

Introduction to DHC Quantitative Modeling Capabilities

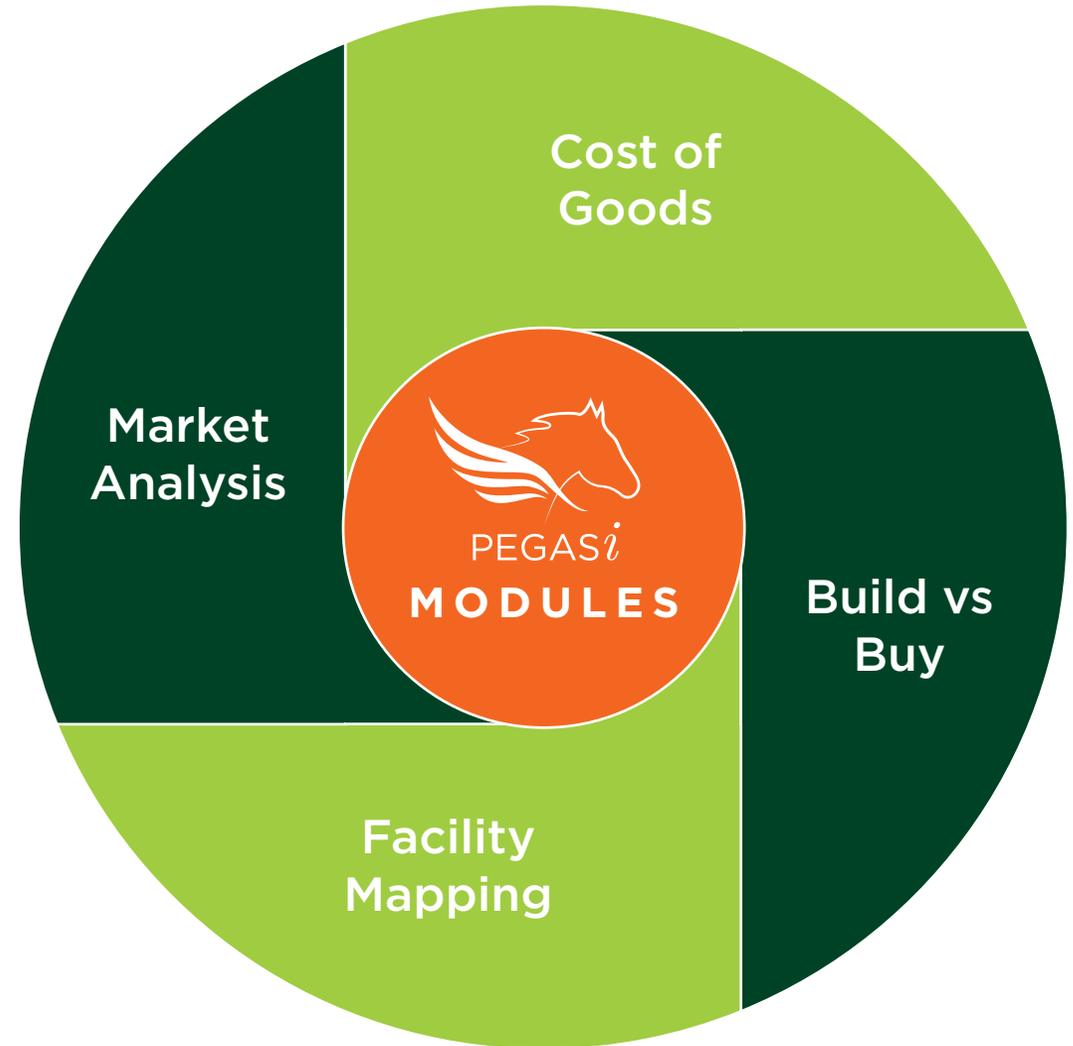


PEGAS*i*

What is Pegasi?

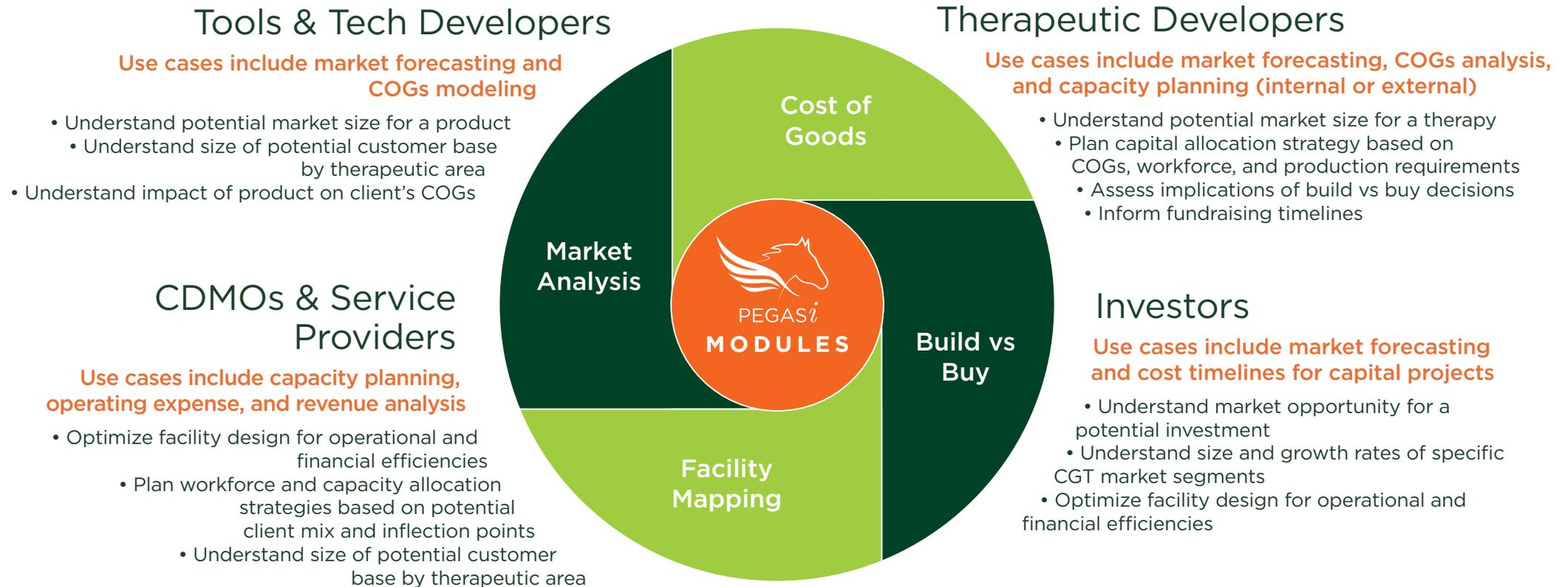
A proprietary platform enabling clients to make data-driven decisions

- DHC built a toolbox for quantitative modeling and data analysis to enable streamlined and flexible support of client needs
- Pegasi platform includes:
 - Templates (Excel, Python, VBA, Tableau)
 - Proprietary database of assumptions and industry insights from DHC SMEs
 - External data sources
- Each project is customized using the relevant tools to provide the output necessary for clients to inform their critical decisions
 - Projects often leverage multiple interconnected tools from the platform (e.g. cost of goods and build vs buy templates)



Pegasi Quantitative Modeling Platform

Providing customized data-driven analyses to a wide range of end users



The background of the slide is a solid orange color. On the left side, there are several overlapping, wavy, light-orange shapes that resemble stylized flames or flowing liquid, creating a dynamic and modern aesthetic.

Customer Type

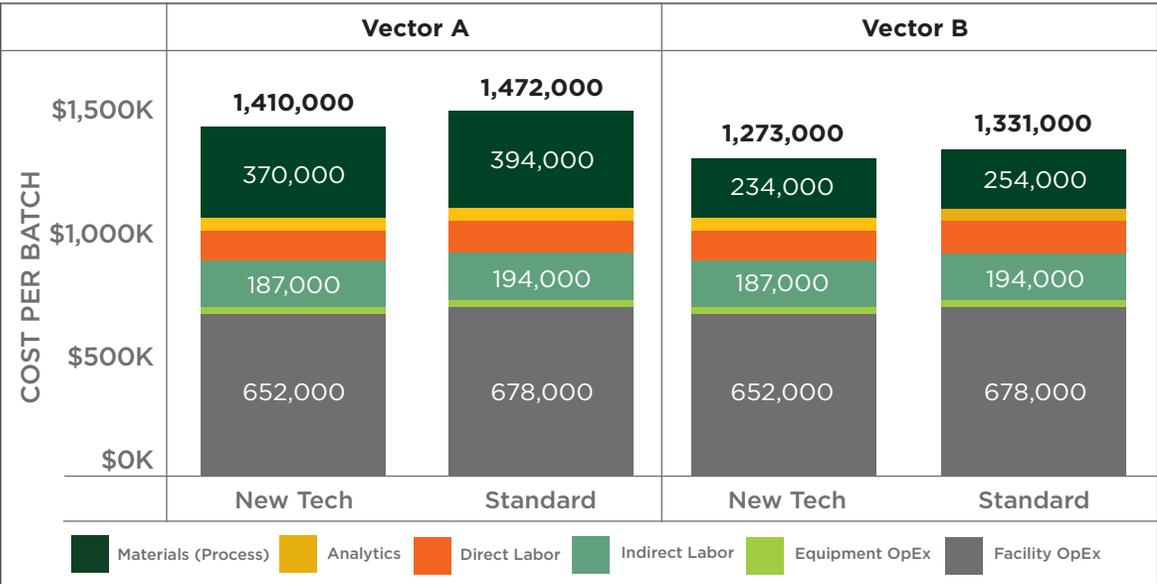
Tools & Tech Developers

Use cases include market forecasting
and COGs modeling

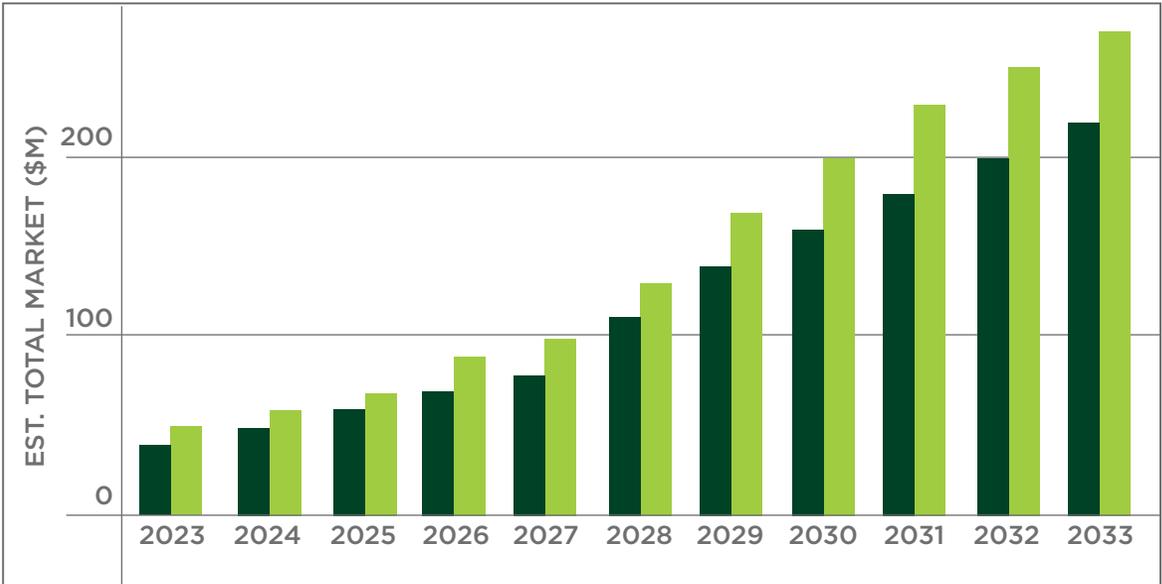
HOW PEGASI CAN HELP:

- Understand potential market size for a product
- Understand size of potential customer base by therapeutic area
- Understand impact of product on client's COGs

Sample Output: COGs Analysis Leveraging Client Tech



Sample Output: Total Market (\$) for Tech vs Standard Tech



Therapeutic Developers

Use cases include market forecasting, COGs, and capacity planning (internal or external)

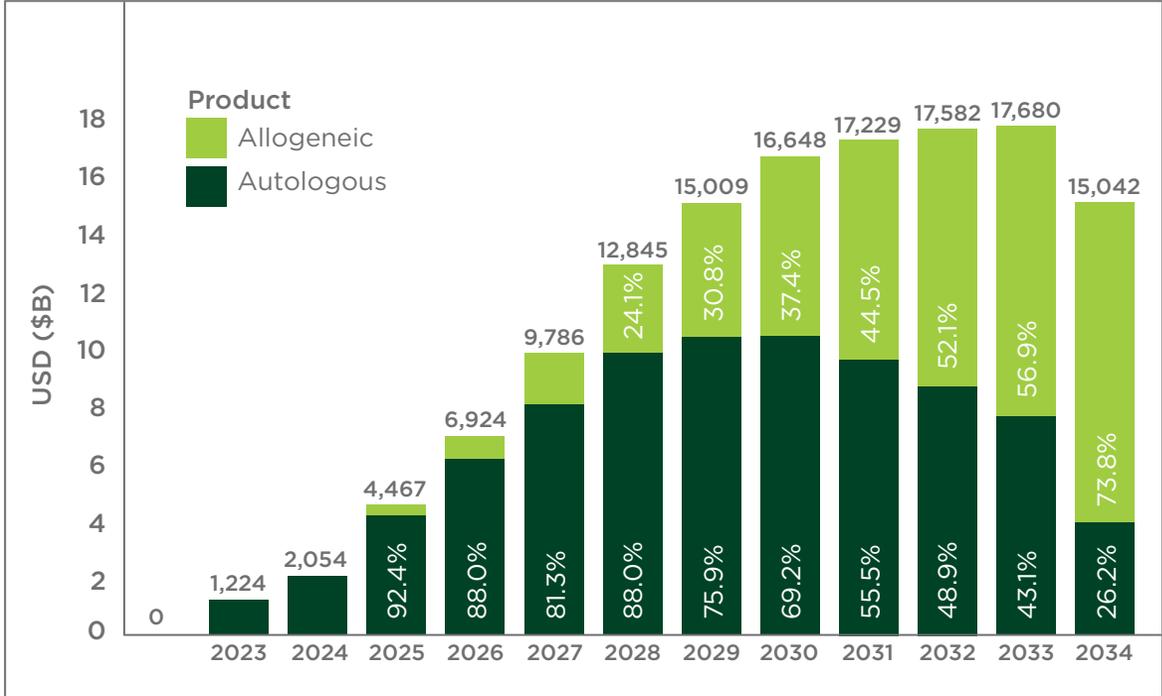
HOW PEGASI CAN HELP:

- Understand potential market size for a therapy
- Plan capital allocation strategy based on COGs, workforce, and production requirements
- Assess implications of build vs buy decisions
- Inform fundraising timelines

Sample Output: Facility Operating Expenses and Revenue Estimates

	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
PRODUCTION Total Suites - Product 1 Annual Lots - Product 1 Max Capacity	Alignment or production targets and capacity										
Capacity Utilization Total Suites - Product 2 Annual Lots - Product 2											
Max Capacity Capacity Utilization											
LABOR Ramped hiring linked to production	Total site FTE										
OPEX Materials (Process) - Product 1 Materials (Process) - Product 2 Materials (Analytics) Labor Equipment - OpEx Facility - OpEx	Capital and operating expenses forecasted based on production targets and phased facility build-out										
CAPEX Equipment - CapEx Facility - CapEx											
REVENUE Production - Product 1 Production - Product 2	Revenue forecasts based on client information or DHC instry knowledge										
RAW PROFIT MARGIN	Financial metrics as defined by client (NPV, cash flow, profit margin, EBIT, etc.)										

Sample Output: Market Size (TAM) Estimates by Product Type



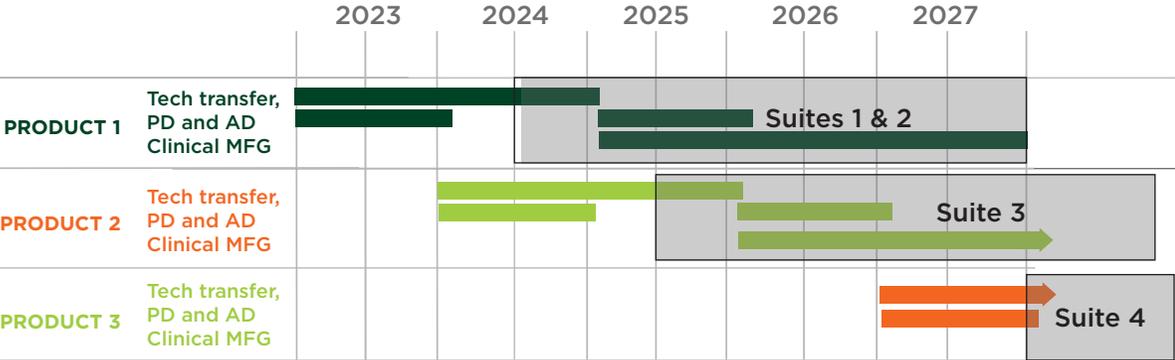
CDMOs & Service Providers

Use cases include facility capacity planning, operating expense, and revenue analysis

HOW PEGASI CAN HELP:

- Optimize facility design for operational and financial efficiencies
- Plan workforce and capacity allocation strategies based on potential client mix and inflection points
- Understand size of potential customer base by therapeutic area

Sample Output: Multiproduct Capacity Planning



Sample Output: COGs and Revenue Analysis

Revenue by Archetype & Phase							Average Breakdown (\$M)		
Phase	Archetype	Revenue				Phase	Line Item	Phase	
Early Clinical	Auto - Product 1	1.6	1.8	1.8	\$5.2	Early Clinical	Review	\$4.7	
	Auto - Product 2	1.6	1.6	1.1	\$4.4		Total Direct Costs	\$1.8	
	Auto - Product 3	1.6	1.8		\$3.9		Total Indirect/OpEx	\$1.6	
	Auto - Product 4	1.6	1.7		\$3.5		Operating Profit	\$1.3	
	Auto - Product 5	1.6	1.8	2.9	\$6.4				
Pivitol Clinical	Auto - Product 1	2.5	2.5	5.7	\$10.7	Pivitol Clinical	Review	\$7.3	
	Auto - Product 2	1.2	1.6	3.2	\$6.0		Total Direct Costs	\$2.0	
	Auto - Product 3	1.2	1.8	.9	\$3.9		Total Indirect/OpEx	\$1.7	
	Auto - Product 4	1.2	1.7		\$3.5		Operating Profit	\$3.6	
	Auto - Product 5	2.5	2.5	7.4	\$12.4				

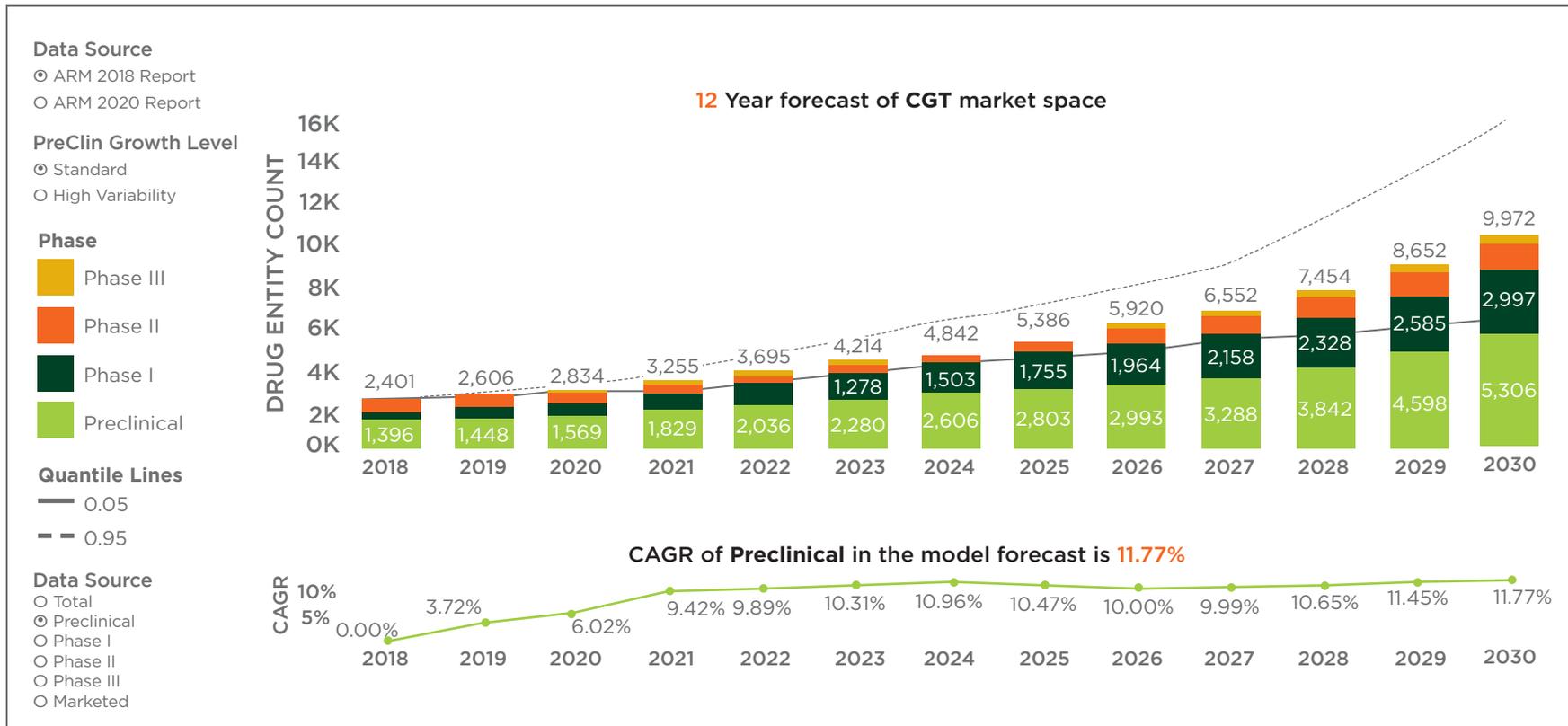
Investors

Use cases include market forecasting and cost timelines for capital projects

HOW PEGASI CAN HELP:

- Understand market opportunity for a potential investment
- Understand size and growth rates of specific CGT market segments
- Optimize facility design for operational and financial efficiencies

Sample Output: Total CGT Market Forecast



Sample Output: Facility Capital Expenditure Estimates

Cost Category	Phase 1 (\$M)	Phase 2 (\$M)
Direct Construction	Cost estimates based on ISO/EU Grade requirements and industry benchmarks	
Interior fit-up		
Process/utility/ lab equipment and controls		
Index Costs		
Design and engineering		
Construction and site management		
Commissioning and site management		
Owner's costs		
Other Costs		
Contingency		
Total Capital Cost		
Total Capital Cost Range (-10/+20%)		

Sample Pegasi Outputs

Tableau dashboards allow for interactivity

Market Forecasting Sample Dashboard

Estimate opportunity for a tool serving viral vector manufacturers



Choose an option for each toggle parameter to update the data in the figures.

Parameter #1

- Large improvement
- Moderate improvement
- Small improvement
- Standard process

Parameter #2

- Large improvement
- Reduce unit ops
- Small improvement
- Standard process

Parameter #3

- Large improvement
- Small improvement
- Standard process

VECTOR A

Figure 1: Total Vector A Market Potential

The total market size for Vector A based on a standard yield and batch cost, using current technology vs batch savings driven by potential improvements using New Tech.

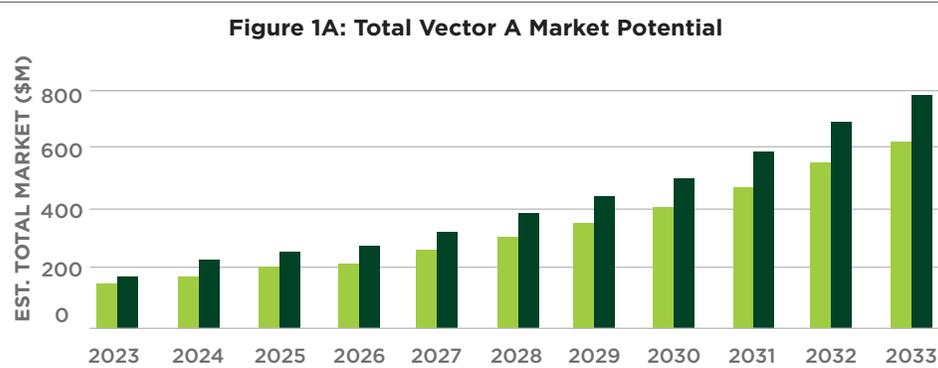
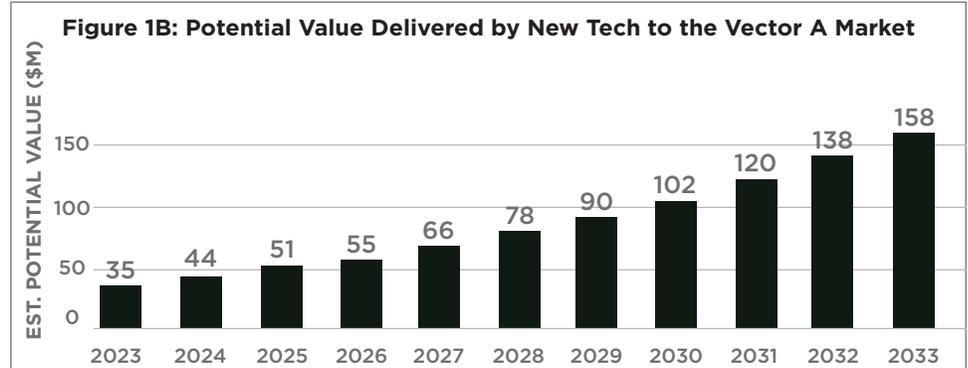


Figure 1B: Potential Value Delivered by New Tech to the Vector A Market



VECTOR B

Figure 2: Total Vector B Market Potential

The total market size for Vector B based on a standard yield and batch cost, using current technology vs batch savings driven by potential improvements using New Tech.

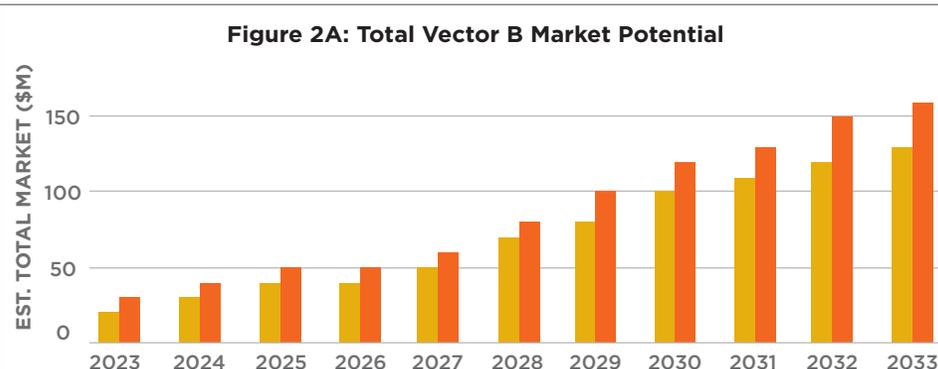
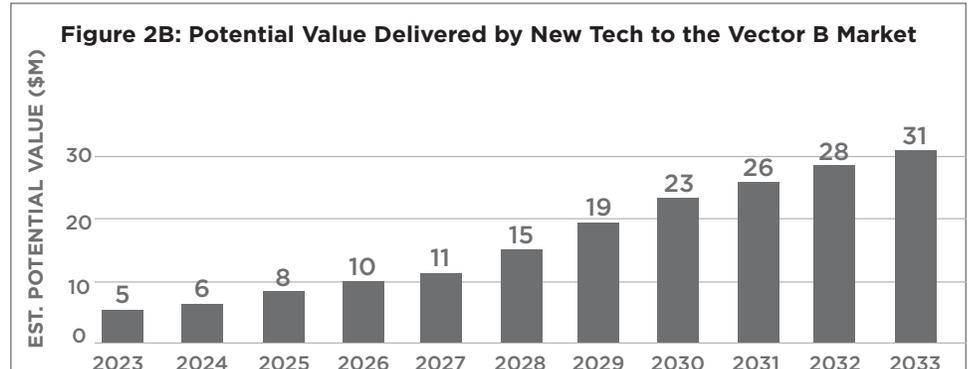


Figure 2B: Potential Value Delivered by New Tech to the Vector B Market



COGs Sample Dashboard

Considering cost per batch or vector cost implications deploying new technology



Choose an option for each toggle parameter to update the data in the figures.

Parameter #1
 Large improvement
 Moderate improvement
 Small improvement
 Standard process

Parameter #2
 Large improvement
 Reduce unit ops
 Small improvement
 Standard process

Parameter #3
 Large improvement
 Small improvement
 Standard process

Cost Category

- Materials (Process)
- Analytics
- Direct Labor
- Indirect Labor
- Equipment OpEx
- Facility OpEx

Figure 1: Cost per Batch by virus type and technology. The cost of producing a batch with New Tech is compared to the cost of a standard production process.

Cost per Batch Difference (%)

Standard: 0.00% New Tech: 1.00%

Yield per Batch Difference (%)

Vector A: 9.00% Vector B: 9.00%

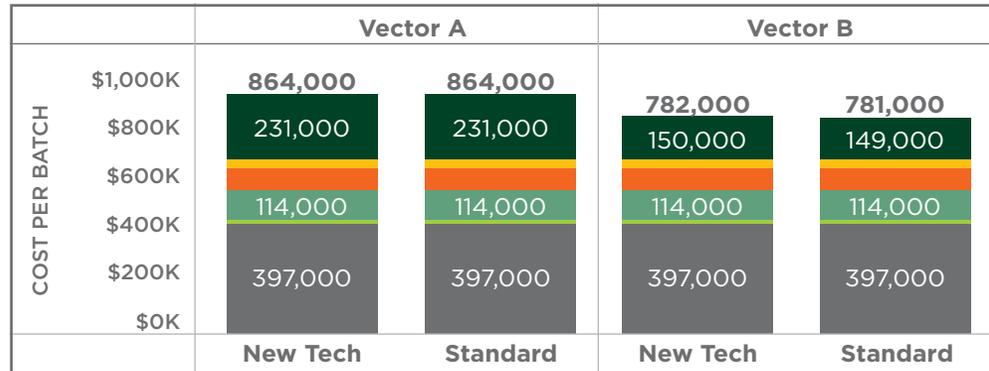
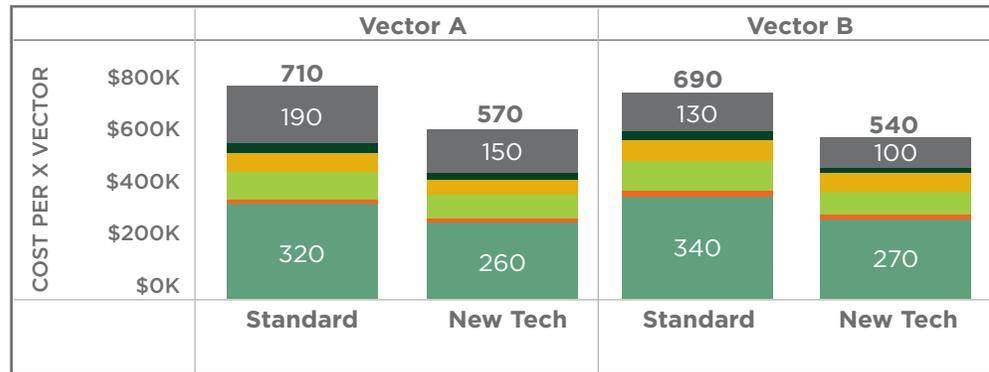


Figure 2: Cost per x amount of vector by virus type and technology. Use of the New Tech may increase titer which affects per production costs relative to a standard production process.

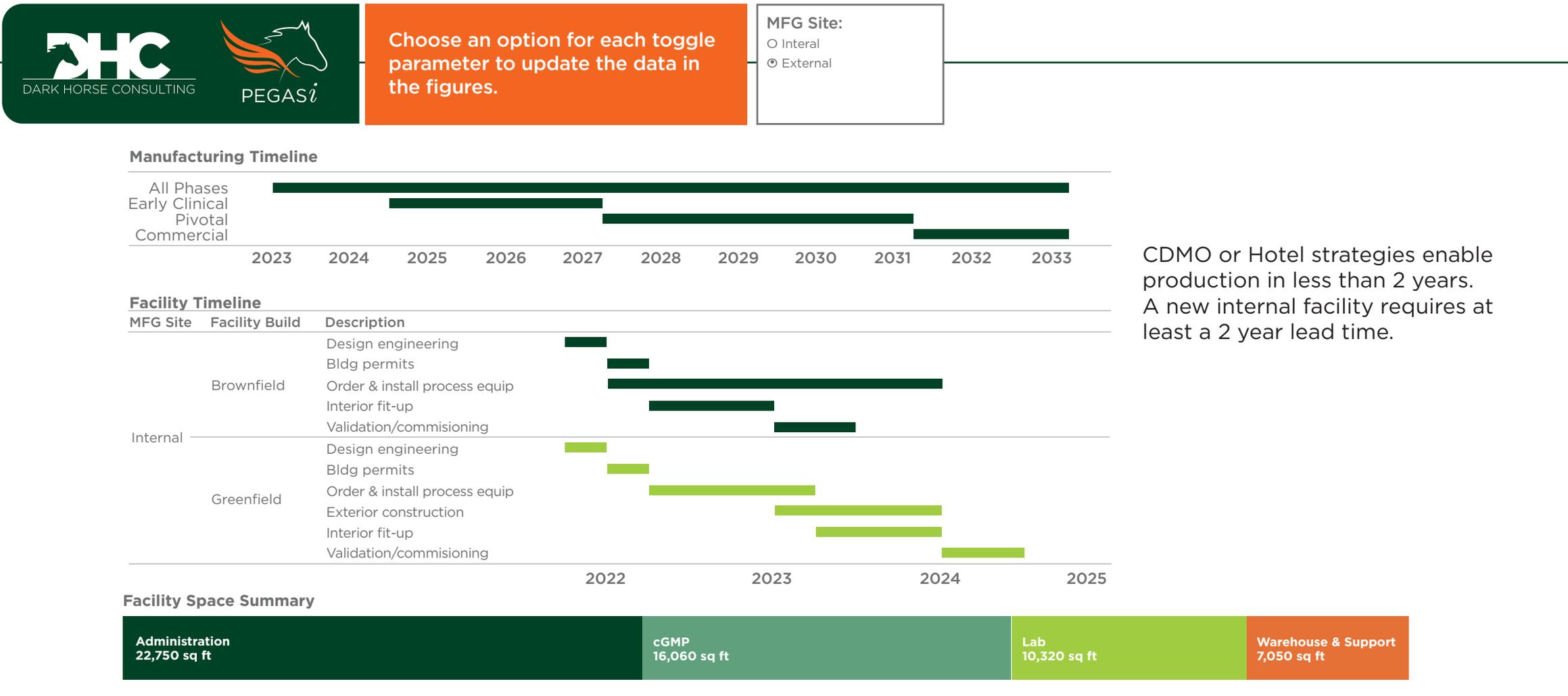
Cost per x Vector Amount Difference (%)

Standard: -6.00% New Tech: -6.00%



Build vs Buy Sample Dashboard

Comparing timelines and space requirements for internal vs external sites

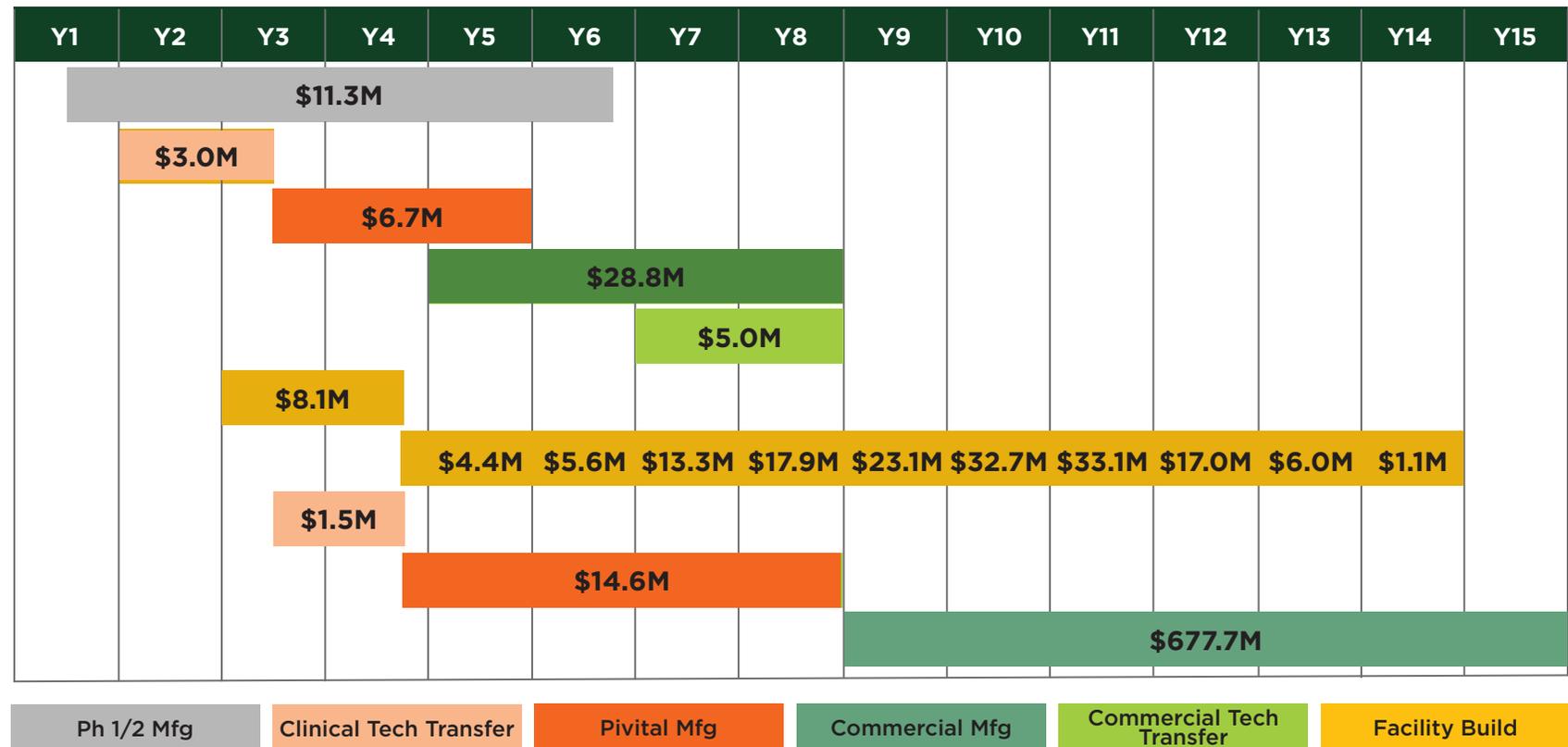


Build vs Buy Financial Planning

Estimating annual financial commitments for external manufacturing and facility build out



- CDMO for all Ph 1/2
- TT* to CDMO for all Program 1 Pivotal
- CDMO for all Program 1 Pivotal
- CDMO for all Program 1 Launch
- TT to Internal for all Program 1 Commercial
- Build Internal for Pivotal
- Expand Internal for all Commercial
- TT to Internal for all Program 2 Pivotal
- Internal for all Program 2 Pivotal
- Internal for all Commercial

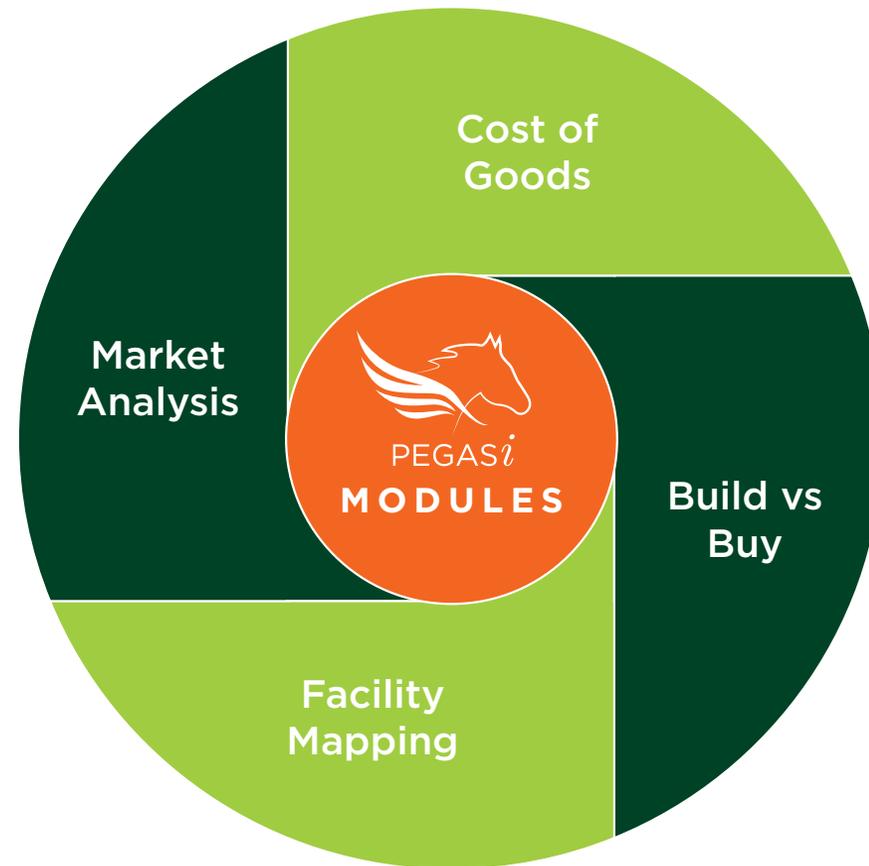


*TT = Technology Transfer

Summary: Pegasi can help crack the code on your CGT problems

Custom solutions provide the data necessary to make critical decisions

- DHC is uniquely positioned to provide support with data analysis given our **deep CGT industry expertise**.
- The proprietary Pegasi platform was designed to support clients in a **streamlined and flexible manner**.
- **Models are customized** to individual clients' needs.
- Projects may leverage **one or more** Pegasi modules.
- Deliverables will include **multiple formats** such as Excel, Tableau, and slides to support varying audiences.
- Dashboards will allow the viewer to **stay at a high-level or drill-down** into the details.



Pegasi Analysis in Action

Our new white paper demonstrates
Pegasi's capabilities

See Pegasi in action via our new white paper

Is CGT Ready for Prime Time?

Analysis utilizing the Pegasi quantitative modeling platform

INTRODUCTION To date, cell and gene therapy (CGT) drugs have predominantly been developed to treat patients with relatively small populations and utilized as late-line treatments. As such, the field has yet to experience the manufacturing capacity demand akin to that of “blockbuster” drugs. In this analysis we utilized the Pegasi platform to explore whether, in its current state, the field could support commercial supply of a CGT drug at blockbuster scale.

ANALYSIS By utilizing the Pegasi platform to model two “prototype” CGT drugs, we have created manufacturing capacity projections for each drug at blockbuster scale (Figures 1-4) as well as modeled the impact of presumptive advanced manufacturing technology introduction on the capacity projections (Figures 5-7).

CONCLUSION The analysis indicates that, in the current state, a successful commercial launch of a CGT drug would be challenged by the lack of available unfragmented manufacturing capacity, as well as the availability of an appropriately skilled workforce. Introduction of advanced manufacturing technologies can meaningfully alleviate these challenges; however, developers would still need to make significant investments to close these capacity gaps, putting further pressure on already borderline prohibitive COGs for these therapies. Thus, a new question emerges: does CGT need to fundamentally rethink its current manufacturing and distribution models?

Scan this QR code to read the white paper with our full analysis.



Pegasi white paper figures 1-4

Off-the-shelf AAV case study

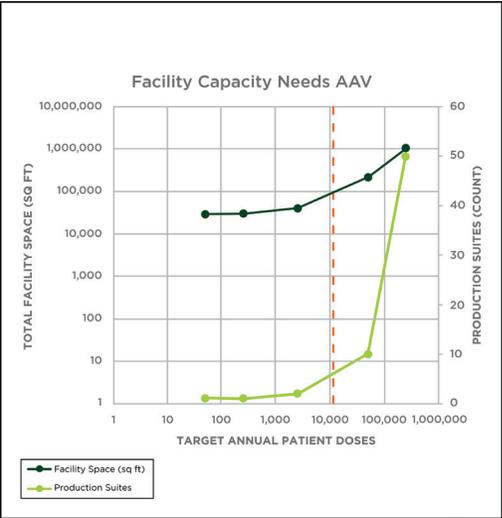


Figure 1. Facility capacity needs for AAV production targets: Total facility space considers cGMP spaces as well as supporting analytics, lab, office, and on-site warehouse and storage. The orange line represents the annual production capacity in a median CDMO facility of 55,000 sq ft.

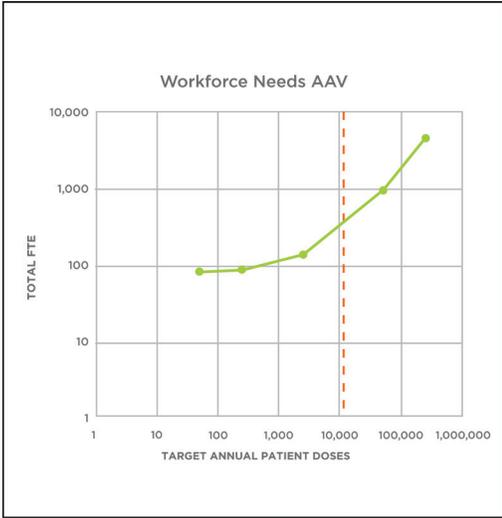


Figure 2. Related workforce needs for AAV production targets: Total workforce needs include all roles and levels needed to release product which includes manufacturing, quality control, quality analytics and environmental monitoring, supply chain, facilities, operations, MSAT, and supportive admin teams. The orange line represents the annual production capacity in a median CDMO facility of 55,000 sq ft.

Autologous CAR T case study

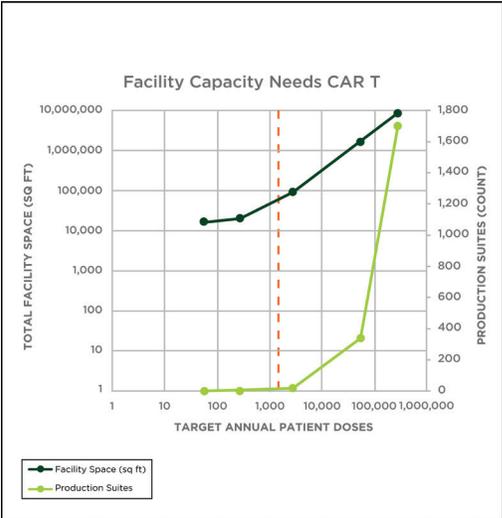


Figure 3. Facility capacity needs for CAR T production targets: Total facility space considers cGMP spaces as well as supporting analytics, lab, office, and on-site warehouse and storage. The orange line represents the annual production capacity in a median CDMO facility of 55,000 sq ft.

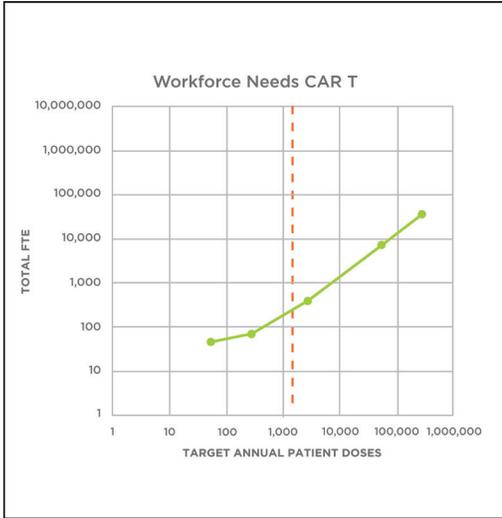


Figure 4. Related workforce needs for autologous CAR T: Total workforce needs include all roles and levels needed to release product which includes manufacturing, quality control, quality analytics and environmental monitoring, supply chain, facilities, operations, MSAT, and supportive admin teams. The orange line represents the annual production capacity in a median CDMO facility of 55,000 sq ft.

Pegasi white paper figures 5-7

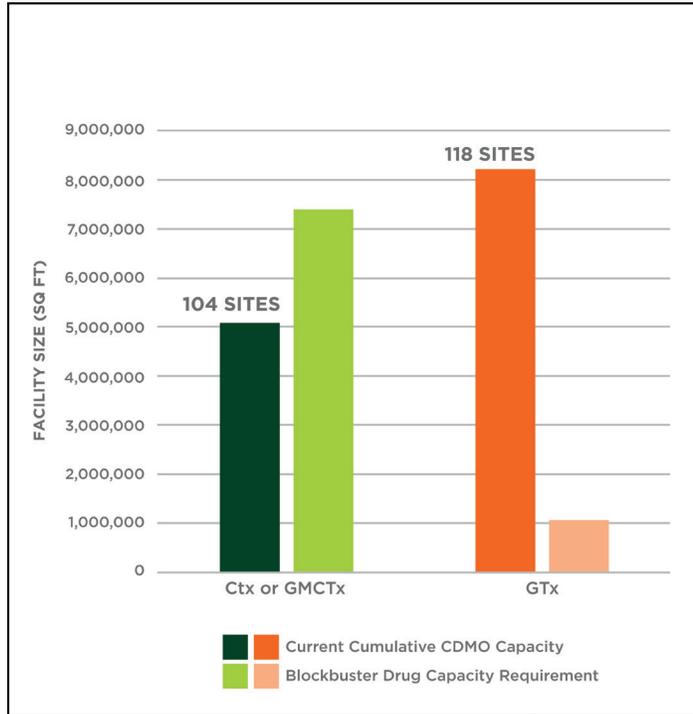


Figure 5. Total CGT CDMO capacity is insufficient to meet blockbuster need: Based on the capacity information from DHC’s global CDMO database, cumulative production capacity available for cell and gene-modified cell products are insufficient to support a single blockbuster product. While the cumulative production capacity for a blockbuster gene therapy appears adequate in scale, the median facility size for the 118 vector CDMO within our database is 55,000 sq ft, which would require this capacity to be heavily fragmented across over a dozen sites/ providers, and thus would be challenging to utilize at scale in a real-life scenario.

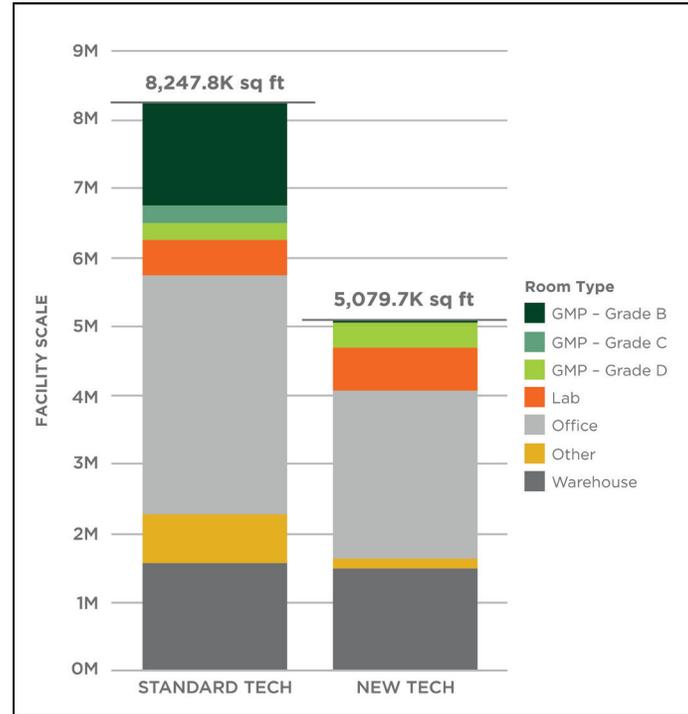


Figure 6. Impact of manufacturing automation introduction on capacity requirements: Utilizing end-to-end manufacturing technologies to implement process automation provides an opportunity to significantly reduce facility capacity requirements.

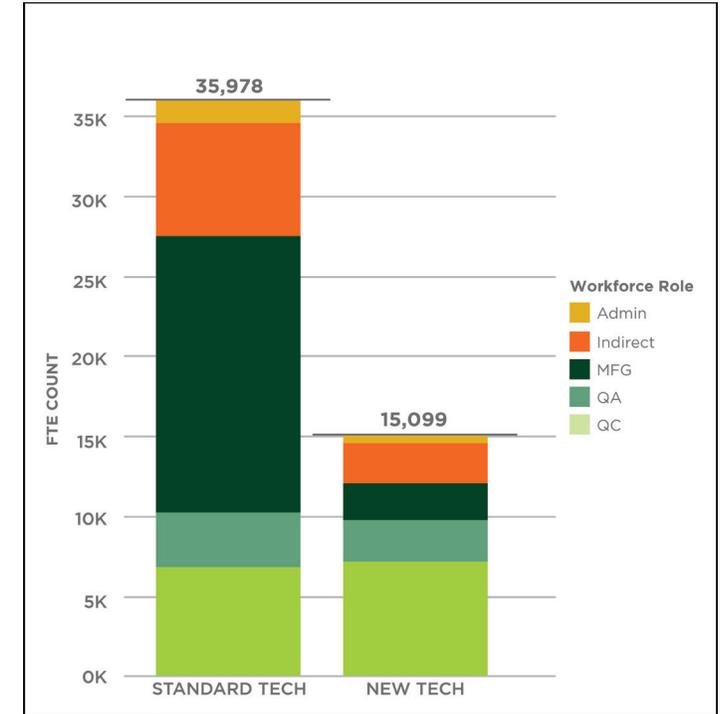


Figure 7. Impact of manufacturing automation introduction on workforce requirements: Methods to reduce facility cost and capacity needs also result in the reduction of workforce requirements. Process automation moves workforce needs away from operator intensive, manual manipulations toward a “set it and forget it” operational strategy where operators would only be required to initiate and terminate the batch production. Notably, as production becomes more automated, the workforce bottleneck shifts onto QC and highlights the need for analytics automation.

Select DHC Modeling Case Studies

DHC has a robust library of case studies available
to showcase relevant past projects

Pegasi: COGs and Facility Planning

CASE STUDY



The Ask

An international tools and technology company requested a market analysis of the gene-editing and advanced therapies space as well as a facility buildout plan to manufacture a critical component for gene therapy applications.

DHC Approach

- Conduct a landscape scan and voice of customer surveys to get a clear picture of the current market need and growth of the market over time.
- Identify and quantify the process equipment and infrastructure systems necessary to meet the production demands.
- Develop a sample facility map outlining production suites and supporting space including expected schedules for the multi-phase facility buildout, aligned with the estimated market growth and market penetration.
- Consider how a manufacturing effort of this size would reside within client's current infrastructure including full complement of labor (how many individuals with which skill sets would be necessary to begin and continue work on a site of this size) down to hazardous materials usage and waste disposal.
- After modeling the demand, infrastructure, and labor, DHC was able to analyze not only the COGs and anticipated revenue but also the sensitivity of the profit ranges in response to changes in any variable fluctuation.

The Impact

- First to consider the final materials was the relevant team in charge of implementation, to ensure an internal alignment of expectations across the responsible project managers and the corresponding in-house technical experts.
- The results also went to senior management to ensure that they had clarity on all decision points necessary to efficiently take the next steps in adding this opportunity to their range of business offerings.

Quantitative Modeling May Yield the Unexpected

CASE STUDY



The Ask

A client who was beginning enrollment for a clinical trial decided to request a quantitative review with a specific manufacturing focus to help isolate any unforeseen future issues. Client's preliminary internal review indicated a range of likely limitations that needed confirmation, including the possible need for more manufacturing capacity.

DHC Approach

- Develop detailed questionnaire help isolate input assumptions: materials costs, process duration and yield, clinical enrollment, and probabilities of success.
- Consider the overlap not only in manufacturing capacity (build vs. buy), COGs, and patient enrollment, but also timeframe ranges for each phase of development.
- After assisting the client in completing the DHC questionnaire, it became clear that the client did not have the set of problems that they expected.
- DHC adapted the expectations of the "ask" and provided a truncated and customized model that was based on the Client's precise situation.

The Impact

- Within a very short timeframe, the client received the answers to their questions and discovered a much quicker and easier fix than they had expected. In this case, the model demonstrated that there were significantly fewer changes required to their existing manufacturing strategy than were expected.
- The client was able to proceed with the trial with peace of mind knowing that not only were they prepared for this stage of clinical trials, but for future stages as well.

Market Analysis for a Manufacturing Reagent

CASE STUDY



The Ask

This client was considering acquisition of a company with a critical reagent used in the manufacture of viral vectors. To understand the market opportunity, DHC was asked to estimate current and future market sizes for this material as it pertained to its use in Adeno-Associated Virus (AAV) and Lentiviral Vector (LVV) manufacturing processes. This market size assessment was one piece of a broader diligence project conducted for this client.

DHC Approach

- **Align on critical assumptions:** Compile key assumptions, including: % of the viral vector markets using this reagent, common price points, and volume requirements of the reagent in standard manufacturing processes.
- **Clinical forecasting:** Leverage external databases to confirm the current number of relevant CGT programs in development using these vectors and forecasted forward for a 5-year period.
- **Patient population:** Estimate current and approximate future patients being treated and calculate the amount of vector required to treat that total expected patient population over time.
- **Market demand:** The total patient population and estimated vector required per patient and in total were used to calculate an estimate for total volume of reagent required to serve the market over the forecast period.
- **Market size:** Calculate the overall size of the market based on a range of estimated reagent volume requirements and price points over the forecast period.

The Impact

- In addition to providing comprehensive diligence support, DHC provided a detailed overview of market size for the reagent in question to build a better understanding of whether this potential opportunity aligned with the client's investment thesis.
- The analysis performed provided the necessary details—including a consideration of the magnitude of potential obtainable market share for this target—to allow the client to make a solid data-driven decision on future investments

Quantitative Modeling of Cell Therapy Mfg. Capacity

CASE STUDY



The Ask

Predicting manufacturing capacity needs for a pipeline of Cell & Gene Therapy products is an exercise with high stakes and enormous uncertainty. A large biotechnology company came to Dark Horse for assistance in identifying the manufacturing facility needs of its cell therapy product pipeline in the face of a wide range of development and commercial assumptions.

DHC Approach

- Gather key inputs from client via a customized questionnaire.
- Build a highly customized model using our proprietary in-house platform. Schedule check-in meetings weekly or biweekly to show interim data, and to alert the client to any places where the model requires more information or where there's conflicting guidance from within the organization.
- Deliver an Excel file and a presentation, complete with a dashboard that highlights major outcomes and walks users through the steps taken. This dashboard allows clients to update input parameters to keep the model current and customized throughout the process.
- The ability to model uncertainty is one of the elements that make Dark Horse's quantitative model offering different. We account for ranges so that you can make a plan and, critically, that plan changes with your real-time experiences because it allows for an adaptive approach. It's the difference between a 2D view of the range of outcomes...and a 4D one.

The Impact

- The client received a highly-customized, probability-weighted picture of the likely range of capacity needs and manufacturing costs for its cell therapy product pipeline, based on Monte Carlo modeling of a range of input assumptions.
- This hard data provided them with the ability to make rational choices in their facility design process, as well as to increase the accuracy of their financial forecasts.



DARK HORSE CONSULTING

darkhorseconsultinggroup.com / contactus@darkhorseconsultinggroup.com