Early Assessment of Economic Viability in Cell and Gene Therapy via Alignment of Cost and Market

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ABSTRACT

Cell and Gene Therapy (CGT) treatment development require significant upfront R&D investment and has relatively lower volumes compared traditional blockbuster drugs to be able to benefit from economies of scale for cost reduction. Therefore, ensuring the economic viability of a CGT treatment is one of the most pivotal considerations for pharmaceutical companies to balance between bringing life-saving innovation to the market and profitability. In this work, we developed an integrated framework for early assessment of economic viability of CGT consisting of a high-level manufacturer neutral model for cost combined with market demand pricing model that is region and treatment/indication specific. For specific oncology cancer indications in the US market, the integrated framework and subsequent models yield economic viability early assessment results with key levers identified for the cost model (Total Fixed cost, Total Labor Cost, Total Material cost and Number of batches) and market demand pricing model (Cancer Stage, Reimbursement and coverage, and Standard of care). The integrated framework highlighted that for multiple myeloma, treatment production isn't viable for localized cancer stage because of the high Cost whereas is viable for distant stage cancer because of the high selling price potential. The proposed integrated framework combined with key levers identified can be used by pharmaceutical companies to evaluate the economic feasibility in the CGT development and commercialization lifecycle to bring life-saving innovative treatments to patients while maintaining profitability for sustainable business operations.

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1. Introduction

1.1 Problem Background

Drug development typically requires significant upfront R&D investment; therefore, ensuring the economic viability of a drug is one of the most pivotal considerations for pharmaceutical companies. It is paramount for them to sustain the supply of much-needed medications, maintaining a delicate balance between innovation and profitability. Within this realm, Cell and Gene Therapy (CGT) products have emerged as a promising class of medical interventions encompassing gene therapies, cell therapies, and tissue-engineered products (Biotech Primer, 2021). These cutting-edge treatments hold immense potential, particularly in addressing rare diseases such as oncology indications for cancer treatment where conventional approaches often fall short.

However, the inherent nature of CGT products, characterized by relatively lower volumes compared to traditional blockbuster drugs, presents a unique set of challenges. Unlike their high-volume counterparts, CGT products struggle to benefit from the economies of scale and volume-driven cost efficiencies (Harrison, 2018). Consequently, ensuring the economic viability of CGT products demands scrutiny and proactive evaluation from the outset.

In light of these complexities, an early assessment of the economic feasibility of CGT products becomes imperative. By strategically analyzing the cost dynamics, market potential, and pricing considerations, pharmaceutical companies can navigate the intricate landscape of CGT development, ensuring sustainable innovation while meeting the needs of patients with rare diseases.

1.2 Problem Statement

The project sponsor, PharmCGT, was seeking an in-depth understanding of the various contributing factors to determine the economic viability of CGT with alignment of cost and market. The project includes two major areas of research: the formulation of a high-level cost model for CGT

technology and manufacturing, and the development of a market demand pricing model. The further alignment of these two key areas between cost and market provided critical insight into the economic viability of CGT.

The key goal was to develop an integrated framework comprised of two models that PharmCGT can utilize for the early assessment of the economic viability of CGT. There were three main areas of focus to achieve this goal, each with its expected outcomes.

1. Cost model (Cost/Volume): Detailed cost models can be highly complex and dependent on the manufacturer and process. The aim of this research area was to establish a high-level cost model adaptable to any manufacturer/process. It provided a rapid and reasonably accurate estimate of the costs associated with CGT manufacturing activities. Additionally, it identified key levers that can either improve or worsen costs.
2. Market demand pricing model (Price/Volume): Given the relatively low volume of demand for CGT, pricing was highly volatile, contingent on factors such as disease type and available treatments. The objective of this research area was to devise a market demand pricing model capable of isolating specific disease types, cancer stages, and lines of treatment. It aggregated data to depict total demand. Consequently, the model pinpointed key levers influencing the market demand/pricing curve.
3. Integrated Framework to align the Cost and Market Demand Pricing models: By integrating the cost and market demand pricing models, we achieved the research objective of early economic viability assessment for CGT. This research combined the various key levers identified in the cost and market pricing models. With the model, PharmCGT was able to evaluate the economic feasibility for specific disease types early in the CGT development and commercialization lifecycle. Moreover, it assessed the impact of key cost and market/pricing levers on the results.

2 State of the Practice

When forecasting demand for a new product, the primary consideration is identification of the potential market size (Goldman and Leising, 2021). When applying forecast for CGT products, additional challenges are introduced due to FDA regulatory requirements and the rare disease definition according to the Orphan Drug Act (1983). The Act caps the indicated patient population to 200,000 people in the United States. Combined with the fact that Cost for cell and gene therapy products are typically higher than those for the small molecule pharmaceutical products (PharmCGT, personal communication, 2023), a CGT may require success across several disease stages and indications to be commercially viable. As a part of our literature review, there are mainly two approaches for when it comes to pharmaceutical product forecasting with disease stage market modeling. The first approach is the top-down forecasting funnel process approach (Cook, 2006), which takes are serial top-down approach from the population segmentation considering disease incidence considering variety of factors such as symptomatic, diagnosed and access. While the second approach is based on epidemiology, companies can leverage the prescription data available in order to estimate market share for market entry (Grabowski, 2007). Due to the limited prescription information available for the rare disease market, we have taken the top-down forecasting funnel process approach.

2.1 Current Challenges in Demand Forecasting

This section covered the current challenges associated with demand forecasting for cell and gene therapy products via the top-down forecasting funnel process approach, which included Cancer Type, Patient Population, Cancer Stage and Treatment Methods, Reimbursement and Coverage, Standard of Care, Relapse and Recurrence rate.

2.1.1 Cancer Type and Patient Population

Cell and gene therapy products have specific oncology indications to target the treatment of specific cancer types. An indication refers to the specific type or subtype of cancer for which a particular treatment, therapy, or diagnostic test is appropriate or effective. Therefore, to build a robust model, the first input to consider was the specific cancer type and the target population associated with the disease. In this project, we explored the three different cancer types listed in Table 1.

Table 1.
Three cancer types: pancreatic, myeloma and melanoma (Cancer.gov, 2023)

Cancer Type	Description
Pancreatic	Cancer of pancreas
Myeloma	Cancer of the plasma cell
Melanoma	Cancer of the skin

The cancer statistics for the US population was publicly available on the National Cancer Institute (NCI) website as a part of the Surveillance, Epidemiology, and End Results Program (SEER). The yearly trend between 2010-2020 in terms of rate of new cancer (incidence) was depicted in Figure 1 and Table 2 (SEER.com, 2023) for myeloma.

Figure 1.
Incident and Death rates: Myeloma.

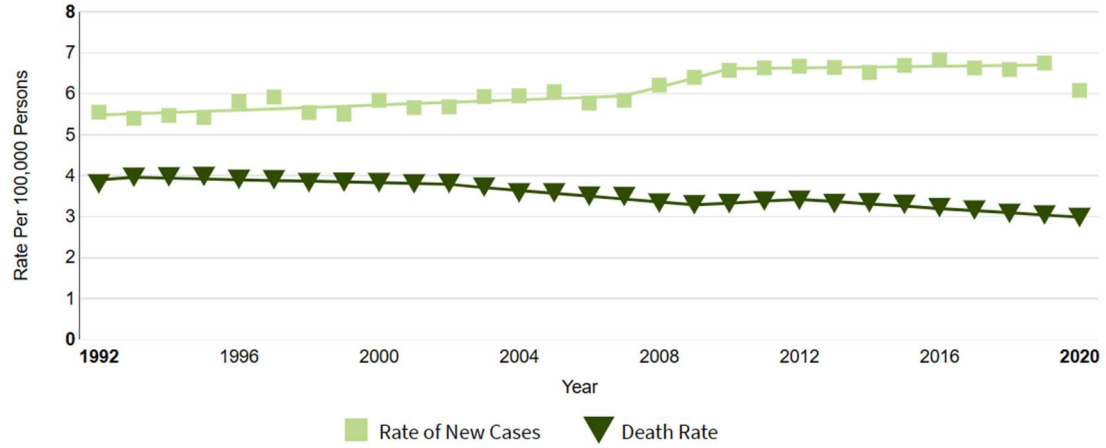


Table 2.

Cancer Stat Facts: Myeloma.

United States								
Mylenoma Epidemiology Age-Adjusted Rates of New Cases/Deaths Per 100,000 & 5-Year Relative Survival Percentages								
Year	Rate of New Cases (Incidence) — SEER 8		Rate of New Cases (Incidence) — SEER 12		Death Rate — U.S.		5-Year Relative Survival — SEER 8	
	Observed	Modeled Trend	Observed	Modeled Trend	Observed	Modeled Trend	Observed	Modeled Trend
2010	6.63	6.67	6.57	6.61	3.32	3.33	54.5%	52.8%
2011	6.94	6.89	6.63	6.62	3.38	3.38	53.6%	54.2%
2012	6.84	6.91	6.67	6.63	3.4	3.42	57.6%	55.7%
2013	6.94	6.92	6.64	6.64	3.32	3.37	58.3%	57.1%
2014	6.73	6.94	6.52	6.65	3.34	3.31	59.5%	58.5%
2015	7.09	6.95	6.69	6.66	3.3	3.26	62.2%	59.9%
2016	7.13	6.97	6.83	6.67	3.22	3.2 -		61.2%
2017	6.95	6.99	6.63	6.68	3.16	3.15 -		62.6%
2018	6.83	7	6.59	6.69	3.08	3.1 -		63.8%
2019	7.1	7.02	6.75	6.7	3.04	3.04 -		65.1%
2020	6.46	7.08	6.08 -		2.98	2.99 -		66.3%
2021		7.10				2.98		67.9%
2022		7.13				2.94		69.2%
2023		7.16				2.90		70.6%
2024		7.18				2.86		71.9%
2025		7.21				2.82		73.3%
2026		7.24				2.77		74.7%
2027		7.27				2.73		76.0%
2028		7.29				2.69		77.4%
2029		7.32				2.65		78.7%
2030		7.35				2.61		80.1%

Based on the specific cancer type and statistics and the use of total prevalence and incidence rate, death rate and survival rate, the overall patient population was estimated. For example, using the SEER statistics and the overall population we estimated the total number of patient population for specific cancer types.

2.1.2 Cancer Stage and Treatment Methods

Stage refers to the extent of the cancer, such as the cancer size and how much has the cancer stayed in a local region/organ or spread within the body. The severity of the cancer and the chance of survival are highly dependent on the cancer staging. For our purpose, we defined the cancer staging via the following (ClevelandClinic.org, 2023):

- Localized—Cancer is limited to the place where it started, with no sign that it has spread.

- Regional—Cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant—Cancer has spread to distant parts of the body.
- Unknown—There is not enough information to figure out the stage.

During our research, we noticed that different cancer staging systems/nomenclatures are available; hence a harmonization table has been developed by Cleveland Clinic for better understanding in Table 3 (ClevelandClinic.org 2023).

Table 3.

Harmonizing different cancer staging system (ClevelandClinic.org, 2023)

Cancer staging (Global Format)	Cancer stage (SEER Format)	TNM Staging	Cancer staging Descripton
StageI	Localized	T1 or T2,N0,M0	The cancer is localized to a small area and hasn't spread to lymph nodes or other tissues
StageII	Localized	T3 or T4,N0,M0	The cancer has grown, but it hasn't spread
StageIII	Regional	Any T,N1 or N2,M0	The cancer has grown larger and has possibly spread to lymph nodes or other tissues
StageIV	Distant	Any T,Any N,M1	The cancer has spread to other organs or areas of your body (Metastasized)

One of the important impacts of cancer staging on the clinical decision is the treatment plan. For different cancer types, there are established treatment guidelines and options available to health professionals (cancer.gov,2023), as shown in Table4.

Table 4.

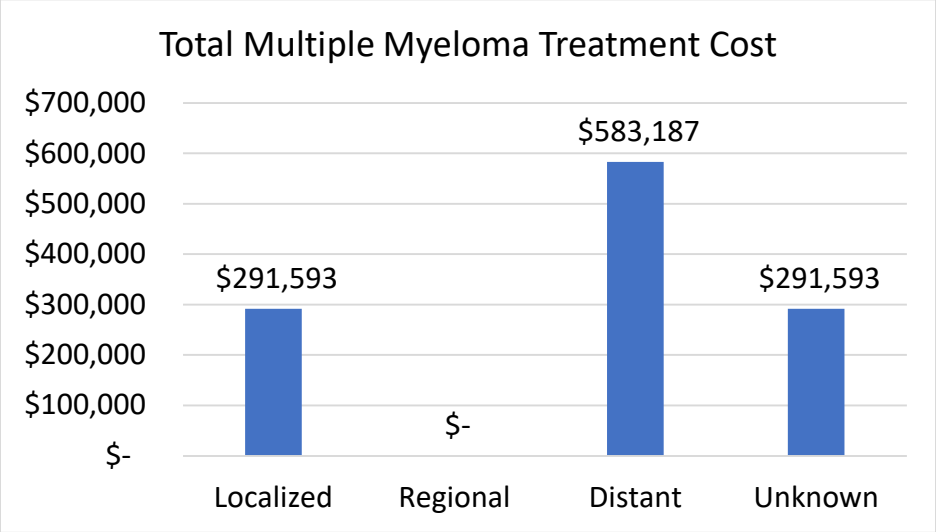
Treatment guidelines and options for cancer staging system.

Multiple myeloma treatment	Melanoma Treatment		Pancreatic treatment
Chemotherapy	Stage 0 melanoma	Excision	Surgery
Other drug therapy	Stage I melanoma	Excision +/− lymph node management	Radiation therapy
Targeted therapy	Stage II melanoma	Excision +/− lymph node management	Chemotherapy
High-dose chemotherapy with stem cell transplant	Resectable Stage III melanoma	Excision +/− lymph node management	Chemoradiation therapy
Immunotherapy	Unresectable Stage III, Stage IV, and Recurrent melanoma	Intralesional therapy	Targeted therapy
Radiation therapy		Immunotherapy	
Surgery		Signal transduction inhibitors	
Watchful waiting		Chemotherapy	
		Palliative local therapy	

(Cancer.gov, 2023)

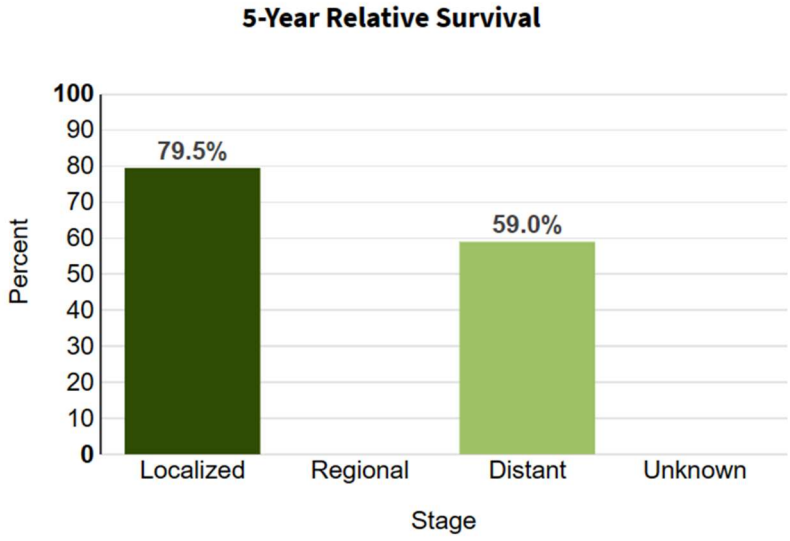
In addition, the tumor stage directly contributes to the overall price of treatment and to the healthcare system. For example, for Myeloma (Bhattacharya, K., 2021) as an example show in Figure 2, the treatment price progressively increases as the advancement of the cancer stage. One of the major contributions to the increased price is for the workup and treatment of metastatic disease.

Figure 2.
Total Myeloma treatment price distribution by clinical stage.



The actual patient survival rate also varies greatly based on the cancer stage and type, shown in Figure 3.

Figure 3.
Survival rate: Multiple Myeloma



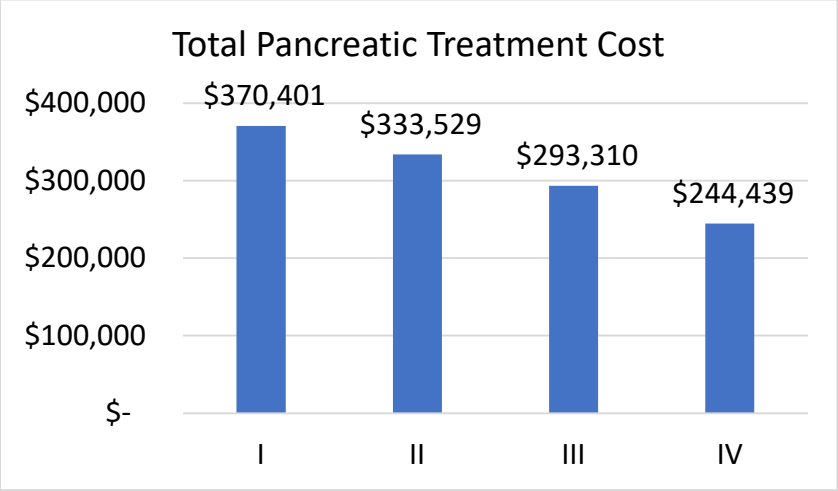
The price determined was on the lower side as significantly better treatment options were available at a higher price (Bhattacharya, K., 2021). But still the model provided us with a way of determining price. Current treatment options include immunotherapy, targeted therapy, chemotherapy, radiation, and surgery. Immunotherapy drugs can be expensive, with price ranging from $150,000 to $300,000 per year which can take the total treatment price for advanced stage between $300,000 to 500,000 per year, as shown in Table 5.

Table 5.
Distribution of various treatment prices as a function of cancer stage of myeloma.

Phases	Cost Driver	Mean Phase Length (Months)	MM group (in US$) (Monthly)	Total Treatment Cost w Patient Time
			Mean	
Disease Lifetime				$ 291,593
Pre-diagnosis phase		1	$ 2,850	$ 2,850
	Outpatient		$ 873	
	InPatient		$ 1,247	
	Prescription drugs		$ 292	
	Other		$ 182	
	Patient time cost		$ 256	
Initial Care Phase		5	$ 13,846	$ 69,230
	Outpatient		$ 4,369	
	InPatient		$ 4,821	
	Prescription drugs		$ 2,508	
	Other		$ 868	
	Patient time cost		$ 1,280	
Continuing Care phase		13.19	$ 10,349	$ 136,493
	Outpatient		$ 2,166	
	InPatient		$ 1,645	
	Prescription drugs		$ 2,751	
	Other		$ 410	
	Patient time cost		$ 3,377	
Terminal Care Phase		5	$ 16,604	$ 83,020
	Outpatient		$ 3,699	
	InPatient		$ 8,411	
	Prescription drugs		$ 1,947	
	Other		$ 1,267	
	Patient time cost		$ 1,280	

In contrast to myeloma, the pancreatic cancer treatment price has a decreasing trend as a function of cancer stage (Tramontan et al., 2019) as shown in Figure 4. Decreasing treatment with increasing cancer stages was primarily because of decreasing continuing phase length and aligned with decreasing survival rate. The decrease further demonstrated the complex task for modeling treatment price for different cancer types. Typical 1-month staging phase begins on the date of diagnosis; the stage of cancer was determined during this time. The initial phase is the period to complete the first treatment cycle. The continuous phase is the follow up period or another round of the treatment cycle.

Figure 4.
Total Pancreatic Cancer Treatment Price



2.1.3 Reimbursement and Coverage

The treatment of cancer can be very costly and the coverage of this treatment price by insurance and reimbursement guidelines is an important economic factor to consider for the viability of launching a new cancer treatment modality. The insurance coverage rate in the US is summarized in Table 6 with annual limits (US HHS, 2022).

Table 6.

Insurance coverage in the US between 2008-2022.

United States		
Year	**Insurance coverage**	**Sources**
2008	84.80%	
2009	84.80%	
2010	84.40%	
2011	84.80%	
2012	85.20%	
2013	86.70%	
2014	88.30%	
2015	90.60%	census.gov
2016	91.20%	
2017	91.20%	
2018	91.50%	
2019	92.00%	
2020	91.40%	
2021	91.70%	
2022	92.10%	

A "reimbursement rate" of 100% was considered for the purposed of this work, as the U.S. Department of Health and Human services prohibits insurance companies from limiting yearly or lifetime coverage expenses for essential health benefits.

2.1.4 Standard of Care

Standard of care (SOC) is a legal term referring to the degree of care a prudent and reasonable person would exercise under the circumstances (Balch et al., 2019). However, in health, this mostly refers to the benchmark of care a patient would receive. For different disease types, the standard of care will be different, and with varying medical and technological advancements and innovations, the standard of care usually improves as a function of time. We incorporated SOC into our model to better determine the health economic outcome for the patient and the overall benefit to health system by introducing a particular therapy product. The SOC was an important lever in the determination of the product share and is a combination of Treatment price, Cancer relapse and recurrence rate and Patient survival rate.

2.1.5 Relapse and Recurrence rate

Cancer patients despite treatment may relapse, and this is usually modeled with cancer recurrence rate. We researched the relapse/recurrence rate for melanoma, pancreatic cancer, and myeloma in the US, as shown in Table 7.

Table 7.
Recurrence rate for different cancer types in the US.

	United States			
Recurrence rate (%)	Localized	Regional	Distant	Unknown
Melanoma	4.20%	8.40%	15.80%	27.90%
Pancreatic	80.00%	80.00%	80.00%	80.00%
Multiple myeloma	62.90%	62.90%	62.90%	62.90%

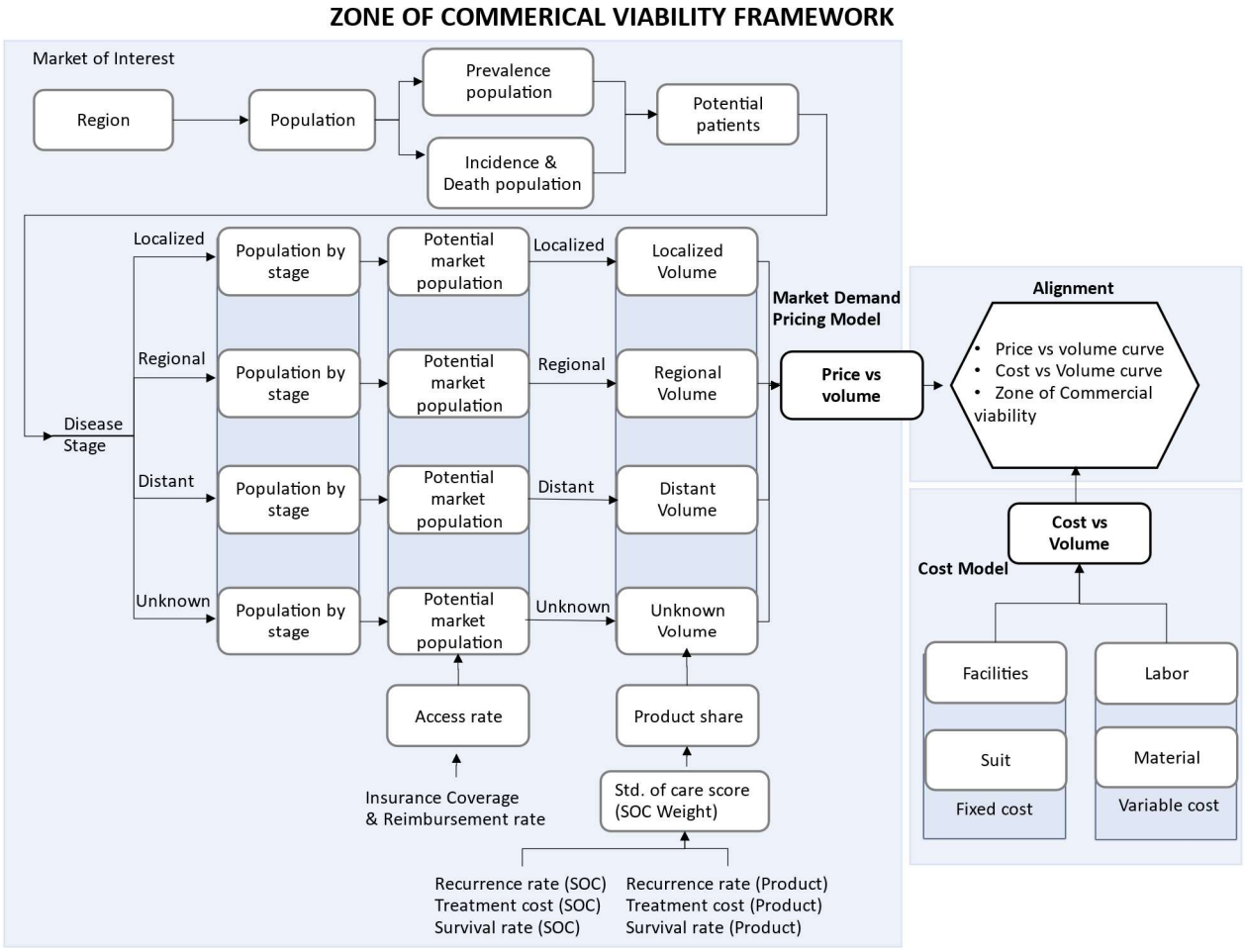
For example, for pancreatic cancer, early diagnosis and surgical resection is one of the important factors for survival because recurrence rate remains as high as 80% (Moletta et al., 2019). In comparison, for multiple myeloma patients, the significance of early vs. late relapse was observed (Majithia et al., 2019) which in term will affect the 2nd and 3rd line treatment strategies for the patient. In contrast, about half of patients treated for melanoma will experience recurrence with most recurrence will develop in the first 2-3 years after treatment (Rueth et al. 2019). These differences in recurrence rate for diseases posed a challenge for accurate modeling of these second order effects.

Based on our review of the current state of the practice, in the Methodology chapter we proposed a model that considers cancer type/patient population, cancer stage/treatment methods, reimbursement and coverage, standard of care and relapse and recurrence rate with underlying assumptions for each, described in more detail in Chapter 3.

3 Methodology

Based on our literature review, we developed an integrated framework for commercial viability by assessing the alignment between market demand pricing and cost. The integrated framework shown in Figure 5 considered both models and the alignment between them to provide a zone in which pharma companies get volume and price flexibility to maximize benefits.

Figure 5.
The Integrated Framework or Early Assessment of Economic Viability via Alignment of Cost and Market



The framework incorporated the major factors such as cancer type, patient population, cancer stage, treatment methods, reimbursement coverage and standard of care (SOC) for the market demand pricing model and facility fixed cost, labor cost, Patient dose, Yield per donor and material cost for the cost model. By combining the output of both market demand price and cost models and applying it to a specific product, PharmCGT can provide an early assessment of the economic viability before the launch of various CGT products.

3.1 Market Demand Price Model

To demonstrate how the methodology works, we first walk through the Market Demand Price model which is dependent on total potential patient volume and product share. Total potential patient volume is based on Epidemiology Data, Disease stage Data, Insurance and reimbursement whereas Product share is based on Standard of Care that is derived from Market Demand Price, Survival rate and Recurrence rate. In the forthcoming subsections, we will delve into an exhaustive exploration of the Market Demand Price Model, elucidating its development with meticulous attention to detail and thorough analysis. Table 8 shows the Input and Output variables used in this model. As a part of this model, we consider the prevalence, disease stage, potential market population and product share and standard of care consideration. More details of the parameters are provided in the Appendix of this report. The key levers identified for the market demand price models are Cancer stage (Refer 2.1.2), Reimbursement and Coverage (Refer 2.1.3), and Standard of Care (Refer 2.1.4), we will be discussing in more detail in Section 5 Discussions.

Table 8:

Input and Output variables for Market Demand Price Model.

Input	Output	Var	Variable Name	Variable Definition	Input Method	Values
In		reg	Region	Market Classification	User	Category
In		dis^{name}	Disease name	Disease name	User	Category
In		pop	Population	Market total population	User	Integer
	Out	pop^{prev}	Prevalence population	# Prevalence of this Cancer	Calculated	Integer
In		r^{inc}	Incidence rate	Rate of New Cases per 100,000	User	Integer
In		r^{death}	Death rate	Rate of deaths per 100,000	User	Integer
	Out	pop^{inc}	Incidence population	New cases with disease ($pop * r^{inc}$)	Calculated	Integer
	Out	pop^{death}	Death population	New deaths because of disease ($pop * r^{death}$)	Calculated	Integer
	Out	pop^{pat}	Potential patients	Total cases in a particular year ($pop^{prev}+pop^{inc}-pop^{death}$)	Calculated	Integer
		dis^{stage}	Disease stage of interest	Disease category		Category
In		r^{stage}	stage population rate	% Diagnosed population by stage	User	%
	Out	pop^{stage}	Population by stage	# Diagnosed population by stage ($pop^{pat} * r^{stage}$)	Calculated	Integer
In		r^{ins}	Insurance coverage	% Insured Population	User	%
In		r^{reimb}	Reimbursement rate	% of insured population are adequately reimbursed for treatment	User	%
	Out	r^{access}	Access rate	% diagnosed population can afford treatment ($r^{ins} * r^{access}$)	Calculated	%
	Out	pop^{mkt}	Potential market population	# patients who can potentially be treated for disease ($pop^{stage} * r^{access}$)	Calculated	Integer
	Out	share	Product share	Product % share in Market	Calculated	%
	Out	vol	Volume	# Patients available for treatment ($pop^{mkt} * share$)	Calculated	Integer
In		$price^{trmt}{}_{soc}$	Treatment price(SOC)	Treatment Price for current standard of care	User	Integer
In		$r^{rec}{}_{soc}$	Recurrence rate (%)(SOC)	Recurrence rate for current standard of care	User	%
In		$surv^{rel}{}_{soc}$	Relative Survival (%)(SOC)	Relative Survival current standard of care	User	%
In		$price^{trmt}{}_{prod}$	Treatment price (Product)	Treatment Price for proposed product	User	Integer
In		$r^{rec}{}_{prod}$	Recurrence rate (%) (Product)	Recurrence rate for proposed product	User	%
In		$surv^{rel}{}_{prod}$	Relative Survival (%) (Product)	Relative Survival for proposed product	User	%
In		$price^{trmtweight}{}_{per\%chg}$	price weightage	Price factor per % change in treatment Price	User	Integer
In		$r^{recweight}{}_{per\%chg}$	Recurrence rate weightage	Recurrence rate factor per % change in recurrence r	User	Integer
In		$surv^{relweight}{}_{per\%chg}$	Survival rate weightage	Sruvival rate factor per % change in survival rate	User	Integer
	Out	$price^{trmtweight}$	Treatment price improvement fa	Treatment price Improvement factor $((price^{trmtsoc}-price^{trmtprod})/price^{trmtweight}{}_{per\%chg})/100$ (1% Change per $)	Caculated	%
	Out	$r^{recweight}$	Recurrence rate improvement fa	Recurrence rate improvement factor $(r^{recsoc}-r^{recprod})*r^{recweight}{}_{per\%chg}$ (1% Change per %)	Caculated	%
	Out	$surv^{relweight}$	Survival rate improvement factor	Survival rate improvement factor $(surv^{relprod}-surv^{relsoc})*surv^{relweight}{}_{per\%chg}$ (1% Change per %)	Caculated	%
	Out	$r^{SOCweightage}$	SOC improvement factor	SOC Weight (1-100%) ($price^{trmtweight}+r^{recweight}+surv^{relweight}$)	Caculated	%
	Out	share	Product Share	%Product Share	Caculated	%

3.1.1 Epidemiology Data (Prevalence, Incidence & Death)

To forecast the portion of population administered as patients, we needed to determine how many people are infected and name it as Potential patient population (pop^{pat}). The model utilized Epidemiology Data available on SEER. SEER is an authorized source for Cancer statistics in the United States. The Surveillance, Epidemiology, and End Results (SEER) Program provides information about prevalence population, incidence rate, and death rate at a country level for a cancer type to help determine the infected population. Potential patient population (pop^{pat}). is a sum of prevalence population ($\mathrm{pop}^{\mathrm{prev}}$), Incidence population (pop^{inc}) and subtracting death population (pop^{death}). Prevalence Population ($\mathrm{pop}^{\mathrm{prev}}$) is the existing population with disease , Incidence population (pop^{inc}) shows the new cases with disease and death population (pop^{death}) shows the cases removed because of death by disease. Incidence population pop^{inc} is derived from total population (pop) and incidence rate. Death population is derived from total population (pop) and death rate (pop^{death}). Equations 1-3 show these relationships:

$$pop^{pat} = \mathrm{pop}^{\mathrm{prev}} + pop^{inc} - pop^{death} \quad (1)$$

$$pop^{inc} = \mathrm{pop} * \mathrm{r}^{\mathrm{inc}} \quad (2)$$

$$pop^{death} = pop * r^{death} \quad (3)$$

3.1.2 Disease Stage Data (Localized, Regional, Distant, Unknown)

After deriving potential patients, the model utilized Disease stage Data available on SEER (refer subsection 3.1.1) for rate of population by cancer stage to find potential patients by stage. As specified on SEER, cancer stages are categorized into Localized, Regional, Distant and Unknown stages (refer 2.1.2) and the associated rates as $r^{localized}$, $r^{regional}$, $r^{distant}$ and $r^{unknown}$. The patient population by stage is important because the treatment type, treatment price, cancer recurrence rate, patient survival rate depend on the cancer stage. Patient population by stage (pop^{stage}) will be a result of potential patient

population (pop^{pat}) and stage population rate (r^{stage}), as shown in Equation 4. So, the population of different stages will be $pop^{localized}$, $pop^{regional}$, $pop^{distant}$ and $pop^{unknown}$ as shown in Equation 5-8:

$$pop^{stage} = pop^{pat} * r^{stage} \quad (4)$$

$$pop^{localized} = pop^{pat} * r^{localized} \quad (5)$$

$$pop^{regional} = pop^{pat} * r^{regional} \quad (6)$$

$$pop^{distant} = pop^{pat} * r^{distant} \quad (7)$$

$$pop^{unknown} = pop^{pat} * r^{unknown} \quad (8)$$

3.1.3 Potential market population

After separating patients by stage (refer 3.1.2), the model utilized percentage of Insured Population (r^{ins}) and percentage of insured population that can be adequately reimbursed for treatment (r^{reimb}) to determine the rate of diagnosed population r^{access} that can afford treatment. The rate of diagnosed population helped to determine Potential US market population (pop^{mkt}) for a specific cancer type. Potential market population (pop^{mkt}) is a result of patient population by stage (pop^{stage}) and access rate (r^{access}). Access rate determined the percentage of population adequately reimbursed and is derived from insurance coverage (r^{ins}) and reimbursement rate (r^{reimb}), as shown in Equations 9-10. Hence, Potential market population for different cancer stages are $pop^{mkt}_{localized}$, $pop^{mkt}_{regional}$, $pop^{mkt}_{distant}$ and $pop^{mkt}_{unknown}$, as shown in Equation 11-14:

$$pop^{mkt} = pop^{stage} * r^{access} \quad (9)$$

$$r^{access} = r^{ins} * r^{reimb} \quad (10)$$

$$pop^{mkt}_{localized} = pop^{localized} * r^{access} \quad (11)$$

$$pop^{mkt}_{regional} = pop^{regional} * r^{access} \quad (12)$$

$$pop^{mkt}_{distant} = pop^{distant} * r^{access} \quad (13)$$

$$pop^{mkt}_{unknown} = pop^{unknown} * r^{access} \quad (14)$$

3.1.4 Product share and Standard of care weight

After determining potential market population (pop^{mkt}) for various cancer stages as $pop^{mkt}_{localized}$, $pop^{mkt}_{regional}$, $pop^{mkt}_{distant}$ and $pop^{mkt}_{unknown}$, the model utilized several input and output variables to determine product share percentage ($share$) for different cancer stages:

The method for determining the product share percentage ($share$) involves first calculating the SOC improvement factor (11) and then using SOC improvement factor to calculate product share percentage. SOC improvement factor (11) is determined by comparing the existing standard of care treatment price, recurrence rate, survival rate with product treatment price, product recurrence rate and product survival rate. SOC improvement factor (11), if positive, determines the percentage of improvement over existing standard of care, but, if negative, provides the insight that the product is not on a par with existing standard of care. It is a sum of Treatment price improvement factor (12) , Recurrence rate improvement factor (13) and Survival rate improvement factor (14).

Treatment price improvement factor(13) is the percentage improvement over price of existing standard of care and is derived by subtracting standard of care treatment price ($price^{trmt}_{soc}$) and

product treatment price ($price_{prod}^{trmt}$) and dividing the result by percentage of price weightage ($price_{per\%chg}^{trmtweight}$). Recurrence rate improvement factor (13) is the unit percentage improvement over recurrence rate of existing standard of care and is derived from standard of care Recurrence rate (r_{soc}^{rec}), product Recurrence rate (r_{prod}^{rec}) and Recurrence rate weightage ($r_{per\%chg}^{recweight}$). Survival rate improvement factor (14) is derived from standard of care Relative Survival ($surv_{soc}^{rel}$), product Relative Survival ($surv_{prod}^{rel}$) and Survival rate weightage ($surv_{per\%chg}^{relweight}$).

Price weightage ($price_{per\%chg}^{trmtweight}$), Recurrence rate weightage ($r_{per\%chg}^{recweight}$) and Survival rate weightage ($surv_{per\%chg}^{relweight}$) are arbitrary input variables used to determine the percentage chance in the respective improvement factors, as shown in Equation 11-14:

$$r^{SOCweightage} = price^{trmtweight} + r^{recweight} + surv^{relweight} \quad (11)$$

$$price^{trmtweight} = \frac{\frac{price_{soc}^{trmt} - price_{prod}^{trmt}}{price_{per\%chg}^{trmtweight}}}{100} \quad (12)$$

$$r^{recweight} = (r_{soc}^{rec} - r_{prod}^{rec}) * r_{per\%chg}^{recweight} \quad (13)$$

$$surv^{relweight} = \left(surv_{prod}^{rel} - surv_{soc}^{rel}\right) * surv_{per\%chg}^{relweight} \quad (14)$$

After determining SOC improvement factor, product share percentage (15) is determined using a power equation as shown in Table 9 in which ($scalecoeff$) variable determined vertical stretch of the curve and ($shapecoeff$) variable influenced the shape of the curve. The values for $scalecoeff$ & $shapecoeff$ are to be decided by the sponsor based on product performance expectations.

Table 9:
Product share and SOC improvement factor power equation.

Var	Variable name	Variable Definition
share	%Product Share (share)	
rSOCweightage	%SOC Weight(rSOCweightage)	
scalecoeff	20	Determines the vertical stretch or compression of the curve
shapecoeff	3	Influence the shape of the curve

$$share = scalecoeff * r^{SOCweightage^{shapecoeff}} \quad (15)$$

The power equation mapped SOC improvement factor (11) and Product Share percentage ($share$) non-linearly. The equation explained the exponential increase of product share with a small increase in SOC improvement factor ($r^{SOCweightage}$). The value for $scalecoeff$ and $shapecoeff$ is country & indication specific and are chosen to indicate the patient adoption rate in a country. Suitable values for $scalecoeff$ and $shapecoeff$ were used in our model to reflect patient adoption rate in U.S. The assumption was that a fully insured patient will prefer to adopt a new effective drug over a less effective existing drug. This adoption mentality is dependent on market demand price, recurrence rate and survival rate. Low survival rate with an existing drug may trigger faster adoption of a new drug with better survival rate. In either case, the adoption will have a slow initial increase as a doctor might be hesitant to try a new drug if it is not substantially trialed or effective. However, once the drug is proven or shown to be substantially more effective than the existing drug, the adoption and prescription rate will increase exponentially.

3.1.5 Volume

After deriving product share percentage ($share$), the model utilized potential market population (pop^{mkt}) and product share ($share$) to determine patients' volume available for treatment (*17*). Patients' volume available for treatment is a multiple of potential market population and share, as shown in Equation 16.

The volume by cancer stage will be a multiple of stagewise potential market population $pop^{mkt}_{localized}$, $pop^{mkt}_{regional}$, $pop^{mkt}_{distant}$ and $pop^{mkt}_{unknown}$ and stagewise product share percentage $share^{localized}$, $share^{regional}$, $share^{distant}$ and $share^{unknown}$, as shown in equation 17-20.

$$vol = pop^{mkt} * share \quad (17)$$

$$vol^{mkt}_{localized} = pop^{mkt}_{localized} * share^{localized} \quad (17)$$

$$vol^{mkt}_{regional} = pop^{mkt}_{regional} * share^{regional} \quad (18)$$

$$vol^{mkt}_{distant} = pop^{mkt}_{distant} * share^{distant} \quad (19)$$

$$vol^{mkt}_{unknown} = pop^{mkt}_{unknown} * share^{unknown} \quad (20)$$

Based on our analysis, we understood that Cancer stage, Insurance coverage and existing Standard of Care are the key levers impact Market Demand Pricing model. We will discuss the key levers in detail in the alignment section 3.3.

3.2 Cost model

As described in Methodology (refer section 3), an integrated framework for zone of commercial viability by assessing the alignment between market demand pricing and cost is developed. We discussed Market demand pricing model in subsection 3.1, we will now walk through the Cost model. The Cost model is dependent on Total fixed cost, Labor cost and Material cost.

Total fixed cost ($TotalfixedCost$) is based on Facility cost ($NetCost_{facility}$), Suite cost ($NetCost_{suite}$) and IT cost ($NetCost_{IT}$). Labor cost is the labor required to produce drugs for ($Num_{patients}$) volume of patients, Number of batches for ($Num_{patients}$) volume of patients, Total number of suites for ($Num_{patients}$) volume of patients, Total number of Facilities for ($Num_{patients}$) volume of patients. Material cost is based on the cost of material to produce drugs for ($Num_{patients}$) volume of patients. ($Num_{patients}$) is the minimum patients volume required for production. After calculating the Total cost to produce drugs for ($Num_{patients}$) volume of patients, we calculated cost per

patient by dividing Total cost by ($Num_{patients}$). We will learn each in detail in the subsections below. Table 10 shows all the needed inputs used in the model. The key levers identified are Total Fixed cost, Total Labor cost, Total Material cost and Number of batches, we will be discussing in more detail in the discussion section.

Table 10.

Cost Model input and output variables.

Output	Var	Variable Name	Variable Definition	Input Method	Values
	reg	Region	Market Classification	User	Category
	$name^{dis}$	Disease name	Disease name	User	Category
	$Cost_{facility}$	Facility cost	Annualized cost of capital investments (30K sq FT)	User	Integer
	$period_{facility}$	Facility Number of periods	Effective facility cost distribution years	User	Integer
Out	$NetCost_{facility}$	Net facility cost	Net Capital cost per year (Partially factoring dep)		
	$Cost_{suite}$	Cost per CT suite	CT Suite cost	User	Integer
	Num_{suite}	Number of suites	Number of Suites	User	Integer
Out	$TotalCost_{suite}$	Total CT suite cost	Total CT Suite cost	Calculated	Integer
	r^{equip}	Equipment cost % of total suite	Equipment cost % of total suite	Calculated	Integer
	r^{Infra}	Infrastructure cost % of total suite	Infrastructure cost % of total suite	Calculated	Integer
Out	$Cost_{Equip}$	Euipment cost	Euipment cost	Calculated	Integer
Out	$Cost_{Infra}$	Infrastructure cost	Infrastructure cost	Calculated	Integer
	$period_{equip}$	Equipment Number of periods	Effective Euipment cost distribution years	User	Integer
	$period_{infra}$	Infrastructure Number of periods	Effective infrastruture cost distribution years	User	Integer
Out	$NetCost_{suite}$	Net CT suite cost	Net CT suite cost	Calculated	Integer
	$Cost_{IT}$	IT cost	MES (IT) system cost	User	Integer
	$period_{IT}$	MES (IT) Number of periods	Effective MES cost distribution years	User	Integer
Out	$NetCost_{IT}$	Net MES (IT) cost per year	Net MES cost per year	Calculated	Integer
Out	TotalfixedCost	Total Fixed cost	Total Fixed cost	Calculated	Integer
	$Labor_{facility}$	Labor per facility	Labor per facility	User	Integer
	$Labor_{suite}$	Labor per suite	Labor per suite	User	Integer
	$Num_{patients}$	Number of patients	Number of patients	User	Integer
	$dose_{patient}$	Patient dose	Patient dose	User	Integer
	$weight_{patient}$	Avg patient weight	Avg patient weight	User	Integer
Out	$Production_{perpatientnum}$	Drug quantity per patient numbers	Drug quantity per patient numbers	Calculated	Integer
	$Yield_{donor}$	Yield per donor	Yield per donor	User	Integer
Out	$Batch_{perpatientnum}$	#batch per patient numbers	Number of batches for patient numbers(#patients)	Calculated	Integer
	$Area_{facility}$	Facility Area	Facility Area	User	Integer
	$Area_{suite}$	Suite area	Suite area	User	Integer
Out	TotalSuites	Total suits per facility	Total suites per facility	Calculated	Integer
	$Batch_{persuite}$	Batches per suite per year	Batches per suite per year	User	Integer
Out	NetSuite	Total suite for production quantity	Total suite for production quantity	Calculated	Integer
Out	Totalfacility	Total Facility for production quantity	Total Facility numbers for production quantity	Calculated	Integer
Out	$TotalLabor_{facility}$	Labor per facility	Labor per facility	Calculated	Integer
Out	$TotalLabor_{suite}$	Suite labor	Suite labor	Calculated	Integer
Out	TotalLabor	Total Labor	Total Suite labor	Calculated	Integer
	$Cost_{labor}$	Cost per labor	Cost per labor	User	Integer
Out	$TotalCost_{labor}$	Direct Labor Cost	Labor cost for production quantity	Calculated	Integer
	$Cost_{material}$	Material cost	Costs per batch	User	Integer
	$TotalCost_{material}$	Total Material cost	Material cost for production quantity	User	Integer
	$Cost^{Impf}_{labor}$	Labor cost improvement	Labor cost improvement per patient number	User	%
	$Cost^{Impf}_{material}$	Material Cost improvement per factor	Material Cost improvement per patient number	User	%
Out	TotalCost	Total Cost for number of patients	Total Cost for number of patients	Calculated	Integer
	$Cost_{patient}$	Cost per patient	Cost per patient	Calculated	Integer

3.2.1 Fixed Cost

The fixed cost is the total cost of setting up a production facility with all machinery, equipment, IT systems etc. Fixed cost **Error! Reference source not found.** is the sum product of yearly total Facility depreciation cost ($NetCost_{facility}$), total number of facilities ($Totalfacility$) and Net CT suite cost ($NetCost_{suite}$), total number of suites ($NetSuite$) and Net IT system cost ($Cost_{IT}$), total number of facilities ($Totalfacility$). Total Facility depreciation cost, Net CT suite cost and Net IT system cost will be explained in subsection 3.2.1 whereas Total number of facilities and Total number of suites will be explained in subsection 3.2.2.

Total Fixed cost is shown in equation 17-23:

$$Totalfixed Cost = NetCost_{facility} * Totalfacility + NetCost_{suite} * NetSuite + NetCost_{IT} * Totalfacility \quad (18)$$

To calculate the cost of running a production facility, we considered depreciation of assets as a linear function of number of years of asset life. Facility depreciation cost ($NetCost_{facility}$) is derived from Facility cost ($Cost_{facility}$) and Facility Number of periods ($period_{facility}$) considered for depreciation.

$$NetCost_{facility} = \frac{Cost_{facility}}{period_{facility}} \quad (19)$$

Total CT suite cost ($Total_{Costsuite}$) is a multiple of suite cost ($Cost_{suite}$) and number of suites (Num_{suite})

$$Total_{Costsuite} = Cost_{suite} * Num_{suite} \quad (20)$$

Equipment cost ($Cost_{Equip}$) and Infrastructure cost ($Cost_{Infra}$) are derived by multiplying them with Equipment cost % of total suite (r^{equip}) and Infrastructure cost % of total suite (r^{Infra}).

$$Cost_{Equip} = Total_{Costsuite} * r^{equip} \quad (21)$$

$$Cost_{Infra} = Total_{Costsuite} * r^{Infra} \quad (21)$$

Net CT suite cost ($NetCost_{suite}$) is derived from Equipment cost ($Cost_{Equip}$), Equipment Number of periods ($period_{equip}$) considered for depreciation and Infrastructure cost ($Cost_{Infra}$), Infrastructure Number of periods ($period_{infra}$) considered for depreciation.

$$NetCost_{suite} = \frac{Cost_{Equip}}{period_{equip}} + \frac{Cost_{Infra}}{period_{infra}} \quad (22)$$

Net MES (IT) systems yearly cost ($NetCost_{IT}$) is derived from IT system cost ($Cost_{IT}$) and Effective Number of periods ($period_{IT}$) considered for depreciation.

$$NetCost_{IT} = \frac{Cost_{IT}}{period_{IT}} \quad (23)$$

3.2.2 Labor Cost

Once Facility fixed cost is calculated, the next step is to calculate the number of labor quantity and cost required to run the facility. For simplicity, batches are produced for a multiple of ($Num_{patients}$) volume of patients. This means that Total suites, Number of batches are calculated for ($Num_{patients}$) volume of patients and increase in the order of ($Num_{patients}$) volume of patients. A minimum order quantity is typical in industrial environment, ($Num_{patients}$) is the minimum patients volume required for production.

Direct Labor Cost ($TotalCostlabor$) is derived from the Total number of Labor ($TotalLabor$) and average salary ($Cost_{labor}$), as shown in Equation 24-32:

In our case, we considered an average salary ($Cost_{labor}$) based on Bureau of Labor Statistics. (2023, December). Employee benefits in the United States (Publication No. USDL-24-0485). Retrieved from https://www.bls.gov/news.release/pdf/ecec.pdf.

$$TotalCostlabor = TotalLabor * Cost_{labor} \quad (24)$$

Total number of Labor ($TotalLabor$) is a sum of Labor required to run all facilities ($TotalLabor_{facility}$) and labor required to run all Suites ($TotalLabor_{suite}$) to produced drugs for $Num_{patients}$ volume of patients.

$$TotalLabor = TotalLabor_{facility} + TotalLabor_{suite} \quad (25)$$

$$TotalLabor_{facility} = Labor_{facility} * Totalfacility \quad (26)$$

Total numbers of labor to meet demand ($TotalLabor_{facility}$) of $Num_{patients}$ volume of patients is the multiplication of Labor per facility ($Labor_{facility}$) and Total number of Facilities required to meet demand ($Totalfacility$) of $Num_{patients}$ of patients.

Suite labor ($TotalLabor_{suite}$) is a multiplication of Labor required per suite ($Labor_{suite}$) and Total suites required to produce drugs ($NetSuite$) for $Num_{patients}$ volume of patients.

$$TotalLabor_{suite} = Labor_{suite} * NetSuite \quad (27)$$

Total number of Facility ($Totalfacility$) required to produce drugs for $Num_{patients}$ patients is derived from Total suites ($TotalSuites$) possible in a facility and Total suite for production quantity ($NetSuite$) for $Num_{patients}$ volume of patients.

$$Totalfacility = \frac{TotalSuites}{NetSuite} \quad (28)$$

Total suites required to produce drugs ($NetSuite$) for $Num_{patients}$ volume of patients and is derived from number of batches required to for patient numbers ($Batch_{perpatientnum}$) and Batches per suites ($Batch_{persuite}$).

$$NetSuite = \frac{Batch_{perpatientnum}}{Batch_{persuite}} \quad (29)$$

Total suites per facility ($TotalSuites$) is derived from Facility Area ($Area_{facility}$) and Suite area ($Area_{suite}$).

$$TotalSuites = \frac{Area_{facility}}{Area_{suite}} \tag{30}$$

Number of batches for $Num_{patients}$ of patients ($Batch_{perpatientnum}$) is derived from Demand for $Num_{patients}$ patients ($Production_{perpatientnum}$) and Yield per donor ($Yield_{donor}$).

$$Batch_{perpatientnum} = \frac{Production_{perpatientnum}}{Yield_{donor}} \tag{31}$$

Drug quantity per patient numbers ($Production_{perpatientnum}$) is the production quantity for Number of patients ($Num_{patients}$), Patient dose ($dose_{patient}$) and Average weight ($weight_{patient}$)

$$Production_{perpatientnum} = Num_{patients} * dose_{patient} * weight_{patient} \tag{32}$$

With Equations 18-26, we calculated Labor required to run the facility. With points 3.2.1-3.2.2, we have calculated the facility and labor cost. We will calculate material costs needed to start production in the next subsection.

3.2.3 Material Cost

Total Material Cost ($TotalCost_{material}$) was an important parameter to find the material cost for the total number of batches to produce drugs for Number of patients ($Num_{patients}$). The $Cost_{material}$ is an arbitrary input variable and chosen for the material cost of one batch.

$$TotalCost_{material} = Cost_{material} * Batch_{perpatientnum} \quad (33)$$

3.2.4 Total Cost per patient

The total cost is based on a production quantity for $Num_{patients}$ volume of patients and is a combination of Total Fixed Cost, Total Labor Cost, and Total Material Cost.

$$TotalCost = TotalfixedCost + TotalCost_{labor} + TotalCost_{material} \quad (34)$$

Economies of scale are typical in the manufacturing industry; cost should decrease with increase in production quantity. Labor cost improvement per factor ($\text{Cost}_{labor}^{\text{Impf}}$) and Material Cost improvement per factor ($\text{Cost}_{material}^{\text{Impf}}$) were used to optimize total cost per $Num_{patients}$ volume of patients. The total labor cost and material cost reduce by a factor of $\text{Cost}_{labor}^{\text{Impf}}$ and $\text{Cost}_{material}^{\text{Impf}}$ with every additional $Num_{patients}$ volume of patients. The reduction results into decrease in total cost with every additional $Num_{patients}$.

$$TotalCost_{labor} = TotalCost_{labor} - TotalCost_{labor} * \text{Cost}_{labor}^{\text{Impf}} \quad (35)$$

$$TotalCost_{material} = TotalCost_{material} - TotalCost_{material} * \text{Cost}_{material}^{\text{Impf}} \quad (36)$$

The cost per patient can now easily be calculated by dividing the total cost is based on a production quantity for $Num_{patients}$ volume of patients by $Num_{patients}$ volume.

$$Cost_{patient} = \frac{TotalCost}{Num_{patients}} \quad (37)$$

Based on our analysis, we understood that $Cost_{patient}$ is dependent on Total Fixed cost, Total Labor cost, Total Material cost and Number of batches which are the key levers that will impact Cost model. We will discuss key levers of both the Cost model and Market Demand Pricing model in detail in the Alignment section 3.3.

3.3 Alignment between Market Demand Pricing and Cost model

With the Market Demand Pricing and Cost model, two important parts of the integral framework are complete. The third part is to combine these two models to understand the alignment between them. We noticed that the vol in Market Demand pricing model and volume of patients ($Num_{patients}$) in the Cost model define is the common scale on which the alignment can be understood. On one end, in Market Demand Pricing, vol is the volume of patients that can potentially use proposed product and is based on Cancer stage, Insurance coverage and existing Standard of Care. Standard of Care is inherently based on treatment price, recurrence rate and survival rate. On the other end, in Cost model, $Num_{patients}$ is the minimum number of patients (vol) required for production and the cost of production is based on Total Fixed cost, Total Labor cost, Total Material cost and Number of Batches.

To understand the relationship between the two models, Market Demand Pricing and Cost are plotted on y axis and volume of patients on x axis. Table 11 shows critical Input and Output variables for the alignment between market Demand Pricing and Cost model. For simplicity, we will mention $Num_{patients}$ as volume (vol) moving forward for further analysis within integrated framework and scenario creation.

Table 11.
Critical Input and Output variables for the alignment between market Demand Pricing and Cost model.

Input	Output	Var	Variable Definition
In		$price^{trmt}_{soc}$	Treatment price(SOC)
In		r^{rec}_{soc}	Recurrence rate (%)(SOC)
In		$surv^{rel}_{soc}$	Relative Survival (%)(SOC)
In		$price^{trmt}_{prod}$	Treatment price (Product)
In		r^{rec}_{prod}	Recurrence rate (%) (Product)
In		$surv^{rel}_{prod}$	Relative Survival (%) (Product)
In		$price^{trmtweight}_{per\%chg}$	price weightage
In		$r^{recweight}_{per\%chg}$	Recurrence rate weightage
In		$surv^{relweight}_{per\%chg}$	Survival rate weightage
	Out	vol	Potential market population
	Out	TotalfixedCost	Total Fixed cost
In		$dose_{patient}$	Patient dose
In		$Yield_{donor}$	Yield per donor
	Out	$TotalCost_{labor}$	Direct Labor Cost
In		$TotalCost_{material}$	Total Material cost

The interaction resulted in a combined plot which highlights several insights about the impact of price, cost, and volume. We will discuss combined plot insights in the results section using scenarios.

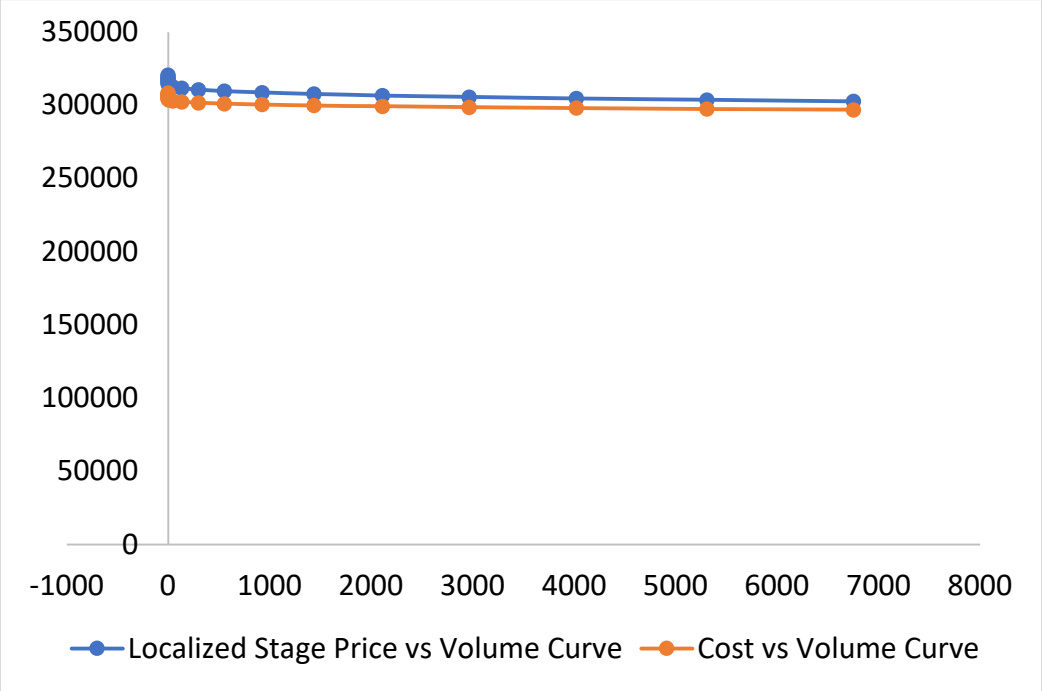
4 Results

For results, we combine the output of the market demand and cost models to assess the viability of launching various gene and cell therapy products. By leveraging the insights provided by each model, our sponsor company gained a comprehensive understanding of the market landscape and potential challenges and opportunities associated with launching products. The "zone of commercial viability" concept can be used to determine the feasibility of bringing a product to market by considering factors such as market demand, competition, and potential return on investment. By applying the combined output of the models to this framework, our sponsor company can make more informed decisions about which gene and cell therapy products are most likely to succeed commercially.

The production cost of the treatment is $308,000 based on Cost model whereas the treatment price based on Market demand pricing model for multiple myeloma in US is $291,593 for localized cancer stage and $583,187 for distant cancer stage.

Figure 6 and Figure 7 are the economic viability plots in which treatment price and cost are shown on y-axis and patient volume is shown on the x-axis. Figure 6 shows the Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for localized cancer stage whereas

Figure 6.
Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for localized cancer stage (Not economically viable).



In Figure 6, for the localized stage of Myeloma the model shows it is not economically viable to launch the therapy because the cost is too high and the existing standard of care exists at a lower price. Figure 7 shows the Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for distant cancer stage. It is clear from the plot that the treatment price is higher than the production cost and hence the treatment is economically viable. For the distant stage of Myeloma, because the treatment price is higher than the product cost, not only the production of the treatment is

economically viable but because the standard of care treatment price is high, a higher treatment price can be sought for a better product.

Figure 7.
Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for distant cancer stage (Economically viable).

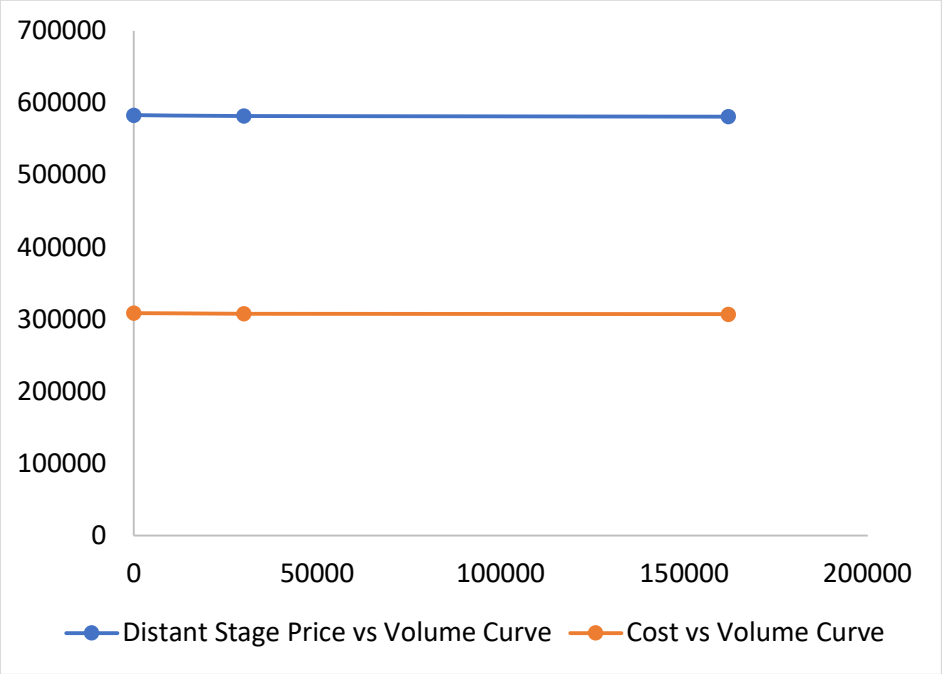


Figure 6 demonstrated it is not viable to produce treatment for localized cancer stage, but different cost and price optimization opportunities are possible to make the treatment economically viable. To discuss the opportunities in detail, we created two scenarios. Scenario 1 involve adjusting the cost to achieve economic viability while keeping Price fixed, while scenario 2 involve adjusting treatment price to achieve economic viability while keeping Cost fixed.

In Figure 8 (Scenario 1), cost of treatment is adjusted using Cost model key levers (refer 3.2.4). Figure 8a shows that treatment cost after reducing Total fixed cost by 25% can make the product economically viable as the adjusted production cost will be $245,000 in comparison to the selling price of $291,593. Similarly, figure 8b shows that after reducing Total labor cost by 65%, the adjusted production cost will be $286,652 which makes the product economically viable to produce.

Figure 8.

Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for localized cancer stage (Cost adjusted using key levers to make it economically viable).

Figure 8a.
(Total Fixed cost reduced by 25%).

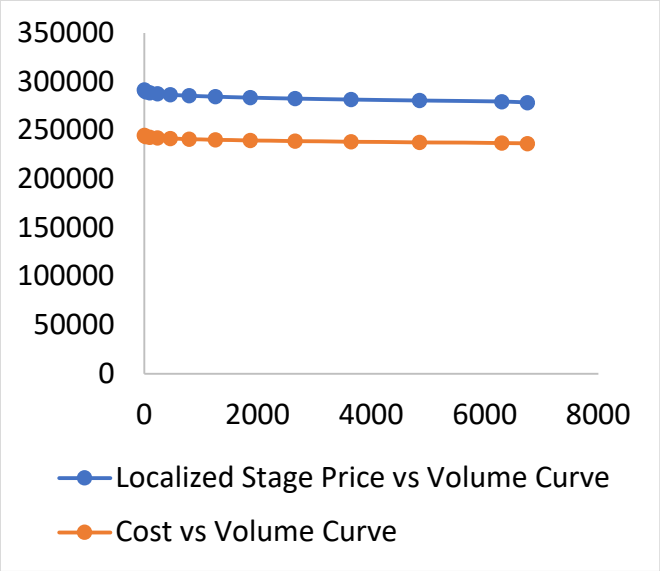
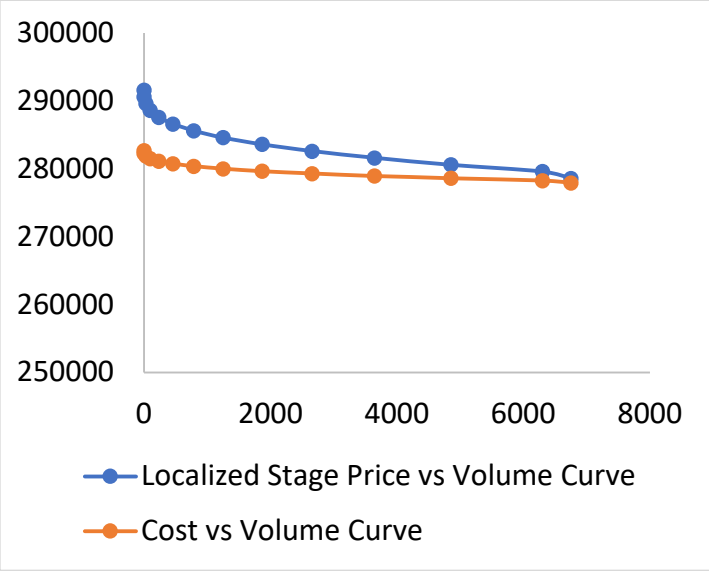


Figure8b.
(Total labor cost reduced by 65%).



In Figure 9 (Scenario 2), treatment price is adjusted using Market demand pricing model key levers (refer 3.1.5). Figure 9a shows that after increasing treatment price by 10% and reducing recurrence rate by 20% can make the product economically viable as the adjusted treatment price will then be $320,752 in comparison to the selling price of $291,593.

Figure 9.

Economic Viability plot comparing market demand price and cost model output for Myeloma in the US for localized cancer stage (Market Price adjusted using key levers to make economic viable).

Figure 9a.
(Total Price increase by 10% & recurrence reduced by 20%).

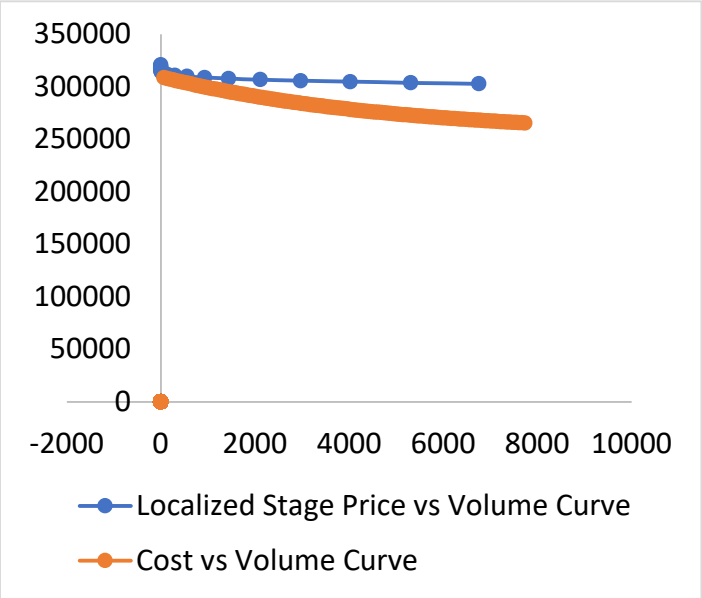
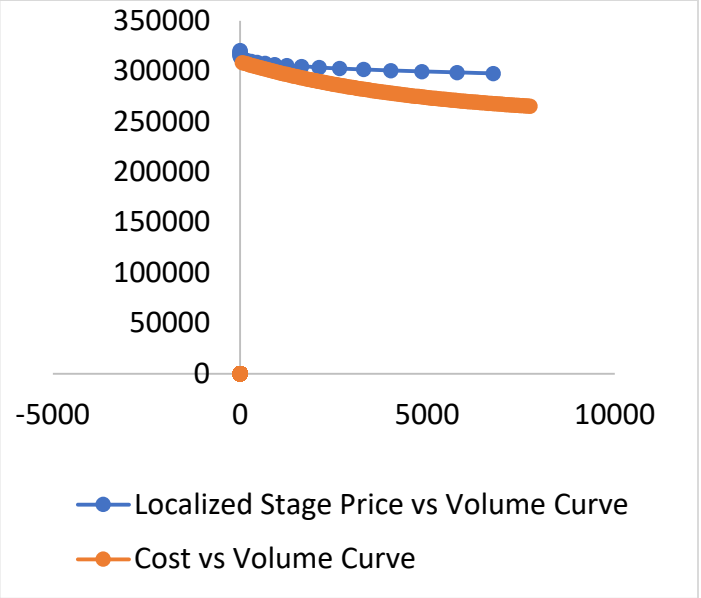


Figure9b.
(Total Price increase by 10% & survival rate increased by 20%).



Similarly, in figure 9b, after increasing treatment price by 10% and increasing survival rate by 20% can make the product economically viable as the adjusted treatment price will then be $320,752 in comparison to the selling price of $291,593. Despite higher price than the standard of care, the product can still gain market share if there is an significant improvement in lowering recurrence rate and higher chances of survival.

5 Discussions

The proposed integrated framework which include market demand pricing and cost models allows for PharmCGT to perform early assessment of economic viability of innovative cell and gene therapy treatments. In section 4, we show several different scenarios of economic viability for the treatment of Myeloma in the US. Figure 7 demonstrate economic viability for distant stage of Myeloma, while Figure 6, 8 and 9 demonstrate examples of starting with not economically viable and the possible levers in the market demand pricing and cost models in order to achieve economic viability. The market demand price

and cost models and the alignment between them provides the critical visibility required for the PharmCGT to start an internal discussion of how to channel efforts in the right direction to provide best marginal benefits to the patient while maintaining sufficient profits to keep the R&D engine running.

5.1 Recommendation and Limitations

In this work, the results generated from the proposed integrated framework focused on a single disease type Myeloma in the US. Therefore, there are two directions for next steps in terms of exploration and application: additional disease types and expansion in terms of geography. In addition to Myeloma, the model can be used to explore additional disease types to test the sensitivity of the market demand price model, and the top-down funnel approach for different cancer types. Similarly, the cost model can be tested to explore sensitivity with respect to different disease types.

Secondly, our model validation used US data because this was the most robust public data available, however exploring Outside of US (OUS) application would be highly recommended. Especially another developed market country (in EU such as Germany) and an emerging market (such as Brazil or China) to have a comparison between developed vs emerging markets.

For the cost model, we intentionally developed a manufacturer neutral model to increase the generalizability of our work. However, one limitation in the cost model is we did not take into efficiencies in economy of scale which can vary depending on the manufacturer, technology, and IP available. This is another area that can be explored to improve the model of the future.

6 Conclusion

As a part of the project, we developed an integrated framework comprised of Market pricing model, Cost model and Alignment between these two models that PharmCGT can utilize for the early assessment of the economic viability of CGT. The three main contributions include:

1. A market demand pricing model to consider the low volume of demand for CGT capable of isolating specific disease types, cancer stages, and lines of treatment with the capability to aggregate data to depict total demand. The key levers that can either improve or worsen the market demand price are identified as SOC, disease Recurrence Rate, and Survival Rate.
2. A high-level cost model adaptable to any manufacturer/process and provide a rapid and reasonably accurate estimate of the costs associated with CGT manufacturing activities. The key levers that can either improve or worsen costs are identified as batch, dose and donor yield.
3. An integrated framework capable of early assessment of economic viability via alignment of Cost and Market Pricing models, with the ability to assess the impact of key market demand price and cost levers on the results.

The integrated framework was developed for the US region and for one Myeloma oncology cancer indication. However, can be generalized in the future for additional countries/regions and various disease indications.

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