by comparing and averaging values across similar firms. This is detailed in **Appendix 11.5**. An average debt/total capital ratio of 0.55 was calculated, which is equivalent to a D/E ratio of 1.22. Whilst not high or low on its own, this number is based on large, multinational, and in some cases state-sponsored enterprises. The riskier nature of starting up a business, combined with the recent skyrocketing interest rates worldwide, means that debt repayment terms may be unfavourable to DPI. Furthermore, due to the 0% corporate tax rate, debt financing is not tax-efficient for DPI. As such, a more conservative D/E of 1 was used.

6.2. Corporate Tax

As stated in **Economics Section 2.5**, companies based in the KIZAD special economic zone pay 0% in corporate in customs taxes. This is currently set for an indefinite period. It is therefore reasonable to assume that this will be in force for the foreseeable future, given that corporate tax across the rest of the emirates is only set to increase from 0% to 9% in 2024 [36].

6.3. Cost of Debt and Equity

6.3.1. Equity

Using the Capital Asset Pricing Model (CAPM), the required rate of return on an equity stake K_e is given by the **Equation 6**:

$$K_e = r_f + \beta(r_m - r_f) \tag{6}$$

Where r_f, r_m and β are the risk-free rate of return, market rate of return and equity risk premium respectively. β represents the systematic risk of an asset compared to that of the overall market, and as such K_e represents the rate of return equity investors would expect for taking on that level of risk. A β of less than 1 indicates that the stock is less volatile than the overall market and vice versa.

The risk-free rate was taken as the yield on the 2.5% Emirate of Abu Dhabi 2029 10Y Municipal bond, calculated to be 2.82% as of 10/03/2023 [37]. β was taken to be 0.424, as calculated above, and r_m was taken as 6.18%, which is the five-year annualized return rate of the Dow Jones GCC Index. Overall cost of equity is thus 8.811%.

6.3.2. Debt

A company's cost of debt is simply the interest they must pay annually on any amount borrowed. Similar to capital structure, an industry analysis, which is detailed in **Appendix 11.6,** was used to estimate an interest rate. A value of 3.2% was decided pending negotiations. This was increased to 6% following negotiations with Hawkes Capital.

6.4. Weighted Average Cost of Capital (WACC)

The Weighted Average Cost of Capital is the average return a company must pay to all of its investors (both equity and debt) to attract and retain their investment. It is also used as the discount rate in NPV and DCF calculations, and is given by **Equation 7**.

$$WACC = \frac{E}{D+E+P} * K_e + \frac{D}{D+E+P} * K_d + \frac{P}{D+E+P} * K_p \quad (7)$$

This equation also includes preferred stock P, which is a stake that pays a fixed dividend K_P as opposed to profit sharing. This means it is usually regarded as a safer option for investors. For simplicity, DPI has assumed that 100% of initial financing will be debt and equity (P=0). Since D/E is 1, E/D+E and D/D+E are both equal to 0.5. The WACC was calculated to be 7.41%. In the GCC, unlisted companies far outnumber listed companies, presenting a unique opportunity to exploit market inefficiencies to gain more favourable terms for DPI's WACC (which is not possible in more developed markets).

6.5. Hurdle Rate

The hurdle rate of a new project, also known as the minimum acceptable rate of return, is the minimum rate of return that a company expects to earn on its investment in the project to compensate for the risks and opportunity costs of investing in the project.

The hurdle rate is typically based on the company's WACC but may be higher if the project involves a new market, a new technology, or a new product that the company has not previously developed or marketed. In this case the hurdle rate was taken to be equal to the WACC.

7. DolutePharm Industries KPIs

7.1. Cash Flow Analysis – NPV, IRR and Payback Period

A cash flow analysis was conducted to assess the performance of the project over its lifetime. This was selected as it can account for the time value of money along with other external circumstances. It is conducted by determining the project cost and first interest payment which will all be paid in year 0 for this analysis. This is the first year (2023) cash outflow. Following this the net cash flow for the consecutive years of operation are calculated and discounted to the present time value of money using the WACC as the discount rate. This is done using **Equation 8**.

$$NPV = \sum_{n=1}^{n=t} \frac{CF_n}{(1+i)^n} \quad (8)$$

The NPV was calculated to be 1.503 billion USD. This indicates that process is highly profitable.

Initial rate of return (IRR) is the maximum discount rate for which the process remains profitable. It is calculated by finding the value for which the NPV is equal to zero. It was found to be 144.61% for this project. This exceeded the WACC calculated in **Section 5.4** by 19.5 times. This indicates that in the event of significant changes to the process, DPI is highly likely to remain profitable.

Payback period is defined as the time (usually expressed in years) for the project cost to be paid off. Therefore, a lower payback period correlates to a lower risk investment. This project's payback period is 2.1 years, whereas the industry average for the pharmaceutical industry is 5 to 7 years. This indicates that this is an attractive investment to potential investors. The relatively short payback period is particularly attractive given the risks posed by patent expiry. Although, the projects profitability is unlikely to be affected by patent expiry, due to its highly competitive price point and business strategy, the relatively short payback period will serve as a comfort to potential investors.

7.2. Cumulative (Final) Cash Balance

The final cash balance is an absolute measure of value creation (as opposed to relative), like NPV. It is a concrete figure of how much cash is available to be shared among shareholders at the end of the investment project. It is useful for analysing cash flow trends over time and assesses the ability of a company to meet sudden financial obligations. It was calculated to be 2,211,057,029 USD.

7.3. Multiple on Invested Capital (MOIC)

MOIC is calculated simply by diving the total value of a project by the initial investment. Whilst it is widely calculated using the exit value of a project, it has been included as it is an easy-to-understand metric which shows the ROI of an investment, and measures actual returns on invested capital, as opposed to percentage returns. A value of 11.08 was found for this KPI.

7.4. Gross, Net and EBITDA Margins

The gross, net and EBITDA margins were calculated to be 91%, 75% and 79% respectively. EBITDA is a widely used and useful financial metric which serves as a measure of a company's profitability that is both industry agnostic and ignores differences in accounting practices. Gross and Net profit margins allow investors to understand how efficient a company's operations are, and how much money is lost to inefficiencies over the accounting period.

8. Sensitivity Analysis

8.1. KPI sensitivity results

Due to the extremely high profitability of the plant, a stress test was conducted as opposed to the sensitivity of test outlined by Towler and Sinnott [34]. Whilst the underlying factors tested were similar, the range of testing was increased to gain meaningful data. The KPIs tested are detailed below.

Table 23. Independent variables tested in the sensitivity analysis.

Factor Varied	Lower Bound	Upper Bound
DTG Sale Price	-90%	0%
Production Rate	-90%	0%
Feed Cost	0%	2560%
Utility Cost	0%	2560%
CapEx Cost	-20%	160%
WACC	-50%	500%
Construction Time	-6 months	12 months

8.1.1. DTG Sale Price and Production Rate

As mentioned above, DPI's sale of DTG is 100% secured by Hawkes Industries. However, in the case of market disruption, it may be necessary to re-negotiate a change in the sale price of DTG. As can be seen, the NPV of DPI is extremely resistant to the DTG sales price and rate of production. This agrees with the very high profit margins seen above, something which is fairly rare to see in capital intensive industries (such as manufacturing). It is worth noting that the NPV varies almost linearly with both sale price and production output, at a rate of around 200 USD per 10%. This suggests that the process is highly scalable, given the relatively low initial investment requirement. The EBITDA margin curve is similar to a 1-exp graph, with a "knee" at -60%. This appears to be limit at which NPV remains positive whilst also maintaining a high level of profitability. Below this, there is a rapid decline in EBITDA margin, which could mean that DPI would not be able to meet short-term financial difficulties. However, if the feed/production rate existed in the area where the EBITDA margin is positive whilst the NPV is negative, a longer production time may allow DPI to reach a net positive value.

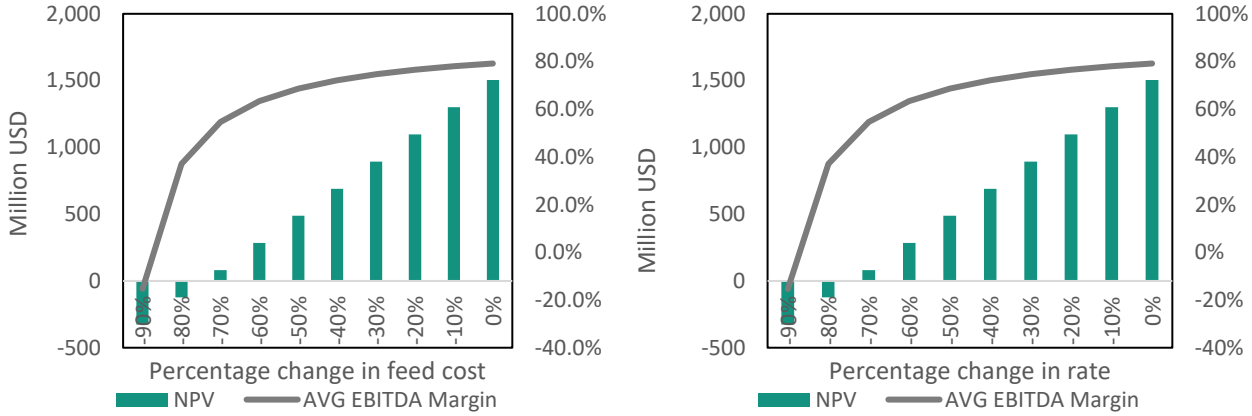

Figure 4. Sensitivity to DTG sale price (left) and plant production rate (right)

8.1.2. Feed and Utility Cost

It is very clear that Feed Cost is one of the less substantial sources of cost in DPI's process. This is somewhat typical in the specialty drugs market, where the value of the product far outstrips

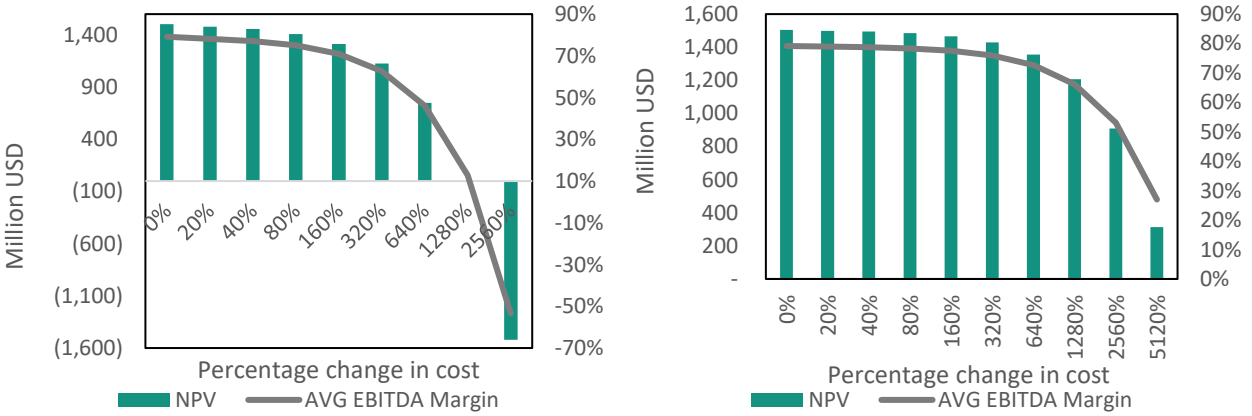

Figure 5. Sensitivity to total feedstock cost (left) and utility cost (right)

its source materials by themselves. It was found that the feedstock had to be over 11 times more expensive than negotiated for the process to become economically unviable. The utilities cost was found to have an even weaker effect on the profitability of the system, with even a 50.2x (5120%) increase utility cost not being enough to make the process unfeasible. This is partly due to the cheap price of electricity in the UAE, which makes up the vast majority of DPI's utility needs.

8.1.3. Capital Cost Misestimation

Estimations of cost can never be 100% accurate. A misestimation of capex was expected to have a more interesting effect on the process feasibility, as the capital cost affects the initial negative cash flow from financing, and also leads to increases in coupon payments to bondholders. There was a linear trend of NPV to increasing initial capital expenditures. EBITDA margin was unaffected as it does not consider depreciation of PPE (property, plant and equipment).

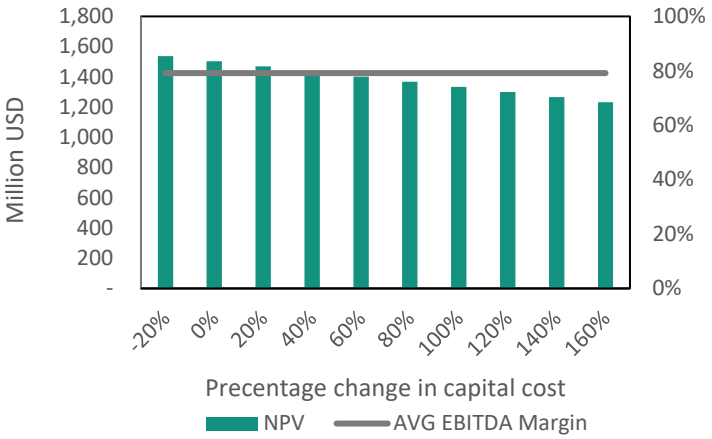

Figure 6. Sensitivity to initial capital costs

8.1.4. WACC

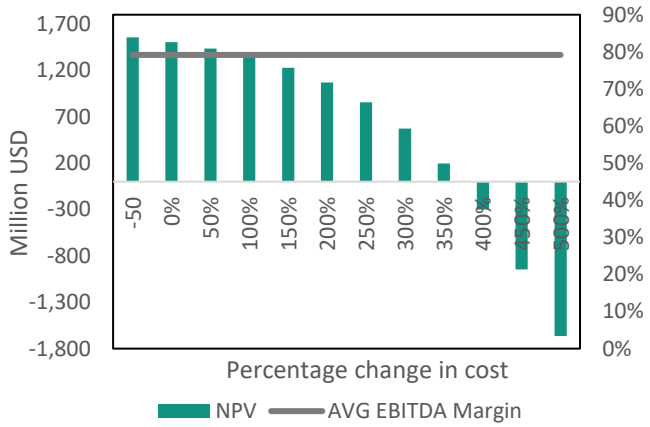

Figure 7. Sensitivity to WACC

The world is undergoing a period of high inflationary pressures. Despite this, it was decided that it was still worth finding the impact of a *decrease* in the WACC. This is because it was believed that DPI qualified for a special loan by the Abu Dhabi Fund for Development given the exclusive distribution of product to lesser economically developed nations. Under the terms of the loan, DPI would receive the sovereign rate of interest, as opposed to a private rate.

8.1.5. Construction Time

The most influential factor was found to be the construction time. Whilst an earlier construction was found to create some additional value, this upside potential is outstripped by the downsides due to late construction, as both loan payment and all fixed costs will have to be paid whilst production is not producing any positive cash flow. A delay of two years is all that is needed to erase value.

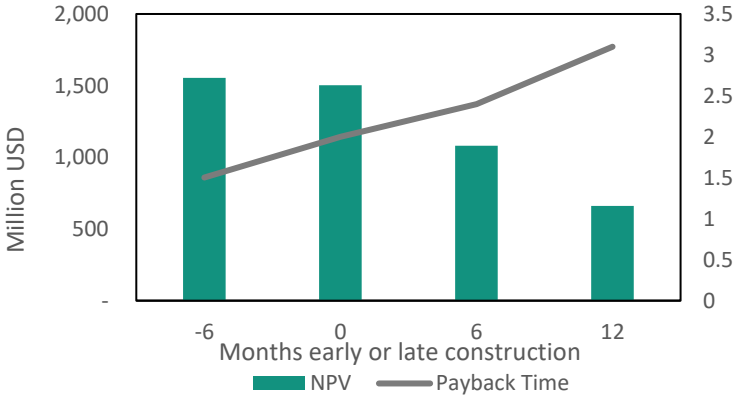

Figure 8. Sensitivity to early or late construction time

8.2. Scenario Analysis

Whilst the above KPI sensitivity tests indicate a tremendously profitable process regardless of all singular feasible market conditions, in the real world such circumstances tend to present themselves in tandem. Thus, a scenario analysis was completed which looked at what several KPIs/factors may look like in a worst case, base case and home-run scenario. Apart from raw KPI values, one risk which is unique to a pharmaceuticals manufacturer is the possibility of manufacturing halts due to newfound dangers. Whilst the profitability of this is vanishingly small due to the fact that Dolutegravir has been an approved medication since 2013, it is still worth testing the potential

impact if production were to be stopped mid-way through the plant lifetime. Furthermore, the entire sale of DTG is underwritten by Hawkes Industries. This creates buyer concentration risk, and the worst case therefore also reflects a sudden loss of buyer. The details of the scenario analyses are in **Table 24**. In the worst case, DPI is loss-making (but two orders of magnitude smaller loss than the potential gain in the positive scenarios). The best case scenario is observed to be ~17% better than the neutral case, and both show a roughly linear trend in value creation.

Table 24. Variable and KPIs explored in scenarios.

	Worst	Base	Best
DTG Sale Price	-50%	0%	+10%
Feed Cost	+200%	0%	0%
WACC	+100%	0%	-50%
Product Recall	Year 5	Never	Never
NPV (M USD)	-16	1,503	1,757
IRR	N/A	145%	166%
MOIC	-0.67x	11.08x	12.96x

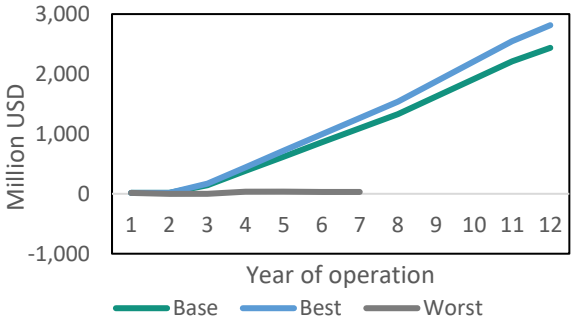

Figure 9. Cumulative cash according to scenario analysis

9. Conclusion and Outlook

DolutePharm Industries (DPI) plans to enter the pharmaceuticals market in 2025, producing 88,000kg of Dolutegravir (DTG) API at maximum capacity, to be distributed exclusively to poorer nations with a high incidence of HIV/AIDS in their populations. The primary markets are South Africa and India, and the plant will be based in the United Arab Emirates. DPI hopes to build reputation to capitalise on the 2026 expiry of the patent for the production of DTG, so as to be protected against any loss of market share after this event. Market conditions, 0% corporate tax rate in the KIZAD SEZ and high margins puts DPI in a favourable position to enter the market. Furthermore, the lack of peer competition gives DPI first-mover advantage to be a central player in the GCC middle-market pharmaceuticals industry in years to come.

The total initial capital investment for the project is 120M USD, which is composed of a 61.4M USD ISBL, 24.6M USD OSBL and a further 34M USD of fixed costs. Corresponding to this, 15.5M USD of working capital was also held to cover any expenses before production. In total, the 135M USD investment cost was decided to be covered by a 50/50 Debt-Equity split, of 67.8M USD each, with debt being raised at 6% and equity being priced at a cost of 8.81%. This led to a WACC of 7.41%. Given this total investment cost, DPI expects to generate an IRR of **144%**, a NPV of 1,500M USD and a project payback of 2 years from the end of construction.

Stress testing was conducted to investigate the resilience of the process' economics. It was found that while greatly profitable, a sharp increase in the WACC or misestimation of the plant's capital cost could be enough to wipe out any potential value.

Given Abu Dhabi's status as a prime exporter of oil and gas products, leading to cheap natural resource costs, it may be worth negotiating with suppliers to provide a CHP or furnace element to ease DPI's reliance on electricity on the heating and cooling elements of the plant. Furthermore, much of the financial analysis was completed through comparisons and extrapolations of public knowledge. Given the fact that most companies in the UAE are not publicly listed, there is an information gap between providers of finance and project managers. It would be worth reaching out to different providers and users of finance to be able to get a more accurate picture of the market landscape.

Finally, it would be worthwhile for DPI to reinvest a portion of profits into research and development, a branch which has been not considered given the singular nature of DPI's aim. With this funding, it could explore less capital-intensive schemes for the manufacture of DTG. This would translate into a lower capital expenditure requirement for any future projects pursued.

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11. Appendix

11.1. WHO Framework for estimation of API Selling Price.

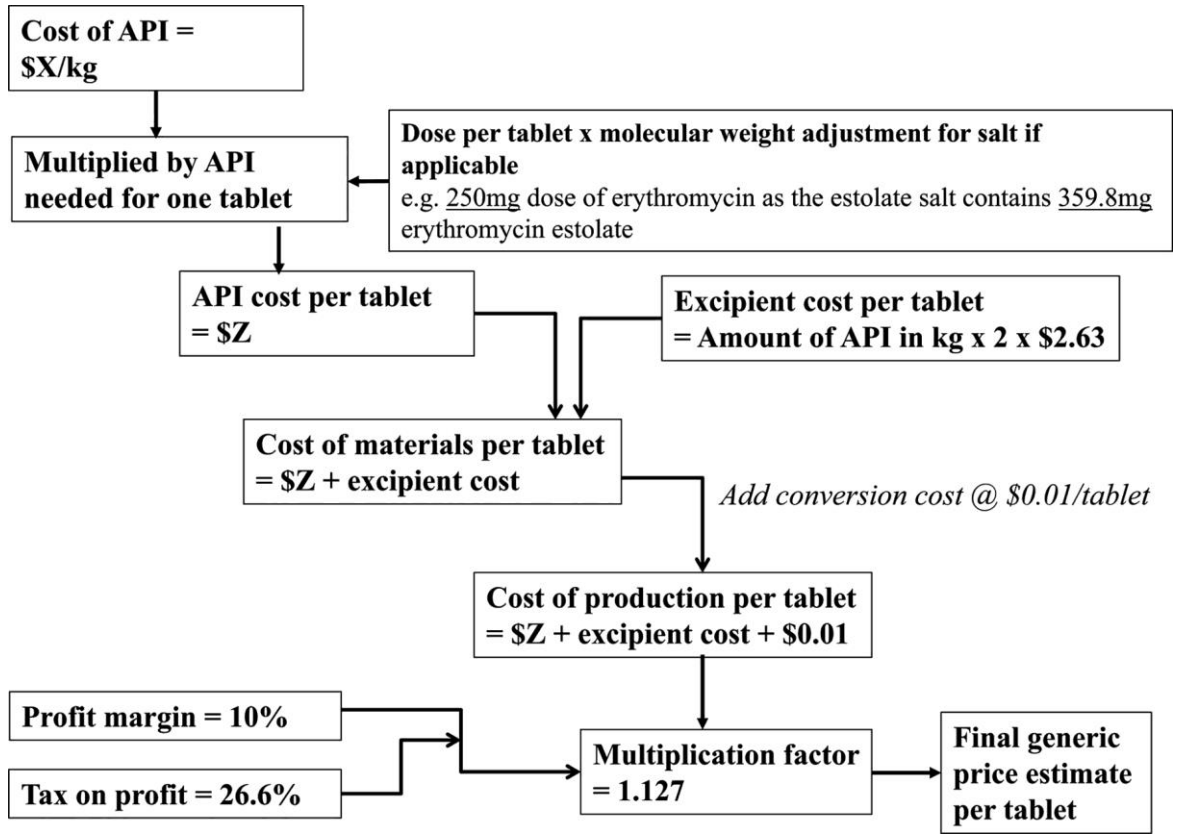

Figure 10. Pricing Framework used for negotiation of DTG Sale Price

11.2. Adjustment Factors for T&S Estimation

Table 25. Adjustment Factors for T&S Estimation

Factor	Value	Source
Location	1.02	[34]
Material	1.3	[34]
Time (2007)	1.59	Using method outlined below
Time (2014)	1.40	"

$$Cost\ in\ year\ A = \frac{Cost\ index\ in\ Year\ A}{Cost\ imdex\ in\ Year\ B} * Cost\ in\ year\ B$$

The CEPCI value used for 2007, 2014 and 2022 are 509.7, 576.1 and 808.7 respectively [38].

s

11.3. Hand Factors for ISBL Estimation

Table 26. Hand Factors for ISBL Estimation

Equipment type	Hand Installation factor
Compressions	2.5
Distillation Columns	4
Fired heaters	2
Heat Exchangers	3.5
Instruments	4
Miscellaneous Equipment	2.
Pressure Vessels	4
Pumps	4

11.4. Detailed Factorials for ISBL Estimation

Table 27. Detailed Factorials for ISBL Estimation

Factorial	Definition	Towler Factor
f_{er}	Equipment Erection	0.5
f_p	Piping	0.6
f_i	Instrumentation and Control	0.3
f_{el}	Electrical	0.2
f_c	Civil	0.3
f_s	Structures and buildings	0.2
f_l	Lagging and Paint	0.2

11.5. Comparisons table for deduction of capital structure and cost of equity

In deciding our capital structure and calculating our cost of debt and equity, the below comparison table (**Table 25**) was formed by collecting data on publicly listed pharmaceuticals companies in the Middle East.

Table 28. Comparisons table for deduction of capital structure and cost of equity

	Location	LTM Total Debt/Capital %	Total Enterprise Value Latest	5 Year Beta
Gulf Pharmaceutical Industries (Julphar)	UAE	48.03%	531.4	0.45
Saudi Pharmaceutical Industries (SPIMACO)	Saudi Arabia	40.01%	950.8	0.4
InterCure	Israel	28.16%	120	-0.09
Tikun Olam-Cannbit Pharmaceuticals	Israel	16.37%	14.3	1.99
Panaxia Labs Israel Ltd	Israel	142.65%	17	-0.46
Cannassure Therapeutics Ltd	Israel	96.21%	7.9	0.36
Seach Medical Group Ltd	Israel	15.95%	23.6	0.32
Teva Pharmaceutical Industries Limited	Israel	71.36%	30,656.00	1.22
IM Cannabis Corp.	Israel	12.17%	17.4	2.37

AVG		55.34%	237.8571429	0.424

Teva was ultimately not included due to its conglomerate structure, as opposed to being a specialised pharmaceutical company. Likewise, IM Cannabis Corp. was excluded due to its relatively novel pharmaceutical offering, which is likely a factor that contributes to its very low D/C percentage.

One limitation to this is the lack of publicly available data on the pharmaceutical manufacturing industry in the ME region, owing to the lesser developed nature of the industry in this market.

11.6. Comparisons table for deduction of cost of debt

Using Julphar and SPIMACO, the state pharmaceutical companies of the UAE and Saudi Arabia respectively, as precedent, an investigation of DPI's cost of debt was conducted by finding the interest expense on the income statements as a percentage of their total balance sheet debt. Given the average interest paid was 3.2%, and DPI's higher credit rating (BBB vs B+ for Julphar), 3.2% was decided to be the maximum theoretical interest payment.

Table 29. Comparisons table for deduction of cost of debt

	Interest expense as % of D	Credit Rating
Julphar	3.29%	B+
SPIMACO	3.11%	Not available