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Predictive Oncology:

Unique, Valuable Assets and Recent Capitalization Present a Promising Opportunity in AI-Driven Drug Development

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Our Thesis

Price ($USD):	$1.18
Ticker (NASDAQ):	POAI
52 Week High/Low:	$2.30/$0.63
Market Cap (Millions):	$77.56
Enterprise Value (Millions):	$51.74
Sector:	Healthcare
Target Price (12 months):	$3.49
Risk:	High

Amidst the growing demand for use of artificial intelligence (AI) in drug development and precision medicine, Predictive Oncology (NASDAQ - POAI: $1.18) is well-positioned to leave its mark in the industry. The contract research services (CRO) industry is currently exhibiting a robust growth rate and is expected to continue to grow at an even faster pace in the future. With, the focus on using its unique assets to enhance the development of drugs for treating cancer with a focus on ovarian cancer, Predictive Oncology is targeting a large, competitive market that could greatly benefit from the increased efficiency, reduced risk, and reduction in costs that AI may offer. A unique database and physical asset of more than 150,000 patient tumor responses, 40,000 FFPE (formalin-fixed paraffin-embedded) blocks, and up to 15 years' worth of patient response data makes POAI stand out from its competitors when it comes to leveraging data in precision medicine. We believe that POAI could be significantly undervalued if it succeeds in securing large or multiple drug development contracts, ideally with big pharma.

Key Risks Overview

Predictive Oncology operates in an industry that is characterized by intense competition, high regulatory oversight, and rapid technological changes. These risks can majorly affect the business and can often lead to business failure. Predictive Oncology has not yet validated their plans by inking R&D collaboration deals with big pharma. The company currently has a somewhat substantial cash burn rate, and if it continues to burn cash without generating any significant revenues (ideally through business development), the company will need to raise additional capital in about three to four years, given the current burn rate.

Catalysts

Through its Helomics division, Predictive Oncology has recently made significant strides in its efforts to build AI-driven models of ovarian cancer by completing key data generation milestones in a retrospective study in collaboration with UPMC-Magee Women's Hospital, an affiliate of the University of Pittsburgh School of the Health Sciences, and completing the integration of Quantitative Medicine. This data will now be used to drive Predictive Oncology's AI models in ovarian cancer and their internal ovarian cancer drug repurposing project. **An oncology R&D contract signed with a large pharmaceutical company for use of Helomics' AI platform, PeDAL, is sought, and an announcement of such a contract, which could come from various large or medium-sized pharma companies, would likely send POAI shares higher. It is anticipated that Predictive's in-house program will help validate the PeDAL platform both to investors and pharma. Currently, further details on this program are pending.** Another subsidiary, Soluble Biotech, may be inking more contracts with pharmaceutical companies

for drug formulation or protein expression and stability. TumorGenesis, an additional subsidiary, is focused on the cancer cells from tumors and tumor heterogeneity, a key to understanding how drugs work and don't work in certain cancers. They combine AI, machine learning (ML), and tools to grow and study cancer cells and mixed populations containing cancer cells. Helomics is approaching answers to drug treatment from the patient's clinical history and treatment and TumorGenesis is approaching answers to drug treatment from the cancer cell to the patient. At some point in the future, both technologies will merge, providing patients, oncologists, and pathologists with better combination treatments.

Valuation

We used the sum-of-the-parts valuation method to ascertain the intrinsic value of POAI shares. For the company's research division, we have used a relative valuation methodology to estimate the value of its research business. For its devices division, we have used a discounted cash flow (DCF) approach to determine the net present value (NPV) of projected unlevered cash flows using a discount rate of 15.3%. We then combined these values to arrive at a firm-wide value. We then performed a sensitivity analysis and scenario analysis to ascertain its value for different scenarios. Performing the base case, bull case, and the bear case scenario valuation, and making informed estimates of expected value, **we arrived at a 12-month price target of $3.49**, indicating that POAI shares are undervalued.

Predictive Oncology:
Unique, Valuable Assets and Recent Capitalization Present a Promising Opportunity in AI-Driven Drug Development

Executive Summary

Predictive Oncology (NASDAQ: POAI) is a biotechnology company that operates various subsidiaries across medical subsectors but is primarily focused on the use of AI for drug discovery and development as well as other CRO services, precision medicine, and improving patient outcomes through its primary subsidiary, Helomics. Its other subsidiaries provide solutions for fluid and medical waste management, drug formulation, solubility, and endotoxin testing. It consists primarily of two divisions, i.e., research and devices/services, and operates through four subsidiaries, namely: Helomics, TumorGenesis, Soluble Biotech, and Skyline Medical.

1. **Growing demand for use of AI in drug discovery:** Historically, drug discovery has been carried out through traditional iterative approaches, but with the advancement of robotics and automation, artificial intelligence and machine learning, the paradigm for pharmaceutical R&D is changing. Advancement in technology is expected to help reduce lead times and costs associated with the discovery and testing of a drug candidate. According to Deloitte, a leading consulting firm, the artificial intelligence R&D market size has increased from $200 million in 2016 to more than $700 million in 2018 and is expected to reach $20 billion in the next five years by 2023, and of July 2019, consisted of 170 AI companies, 50 corporations, 400 investors and 35 major R&D centers.
2. **Contract research service is a multi-billion-dollar market:** Contract research organizations (CRO) are the companies that offer research-based services on a contract to many pharmaceutical and biotechnology companies, medical device companies, and various government research organizations. According to Fortune Business Insights, the contract research organization market stood at $38.4 billion as of 2018 and is projected to reach $91 billion by the end of 2026, exhibiting a CAGR of ~11.5% in the forecast period. Predictive Oncology appears to have a positional advantage in the CRO market because it may work in a space that is perhaps less saturated (drug discovery and preclinical) but can be scaled and have high value (oncology).
3. **Valuable data assets:** Helomics has a large database of more than 150,000 patient tumor samples (believed to be the largest in the world of its kind) and up to 15 years' worth of patient drug response data. The data contains information on more than 130 tumor types, 330 tumor subtypes, and 640 anatomic sites. This data is complemented with clinical and demographic information, various biomarkers, mutational profiles, and longitudinal response data, which makes Predictive Oncology's assets stand out from its competitors. This asset of Helomics' represents a significant competitive moat. Other direct competitors must make significant monetary investments to acquire patient tumor biopsies

and sequence their gene or analyze their secretome, etc. Additionally, the look-back patient response period that Helomics has developed over time because of its legacy business took time to develop; any competitor desiring to replicate this asset will have to do so over at least a decade as Helomics did or find some way to purchase it, and it is unclear whether data like this is available for purchase or acquisition. It is important to note that back in 2018, Roche (OTCMKTS: RHHBY) acquired Foundation Medicine for a total valuation of $5.3 billion; Foundation reported about 68,000 cases at the time in its molecular information database, which, as far as we know, only included genomic information.

4. **Aggressive and meaningful acquisitions potentially keep Predictive Oncology ahead of its competitors:** The range of specialized assets that is gathered in its arsenal has been obtained through mergers and acquisitions. Management has strategically acquired different companies complementing each other's business model, thus creating synergies. For example, Predictive Oncology acquired and recently finished integrating Quantitative Medicine (QM) in mid-2020 to pair its TumorSpace knowledge base and testing capabilities with QM's AI/machine learning platform, CoRE, to make efficient use of the TumorSpace to drive internally-operated drug discovery and also partnerships with other biopharmas in cancer drug development. The combination of CoRE and the TumorSpace is called PeDAL (Patient-Centric Drug Discovery using Active Learning). Few other AI companies in the pharma space have both the AI and physical/biological human tumor assets to pair together.
5. **Significant opportunities in drug repurposing:** Drug repurposing involves the investigation of existing drugs for new therapeutic purposes based on new insights. Predictive Oncology recently announced that it will start an in-house drug repurposing program, focusing on ovarian cancer. The company believes that its drug repurposing program could become a significant segment of its operations and value and can also demonstrate the value of the PeDAL platform and Helomics' knowledge base for further collaborations.
6. **Experienced Management:** Predictive Oncology has a management team with years of experience working in the pharmaceutical and biotechnology industry, which is crucial for the company's long-term goal of becoming a leader in precision medicine.

Aforesaid, we believe that Predictive Oncology is poised for rapid growth. The data and tumor assets it possesses could drive significant value for potential drug development and CRO-based collaborations and contracts with major pharmaceutical companies. Given the potential of CROs and the nature of big contracts, we believe that POAI shares could be significantly undervalued if the company succeeds in securing large or multiple drug development contracts. However, if the assets fail to impress potential partners and if Helomics tests do not significantly offset the operating expenses of Helomics, Predictive Oncology may continue to be cash-flow negative.

We are initiating coverage on POAI with a price target of $3.49 per share, achievable in 12 months, using a sum-of-the-parts valuation as our preferred methodology for valuing the stock. It incorporates a long-term view of the company's operation. This model is highly dependent upon the contracts it inks with potential partners and will be adjusted accordingly based upon future contracts.

Company Profile

Predictive Oncology is focused on the use of data and artificial intelligence to develop personalized cancer therapies that can lead to more effective and patient-oriented treatments. It is specially focused on developing methods to improve drug discovery for the treatment of ovarian cancer, as ovarian cancer and its increasing

incidence is a growing concern worldwide with patients generally receiving poor prognosis compared to other cancers (~50% versus ~70% five year survival). Predictive Oncology was a fluid medical waste disposal systems manufacturer selling its proprietary STREAMWAY System, and over the last few years, a range of specialized assets in predictive oncology has been assembled through recent mergers and acquisitions. Skyline was the lone company, and it produced the STREAMWAY System. After the acquisition of Helomics, management completed a forward triangular merger into Precision Therapeutics, which was subsequently renamed Predictive Oncology. Predictive Oncology currently operates through its four subsidiaries: Helomics, Skyline Medical, Soluble Biotech, and TumorGenesis, each of which will be discussed in subsequent sections of this report.

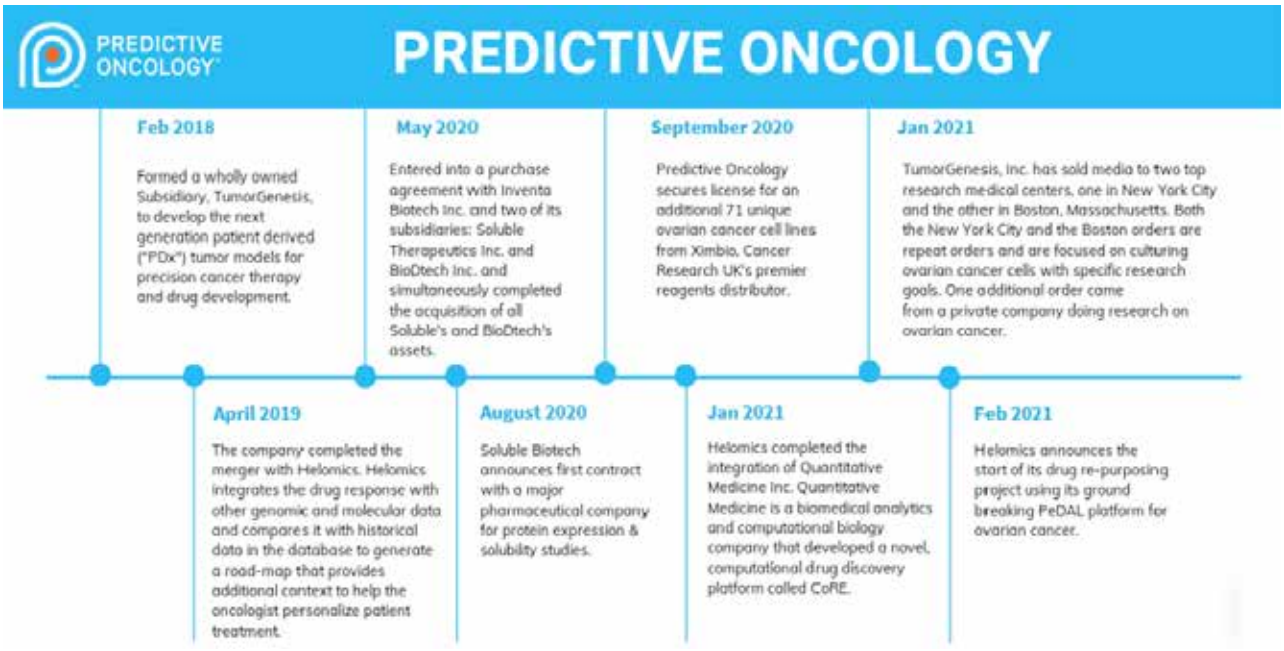


Exhibit: Evolution of the company from a medical device manufacturer to an AI-driven R&D company
Source: company reports, Quantum Research

Through these subsidiaries, Predictive's portfolio of key physical/digital assets includes the following:

- A database of clinically validated historical and outcome data from patient tumors.
- An in-house clinical laboratory improvement amendments (CLIA)-certified lab.
- A "smart" patient-derived tumor profiling platform.
- An in-house bioinformatics artificial intelligence (AI) platform.
- A new computerized approach to growing tumors in the lab to rapidly develop patient-specific treatment options.
- An FDA-approved medical fluid collection and disposal system company.
- Another separate lab including technology for optimizing drug formulations.
- Patent rights for all the relevant technologies listed above and also on specialty media for culturing patient-derived tumors.

Business Model

For purposes of valuing the company, we view Predictive Oncology as operating in two separate ways: an R&D division which comprises Helomics and TumorGenesis, and a product division which includes Skyline Medical which markets and sells fluid disposal systems and their respective disposals for hospital operating rooms, and Soluble Biotech which markets and sells solubility kits and services for rapid, low-cost drug formulation solutions.

Through R&D, it is focused on:

1. The use of data and artificial intelligence (AI) to develop personalized cancer therapies that can lead to more effective and patient-oriented treatments (through Helomics).
2. The use of artificial intelligence and machine learning to provide predictive models of tumor drug response to improve clinical outcomes for patients and to assist pharmaceutical and biotech companies in the development of personalized drugs and diagnostics (through Helomics).
3. Contract service and research focused on solubility improvements, stability studies, and protein production (through Soluble Biotech).

   Monetization Method: The company provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis. While the company has recently readied its AI platform for pharmaceutical R&D, we don't have any revenue guidance from the company. However, we believe that, given the data assets that Helomics possesses, the company is positioned to enter into multi-target, multi-compound R&D contracts with notable pharma companies.

Through selling products,

1. Predictive Oncology is focused on the manufacture and sale of an FDA-approved STREAMWAY system for automated, direct-to-drain medical fluid disposal and associated products (through Skyline Medical).
2. The STREAMWAY system caters to both domestic and international markets and currently drives most of the company's revenues.
3. The company also sells drug solubility kits through its Soluble Biotech subsidiary; although it constitutes an incredibly low share, it is a very high margin business.
4. Helomics will continue to provide clinical testing to oncologists to help them make informed decisions for their cancer patients' therapies.
5. TumorGenesis has introduced its novel line of cancer cell media, used for difficult to grow ovarian, breast, and leukemia cells in culture. In addition, they are adding novel test kits for cancer researchers around the world, including a biomarker discovery kit and new nano spun matrices that can be designed and decorated with biomarkers that help cancer cells grow.

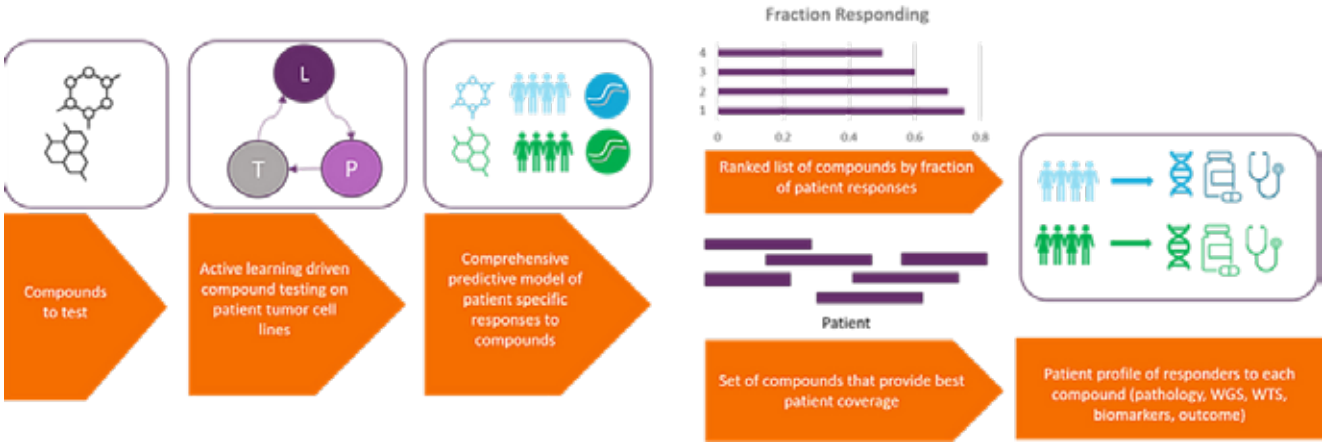
   Monetization Method: The company's Skyline Medical division sells its STREAMWAY system in a B2B setup using partners and medical representatives. Hospitals are the biggest customers of the STREAMWAY system. The company has developed some innovative and technological advancements in waste fluids management systems in the last 2 years. Although there are many competitors in the market, management's increased focus on technological advancement in waste fluids management systems can make it better positioned in the playing field, potentially helping it capture greater revenue

and market share. Helomics, on the other hand, will continue to sell tumor profiling tests to physicians as its legacy business, which allows physicians to individualize treatment of gynecological cancer patients with existing therapies.

Helomics: The Primary Value Driver

Predictive Oncology, through Helomics, is positioning to become a leader in precision medicine. Its historic/legacy business, the unique functional tumor profiling platform, determines how a specific tumor type responds to a drug. The tumor profile is then compared to the knowledge base. Genomic biomarker testing and tumor profiling guide the oncologist in personalizing the patient's treatment by helping them determine which therapy will have the greatest effect and the best tolerability. The tumor drug response testing (TDRT), formerly known as ChemoFx, has been associated with a 49% improvement in progression-free survival and a 14-month improvement in overall survival when patients receive a sensitive therapy. Patients treated with a sensitive agent identified by ChemoFx live 2.5x longer than patients treated with a resistant agent. As a result of running the TDRT platform and genomic profiling for several years, Helomics has amassed ***the world's largest patient tumor drug response and genomic knowledge base***, which consists of at least 150,000 clinical cases covering at least 137 tumor types in the unique, clinically validated, PDx (patient-derived xenograft) platform.

Helomics continues to offer clinical testing as well as offer contract research services that use the CoRE/PeDAL AI technology, since its acquisition and integration (completed as of January 2021) of Quantitative Medicine (QM). Helomics and QM have developed a unique technology called Patient-Centric Drug Discovery using Active Learning (PeDAL) that combines their ***1a)*** clinically validated primary tumor cell assay, named TruTumor, and the ***1b)*** 10-year drug response data, which have been obtained after testing over 150,000 tumors, called TumorSpace, together with ***2)*** their proprietary CoRE AI. This combination of robust data and active machine learning enables Helomics to predict what tests to run, in an iterative fashion. Predictions (made using over 200 million historical discovery data points) can include types of patients (exclusion and inclusion criteria, biomarkers, etc.) or recommending actual compounds that may be promising. This enables the company to much more rapidly and cost-effectively gather the most useful data that can further drive clinical development, which can result in a drastic decrease in time and cost of clinical development. Depending on the application, size and scope of a project, and the performance of PeDAL, this approach could save Helomics, or companies contracted with Helomics, tens or hundreds of millions of dollars in the drug development process. Their offering includes services ranging from understanding the basic biology of the new chemical entity to lead optimization that is before the 1st phase of clinical trials.



Source: Helomics Website

To understand the importance and future of AI in pharmaceutical R&D, we must first frame the problems that are mounting for pharma's R&D programs and pipeline assets.

Current Challenges in Drug Discovery

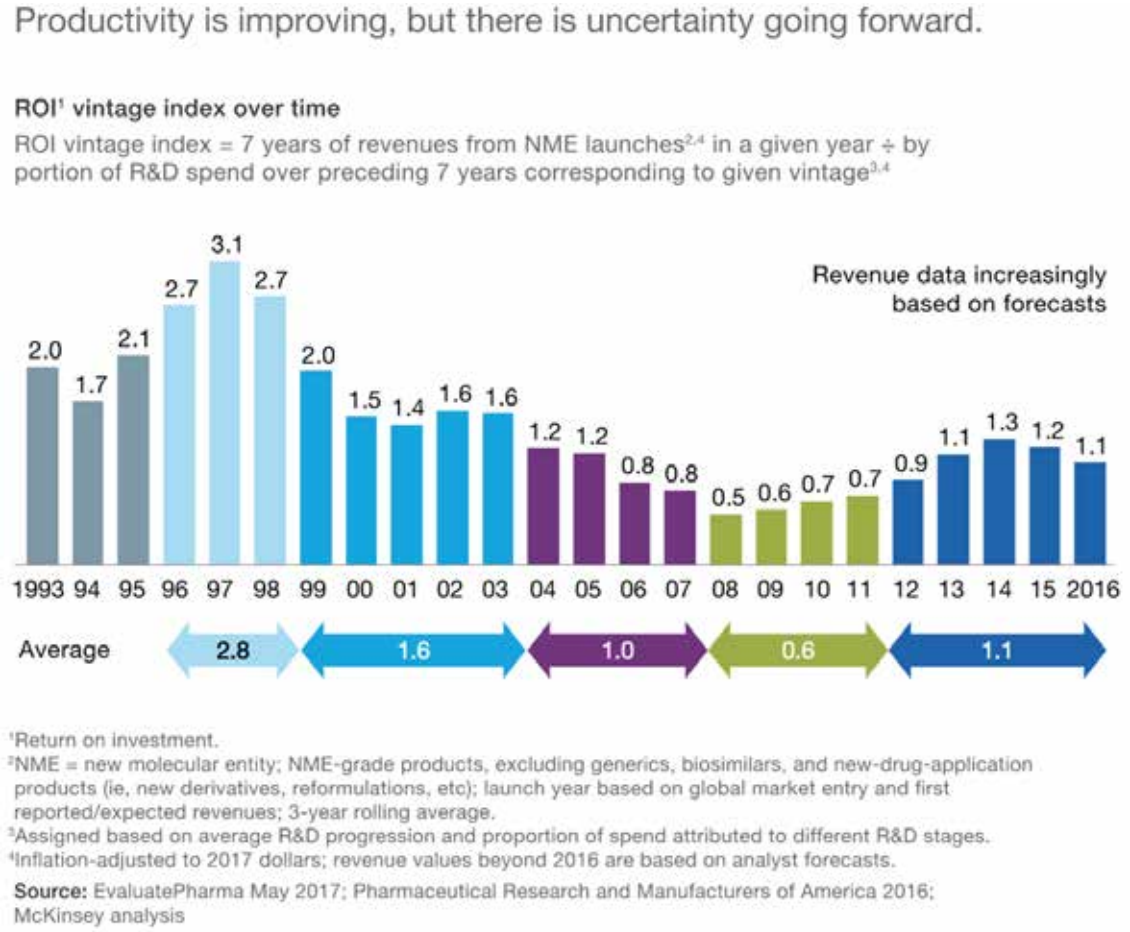
The pharmaceutical industry has provided society with life-saving and life-changing drugs that involve colossal upfront investment in research and development. This process typically takes more than a decade and results in many failed product candidates as drugs either fail to prove efficacy or safety through preclinical and clinical research, as well as regulatory scrutiny. According to Deloitte, the average cost of drug discovery and development has nearly doubled from $1.188 billion to $2.168 billion, per successfully launched drug, from 2010 through 2018.

Figure 6. Average R&D cost to develop a compound from discovery to launch, 2010-19 – original and extension cohorts

Source: Deloitte Centre for Health Solutions. 2019. "Ten Years on Measuring the Return from Pharmaceutical Innovation 2019."

On average, about one-third of this two billion dollars is invested during the drug discovery phase, which is almost $600-$700 million per successful launch. Even after spending more than half a billion dollars, the chance of a compound entering phase 1 of the trial, according to various sources, tends to be close to 10%. On the other hand, according to Deloitte, the average forecast peak sales have decreased to $407 million in 2018, which is less than half of the 2008 average forecast of $816 million. This has led to a steady decrease in the IRR for late-stage pipeline candidates from 10.1% in 2010 to 1.8% in 2018.

The graph below indicates the seven-year average revenue from NME launches divided by the portion of R&D spend over the preceding seven years. According to McKinsey, productivity of the new launches peaked in the year 1997 at 3.1% and has been in the down trend since. It is clear that a variety of sources and data show that ROIs are waning for pharma R&D, on average. What can improve this metric is improvements in R&D efficiency, cost, and time through AI.



Source: Digital in R&D: The $100 billion opportunity. *McKinsey & Company, 2017*

One factor affecting ROI is the failure of drug candidates to live up to their expectations as consecutive tests are carried out. Even after a drug is discovered, tested in preclinical (nonhuman) trials, and is then moved to a clinical trial where it is tested on humans, it doesn't necessarily mean the drug would work as expected on humans; efficacy or safety often do not live up to expectations. For instance, one notable example was a drug designed to treat leukemia, where the drug TGN1412 was tested in monkeys and was well tolerated. Unfortunately, when just 1/500th of a dose was given to six healthy young men in the first phase of clinical trials in 2006, they immediately developed fever, vomiting, and diarrhea. Within hours, they were in an intensive care unit with multiple organ

failures. Drug R&D is a long and expensive process filled with unexpected failures. The table below shows the problem very clearly. For new drug development within the 10 deadliest cancers, the FDA approval rate is an abysmal 7.8%, and with the estimated costs of each over $2.4B, inefficiency and waste in the system created by drug failures is massive, so the field is ripe for the help of AI.

Oncology Drugs- Winners & Losers*

Cancer	Failed	Approved	Total	Percent +	Percent -
Malignant Melanoma	158	12	170	7.1%	-92.9%
Brain Cancer	122	3	125	2.4%	-97.6%
Acute Myeloid Leukemia	91	7	98	7.1%	-92.9%
Kidney Cancer	96	11	107	10.3%	-89.7%
Liver Cancer	73	5	78	6.4%	-93.6%
Lung Cancer (all)	268	32	300	10.7%	-89.3%
Small-Cell Lung Cancer	51	4	55	7.3%	-92.7%
Pancreatic Cancer	131	7	138	5.1%	-94.9%
Ovarian Cancer	139	13	152	8.6%	-91.4%
Prostate Cancer	237	21	258	8.1%	-91.9%
Totals	**1,366**	**115**	**1,481**	**7.8%**	**-92.2%**

* Reported by PhRMA in 2020https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRma_Cancer_Research_7142020.pdf

The 10 Deadly Cancers*

New Cases	Deaths	Percent +	Percent -
324,635	57,043	82.4%	-17.6%
308,102	251,329	18.4%	-81.6%
474,519	311,594	34.3%	-65.7%
431,288	179,368	58.4%	-41.6%
905,677	830,000	8.4%	-91.6%
2,210,000	1,800,000	18.6%	-81.4%
331,500	270,000	18.6%	-81.4%
495,773	466,003	6.0%	-94.0%
313,959	207,252	34.0%	-66.0%
1,410,000	375,304	73.4%	-26.6%
7,205,453	**4,747,893**	**34.1%**	**-65.9%**

**Global Cancer Observatory: WHO Cancer Statistics- https://gco.iarc.fr/

Helomics: Artificial Intelligence in Pharmaceutical R&D

Not only can Helomics' PeDAL platform be used to run preclinical tests to help translate preclinical to clinical research, but also it can be used to aid in the discovery process for new compounds. The difficulty in finding new drugs and targets lies in the high number of variables by which biological systems interact. One target may affect multiple downstream targets, and those targets may interact with an exponentially increasing number of secondary targets, eventually even affecting upstream pathways to the original target or affecting unintended pathways. Current approaches rely on prior knowledge of biological signaling pathways and investigator/scientist intuition and are prone to errors associated with intuition and prior knowledge only.

The "experimental space" for drug discovery is extremely complex. Given a hypothetical multivariate analysis of understanding the effects of different drugs affecting different targets in different cells, it was estimated that the entire experimental space would take about 10 billion plates for analysis (hundreds of wells on each plate), which would of course take thousands of years to analyze. Adding variables such as drug dose, which can be critical since many drugs may have hormetic dose responses, as well as drug combinations or cell combinations, may increase the difficulty of analysis. Thus, the practical solution is to use guided iterative solutions.

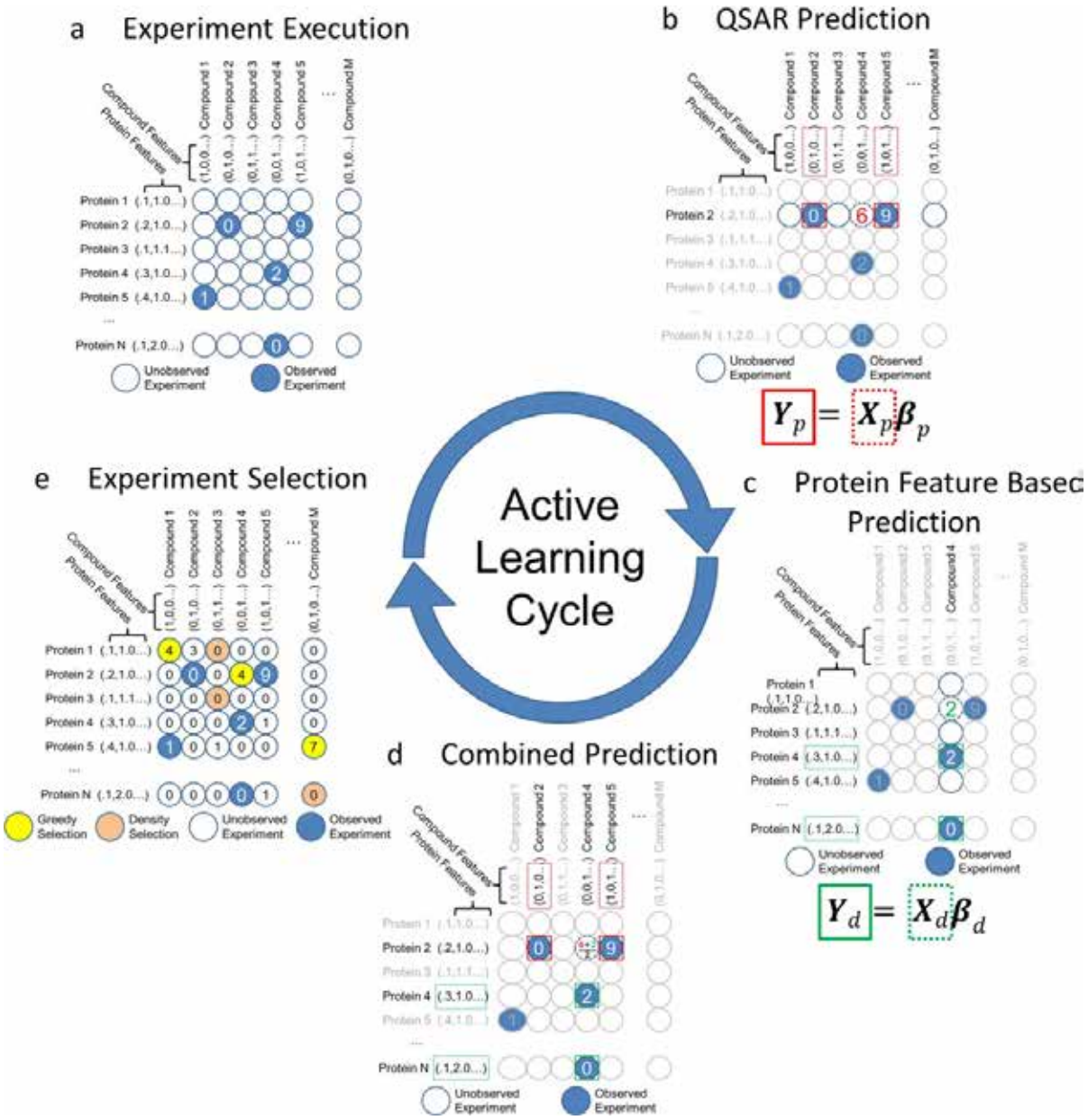
According to a 2011 paper penned by QM/Predictive Oncology's Dr. Murphy:

> *"At a fundamental level, the central problem of screening for potential drugs is the dimensionality of the experimental space within which screening takes place. As highlighted in Fig. 2, the number of experiments required to directly screen for compounds that affect one target while not affecting others can quickly become intractable.*

> ***The only practical solution is to carry out a subset of the possible experiments.*** *Current approaches in drug development require scientists to choose a path through experimental space guided by existing knowledge (e.g., signaling pathways), investigator insight and intuition. This process is often hindered by incomplete or incorrect pathway information and the* ***difficulty of making predictions about complex pathway interactions.*** *An alternative described here involves the use of active machine-learning methods to build statistical models of the entire space and iteratively choose experiments that are expected to best improve the model.* ***The major strength of this approach is that experiment choice is guided on a purely empirical basis and in full consideration of the potential complexity of the system.*** *Active learning is well established in some domains, and it has been applied in a few cases to biological problems."*

A subsequent CMU paper, published in 2014, Kangas, Naik, and Murphy describes the iterative approach that formed the foundation of Predictive Oncology's CoRE/PeDAL platform as follows:

> *"Active learning consists of three phases performed in a loop (as illustrated for the work described here in Figure 1). A campaign of experiments can be initialized either using prior results from literature or databases or by randomly selecting a batch of experiments from an experimental space.*
> ***(1)*** *A model is generated to represent the currently available data.*
> ***(2)*** *From that model, experiments are selected for execution that are expected to improve the model.*
> ***(3)*** *The set of experiments is executed and the resulting data are combined with previously collected experimental data. The loop then continues from Step 1 until either a desired accuracy of predictions is achieved or a specified budget has been exhausted. There have been limited previous applications of active learning to the drug discovery process. In these efforts, compound activity was considered to be binary (active or inactive) and effort was focused on only a single target [22, 23]."*



From: Kangas, J. D. (2014). Efficient discovery of responses of proteins to compounds using active learning. *BMC Bioinformatics, 15(1), 143.*

"An active learning pipeline for an experimental space with N proteins and M compounds. (a) *A round of active learning begins with the data for all of the experiments that have been observed so far.* ***(b)*** *A separate model is constructed for each protein using the compound features to make predictions for the effect of each compound on the activity of that protein. This is illustrated for Protein 2 for which regression using the observed experiments for Compounds 2 and 5 predicts that Compound 4 would show an activity of 6. This model is referred to as CFO [analogous to QSAR, which checks for the presence or absence of specific structural elements in the drug compound, to predict interactions between endogenous proteins and drugs].* ***(c)*** *A separate model [molecular docking model] is constructed for each compound using the protein features to make predictions for the effect of that compound on the activity of each protein [which requires info on both the protein target and the drug]. This is illustrated for Compound 4 for which regression using the observed experiments for Proteins 4 and N*

> *predicts that Protein 2 would show an activity of 2. This model is referred to as PFO.* ***(d)*** *For the CCT approach, if predictions from both methods are available, they are averaged. (In the early rounds when no experiments may have been observed for a given protein or compound, predictions from both models may not be possible).* ***(e)*** *The complete set of observations and predictions is shown, and experiments that would be chosen for the next round of acquisition by different methods are shown (greedy selection would pick the experiments with the highest predicted values, while density selection would pick experiments for compounds and proteins that are most different from those previously selected). The results for the chosen experiments will be added to those observed so far to begin the next round of active learning."*

So basically, the researchers created two separate models, one using compound features only (CFO), and one using protein features only (PFO), then averaging the two for selection of experiments. Moving forward with the experiments targeting information where experimental success is most likely or where the most unknown information can be gained enables Predictive Oncology to generate the most amount of *useful* data while *minimizing* the amount of experimentation (time and money) required to obtain that information:

> ***"The most important difference of the work described here from previous approaches is our emphasis on active machine learning to simultaneously model the effects of many compounds on many targets.*** *To demonstrate the utility of active learning for drug discovery in the context of multi-target modeling, we combined two modeling approaches to make predictions about activities for large numbers of combinations of compounds and targets. Our model uses features developed for virtual screening to describe compounds, and features from sequence analysis to describe target proteins. As a part of this effort,* ***we did not endeavor to make the most accurate predictive model possible. Rather, we investigated the utility of applying active learning in combination with predictive models in order to efficiently discover active compound-target pairs.*** *In tests using data from the PubChem database,* ***we found that active compound-target pairs could be discovered as much as twenty-four times faster using active learning than by random selection of experiments. The algorithms we describe are also computationally efficient, making application to very large experimental spaces practical."***

The company's contract research business applies this approach, now called PeDAL, to address a range of needs from discovery through clinical and translational research, to clinical trials and diagnostic development and validation as noted below:

- Research
  - a. Biomarker discovery
  - b. Drug discovery
  - c. Drug repurposing

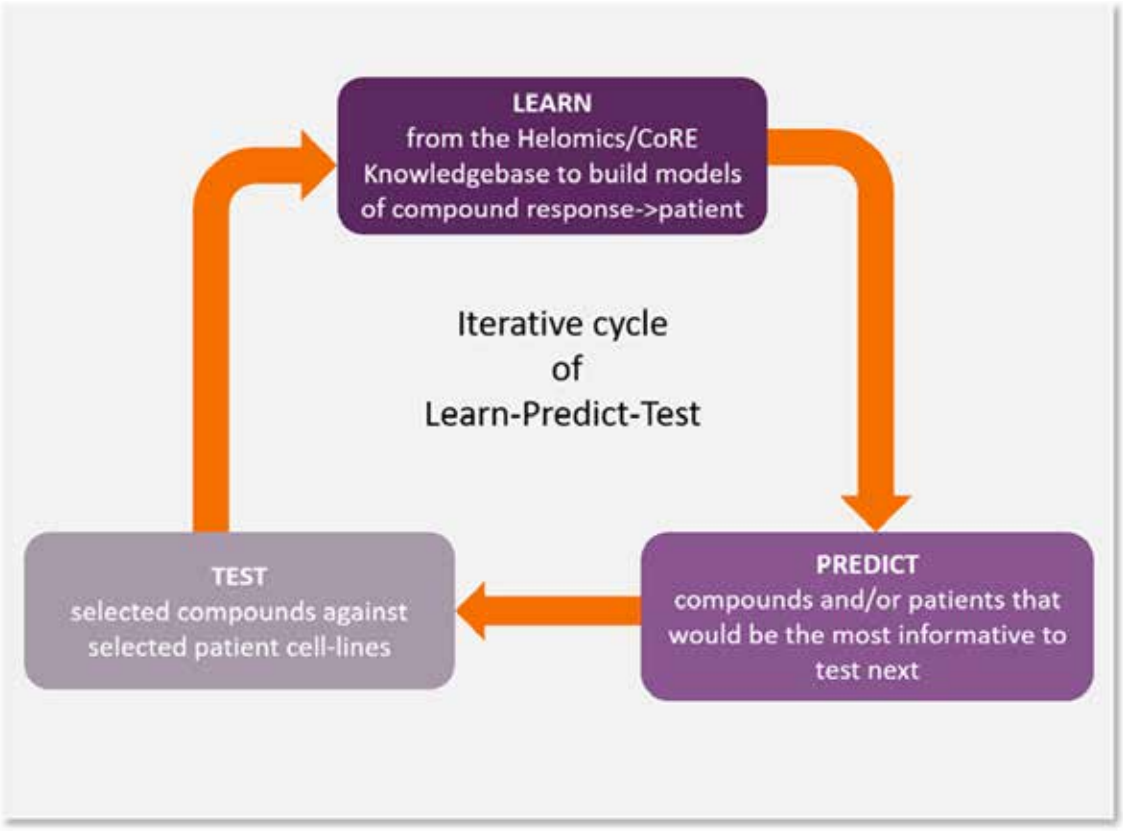
- Development
  - a. Patient enrichment & selection for trials
  - b. Clinical trial optimization
  - c. Adaptive trials

- Clinical Decision Support
  a. Patient stratification
  b. Treatment selection

The company's computational research engine (CoRE AI) is an extensive in-silico platform that employs a polypharmacological/pharmacogenomic approach that builds a large set of predictive models and selects the optimal pair of data and algorithms using extensive machine learning methodology. Predictive Oncology acquired Quantitative Medicine which was a spin-out of Carnegie Mellon University that had developed the adaptive learning platform, CoRE AI. Predictive Oncology has completed various case studies wherein it has demonstrated that:

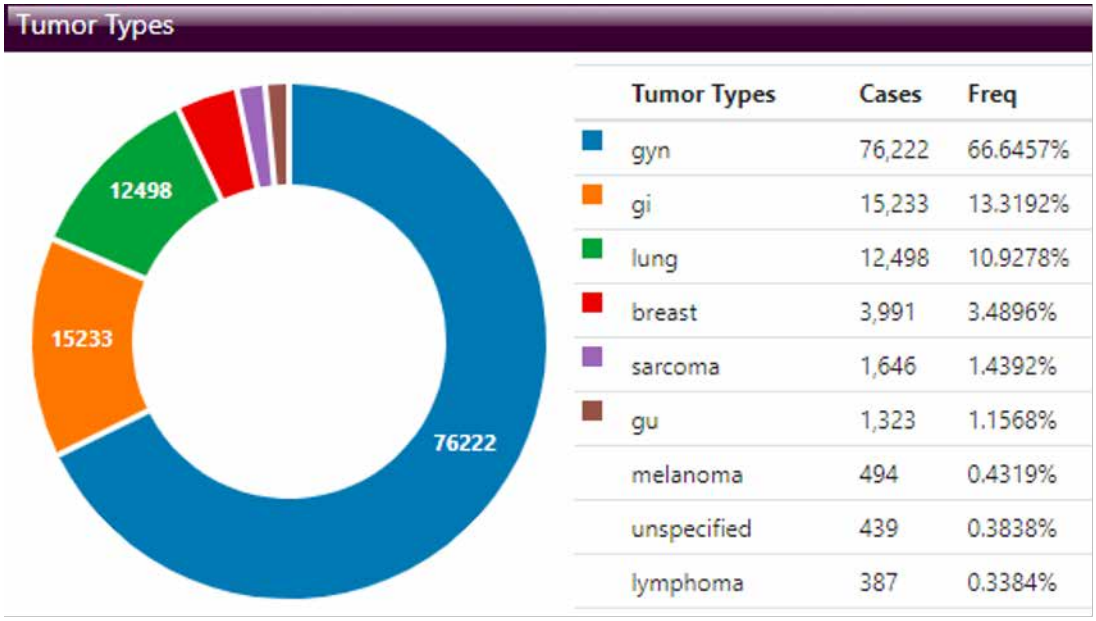
1. CoRE has successfully reduced compound synthesis required to discover promising drug leads, as well as
2. reduced experimentation cost to develop accurate predictive models compared to industry-standard approach, and finally,
3. reduced experimentation by using historical experimental results.

In addition to data within TumorSpace, Helomics has a large bank of FFPE (formalin-fixed paraffin-embedded) blocks—its preserved tumors (~40,000)—that under appropriate circumstances can be used for further data generation, such as the whole genome, whole exome, and whole transcriptome sequencing, as well as immunohistochemistry (IHC/H&E—of which Helomics/TumorGenesis have access to about 100,000 slides), and imaging. So, depending on the application, CoRE can be used in different ways to save time and money, obtain more accurate models, or both.



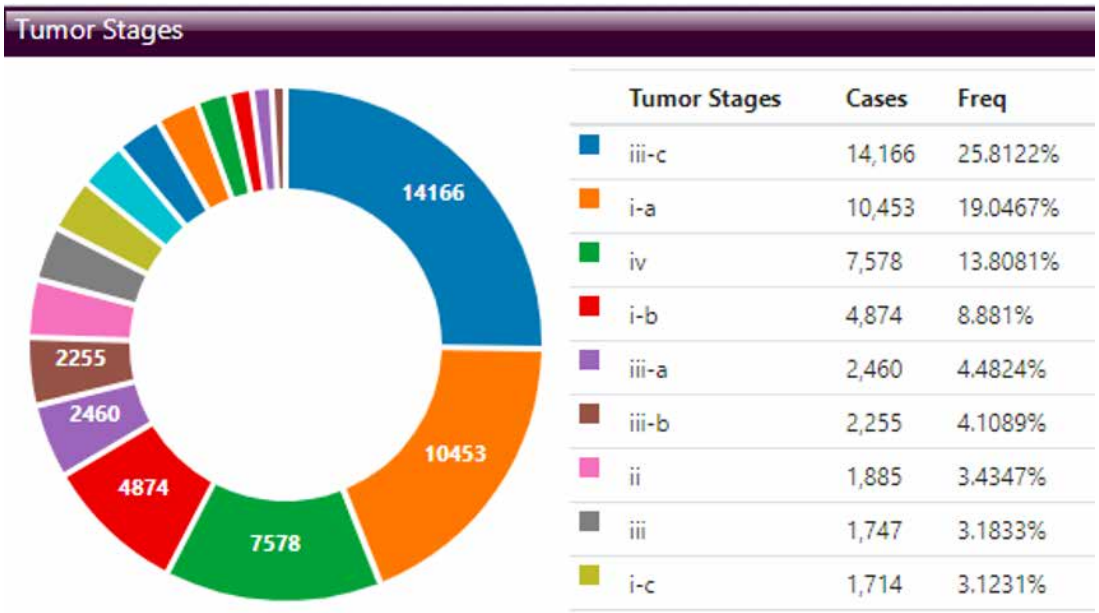
From: Helomics Website

Helomics recently announced that it will begin a drug repurposing program focusing on ovarian cancer using its AI-driven PeDAL approach. Under the program, the company would profile panels of existing drugs against numerous patient-derived cell lines. There are over 300 non-cancer drugs that have shown some published evidence of anti-cancer effect, and these drugs might possibly be new candidates for new cancer therapeutics. Helomics' in-house program will help create clinical validation of the PeDAL approach.



Tumor Types	Cases	Freq
gyn	76,222	66.6457%
gi	15,233	13.3192%
lung	12,498	10.9278%
breast	3,991	3.4896%
sarcoma	1,646	1.4392%
gu	1,323	1.1568%
melanoma	494	0.4319%
unspecified	439	0.3838%
lymphoma	387	0.3384%

From: Helomics Website

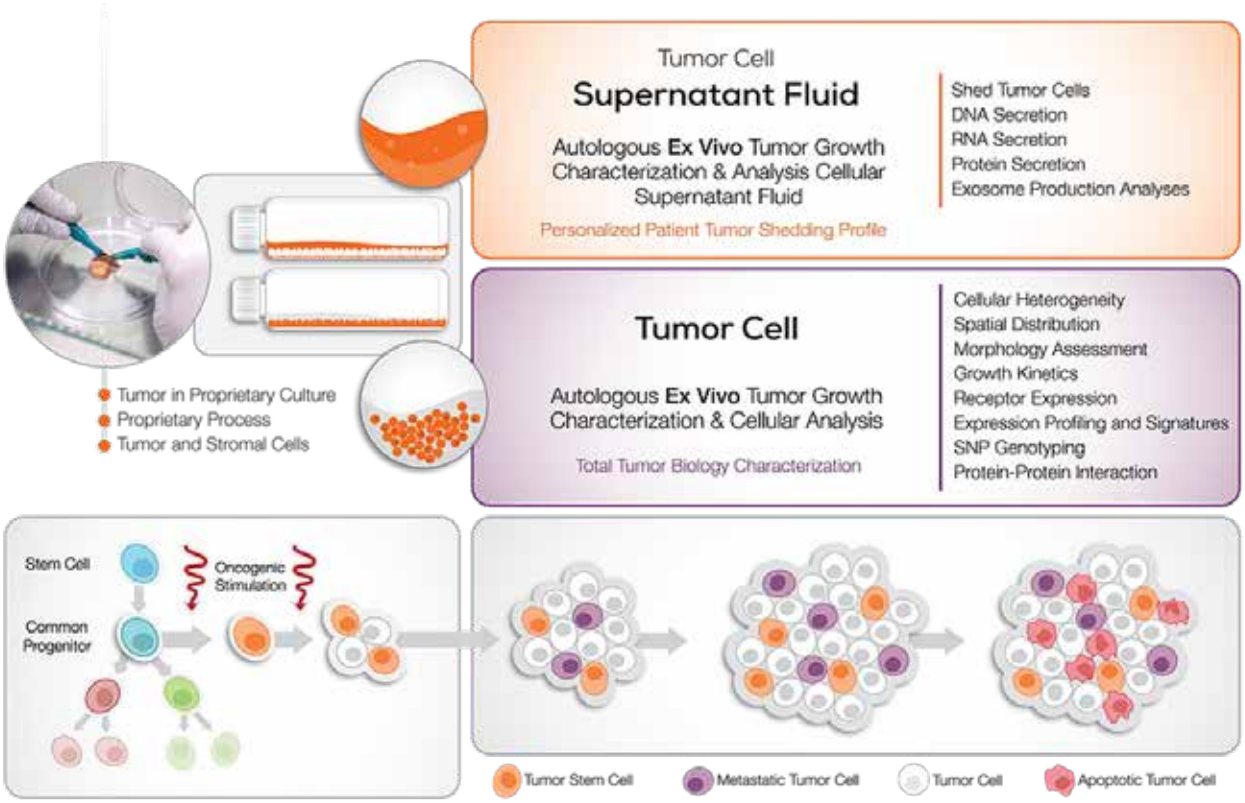


Tumor Stages	Cases	Freq
iii-c	14,166	25.8122%
i-a	10,453	19.0467%
iv	7,578	13.8081%
i-b	4,874	8.881%
iii-a	2,460	4.4824%
iii-b	2,255	4.1089%
ii	1,885	3.4347%
iii	1,747	3.1833%
i-c	1,714	3.1231%

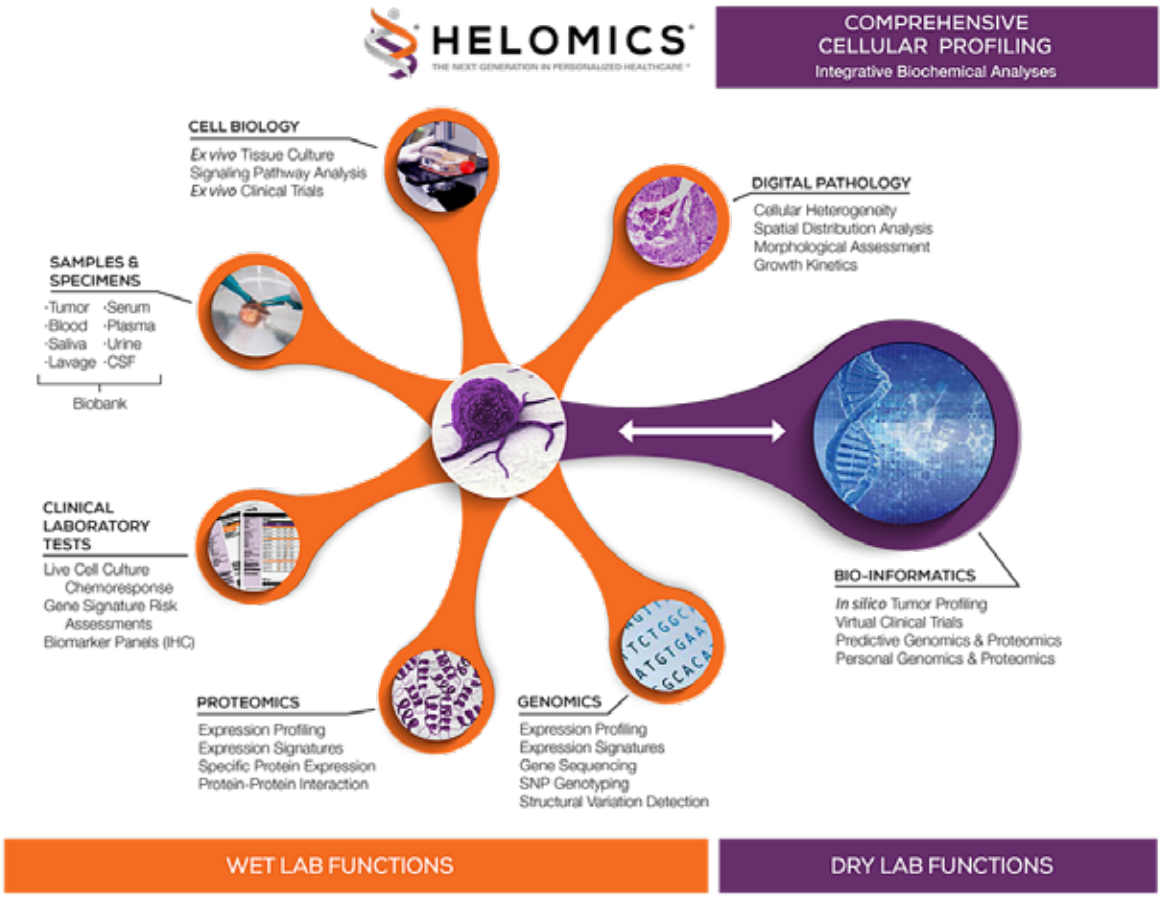
From: Helomics Website

Helomics has developed a significant amount of detailed patient tumor data in the oncology segment, primarily concentrating on gynecological (GYN) tumors. It has created an exhaustive database which, when combined with their proprietary CoRE AI, could be leveraged to work with various pharma companies, helping them reduce their development cost and time while improving accuracy and predictability. This is somewhat similar to how Predictive Oncology is starting up its own drug repurposing program. The company aims to close certain pilot studies with these partners in 2021. We believe that the robust, large amount of data obtained and developed by Helomics will help the company in landing contracts with pharma as research partners.

It is important to note that Helomics, as opposed to various competitors, uses a testing approach using live tumor cells. This approach allows them to monitor many more points of data that are relevant to clinical responses, as shown below.



From: Helomics Website



From: Helomics Website

TumorGenesis: Complementing Growth

In addition to historical data for many oncology patients as well as a bank of patients' tumors and their characterization (cell type and genetics, shedding profile—proteins, exomes, cells, and nucleic acids), Predictive Oncology has a subsidiary, TumorGenesis, that has developed proprietary cell culture media which allows the company to develop and retain cell lines that mimic human tumors *much* more than industry-standard immortalized cell lines. Human tumors are challenging to grow in a cell culture flask, and even if they are grown, a typical immortalized cell line culture does not imitate the original tumor because these cells tend to be chromosomally unstable, and unnatural selective pressures in simplistic experimental environments causes the cells to drift rapidly in terms of genetic and phenotypic (trait) characteristics. TumorGenesis has developed a technology that helps preserve the patient's derived cancer tissue's biological signature and allows researchers to study cancer in preclinical models that should mimic real tumors much more closely. This ideally translates to scientific findings, translating more accurately into the clinic. The objective is to create better models for culturing and screening patient-derived cell lines (PDCL), which will help with scientific advances at the preclinical level as well as higher clinical success rates. Just how useful are the PDCLs? According to TumorGenesis,

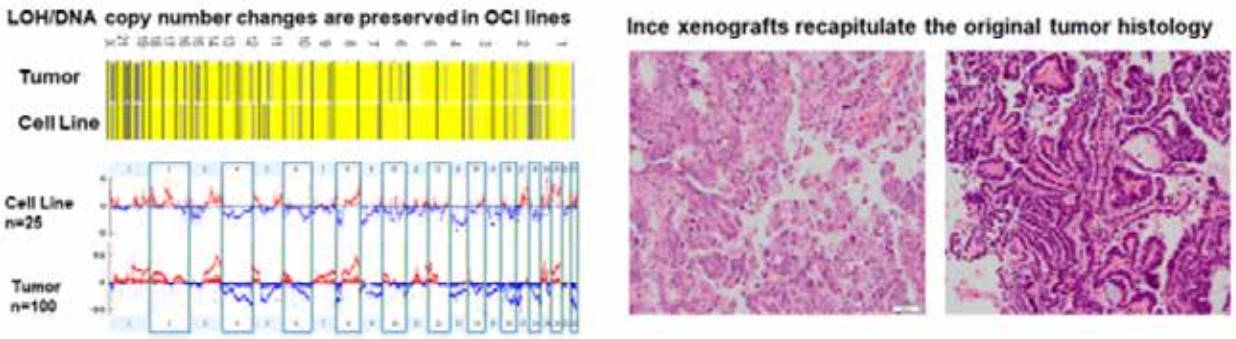
"It is remarkable that the UK cancer researchers using the same media mixes now being offered by TumorGenesis for researchers around the world, independently isolated, and identified another unique set of ovarian cancer cells from patients. Adding these 71 cell lines to our existing 25 cell lines (11 of the first 25 are representative of about 95% of ovarian tumors) adds a powerful new resource for researchers. The media used to grow the novel and unique ovarian cancer cell lines, licensed by Predictive Oncology and its partner, GLG Pharma, is able to retain 95%+ of the cell's DNA and RNA as well as crucial proteomic signatures [and generally differ significantly from standard cell lines]. Our media will be used for the isolating and growing of ovarian cancer cells, which are often found in the 'ascites' fluid located in the abdomen of women with advanced ovarian cancer. Ovarian cells cultured from these ascites fluids are notoriously difficult to work with and when using standard media mixes are often prone to failure. In addition, these cell lines, generally speaking, are not representative of the patient's unique ovarian cancer.

"This new media will allow researchers around the world to isolate and culture ovarian cancer cell types and, in addition, culture them reproducibly to find new targets for the diagnostics and treatment that withstands tests of generalization to new patient test sets. A new array of experiments will also become possible, on how ovarian cancer tumor lineages—many of which are difficult to observe during immunohistopathology or even in genomics analysis—are able to fool a patient's immune system and contribute to relapse after first-line therapy."

90% of published cell line research in breast and ovarian cancer is done with ten standard cancer cell lines (SCCL), and many of the SCCL cells have been found post-xenographic to have lost the relevant lineage biomarkers as well as deeper genomic signatures of their originating breast and ovarian primary tumors—even hardly resembling breast and ovarian tissues. TumorGenesis (TG) has developed media that can be used to culture complex ovarian cancer cell lines from patients that retain 95%+ of the DNA and RNA (even after 70 expansion cycles, as opposed to the standard 20 cycles) as well as crucial proteomic signatures. These cell lines have been developed by culturing PDCLs in proprietary TG media, and as such, they more closely mimic various real human cancers. Because of this, they are expected to better aid in accurately predicting actual patient outcomes on a compound-by-compound basis.

TumorGenesis Cancer Culture Media
Source: Company Website

Primary Culture Success	Less Than 1%	Over 95% (36/37)
Histotype	Mostly unknown	All subtypes
Xenograft Phenotype	Undifferentiated	Similar to patients
Genotype	Discordant	Similar to patients
mRNA profile	Discordant	Similar to patients
Correlates with	Better survival	Poor outcome
Drug response	Sensitive	Resistant
Number available	Total 49	46 (2015)



Source: TumorGenesis Website

TumorGenesis participates in the evolving 3D cancer cell culture media market. This market is expected to grow at a CAGR of approximately 11.3%, to $3.2 billion worldwide in sales in 2027, according to Allied Market Research. TumorGenesis currently has access to 98 different ovarian cancer cell lines with unique, stable signatures. These cell lines respond differently to treatment and can easily be used to increase the reach of ovarian cancer drug discovery and help secure a considerable share of a substantial, growing, market opportunity. TG's solution complements what Helomics offers, synergistically and mechanistically complementing each other to increase the quality of preclinical research. Specifically, the PeDAL approach could utilize TG-based PDCLs which could greatly improve the insights gained from preclinical research and help guide more successful, tailored clinical trials.

Helomics amasses a proprietary knowledge base of over 150,000 patient cases across 137 cancer types that include lung, breast, pancreatic, colon, ovarian, and head and neck. 38,000 of the database samples are ovarian tumors. TumorGenesis' first media product is designed specifically for ovarian cancers and combines with recent TG advances in 3D ex-vivo growth substrates, which utilize nanospun matrices that are highly customized for both tumor/tissue types and, as TG is presently developing, patient-specific materials to recreate the original tumor microenvironment more accurately than has ever before been possible. With an intricately reproduced microenvironment, TG expects to entirely eliminate genetic and phenotypic drift and allow expansion of the cells such that far more comprehensive drug compound libraries can be screened for each sample/patient. This is expected to dramatically widen windows of novel compound and diagnostics discovery to a degree not yet achieved. Initial discoveries by the TumorGenesis team will be used exclusively by the Helomics team to further help focus the Helomics programs for its clients and Predictive's goal for its own compound discovery programs for approved drugs in new indications and just as importantly, new biological and small molecule drugs and companion diagnostics. Once the discoveries are validated and the value has been extracted for Predictive

Oncology via the Helomics/TumorGenesis efforts, the cell lines and other components will be sold to the market for researchers to use. TG will similarly use the combined efforts of Helomics and TG teams to look at early drug discovery services, that as they advance to clinical trials will be passed on to Helomics

We do not assign a significant amount of value to TumorGenesis at this time, but in the future, the TumorGenesis technology may augment Helomics' capabilities and drive its own revenue.

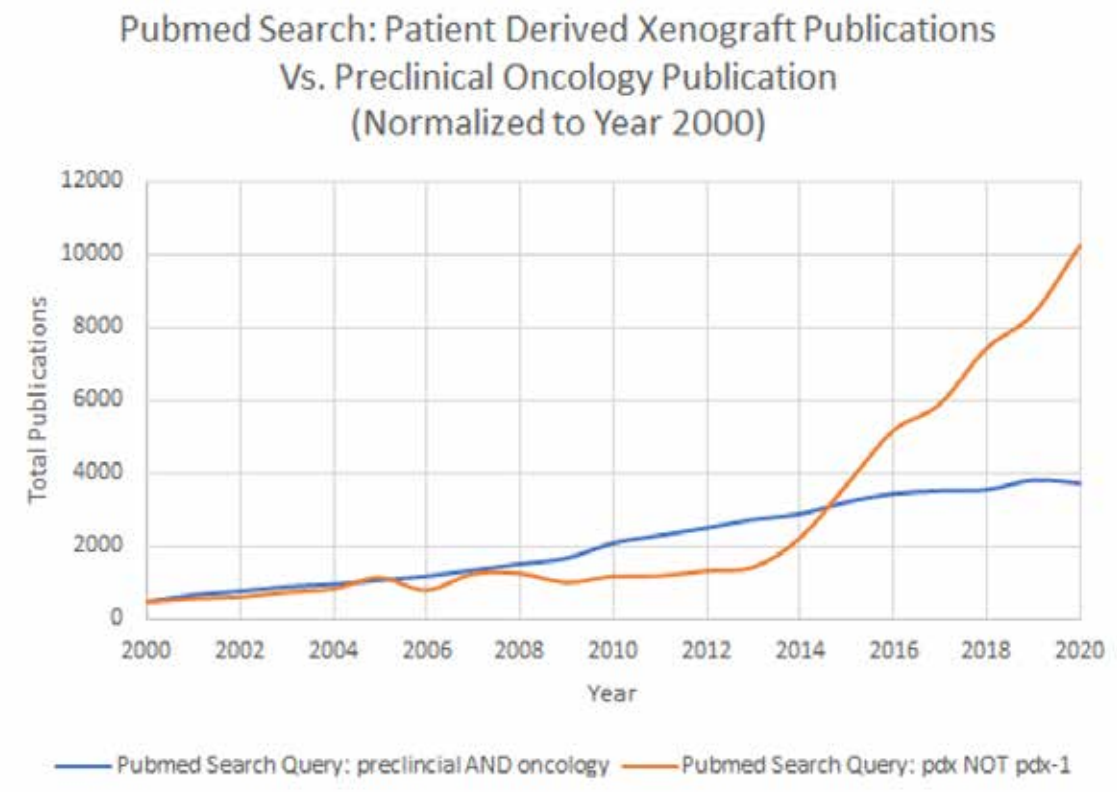
TumorGenesis: Long-Term Outlook

One long-term goal of TumorGenesis is to develop an ex-vivo 3D culture platform including patient and cancer specific nanomatrices, genomics profiling tools and protocols, quality assurance modalities and specialty medias for the growth of PDCLs that more closely resemble those of real patient tumors. This will take a long time; for the medias alone, various medias need to be tailored, tested, and validated for various human tumors and tumor subtypes, and then these medias need to be accepted in the research community as standard. When that process has matured, TumorGenesis may have developed a profitable, high margin business with a significant competitive moat due to the network effect of the research done, as well as the trade secrets that contribute to the platform components and media recipes.

A decent comparison for the scale of this business as well as potential future margins (especially for the 3D specialty cultures) could be Corning's Matrigel, which is ubiquitously used in experiments all over the world. As mentioned before, this market is also growing very rapidly. Of course, specialty media would likely carry a higher price with higher margins but be used in select experiments according to the specific tumors being studied. With Matrigel doing hundreds of millions (USD) in sales, the future business for TumorGenesis' proprietary, specialty media and 3D cultures could be robust and high margin.

Ever since the National Cancer institute (NCI) retired the NCI60 cell lines preclinical models (around 2016) in favor of patient-derived xenografts (PDx) due to their ability to more closely mimic real growth conditions and real patient tumors, the growth of research using PDx has increased. The institutions are well on their way to creating over 1,000 different models for various tumors. According to ESMO,

> *"Like most other cancer cell lines, the NCI-60 have lived in an environment that differs radically from their native one. Over time, the cells have adapted to life in plastic petri dishes, altering their genetic make-up and behaviour. To replace the cultures, the NCI is turning to patient-derived tumour xenografts (PDXs), the models in which the tumours grow in an environment that, although not human, better mimics their native environment. The NCI will distribute cells from those PDXs, as well as data regarding each tumour's genetic make-up and gene expression patterns, and the donor's treatment history."*

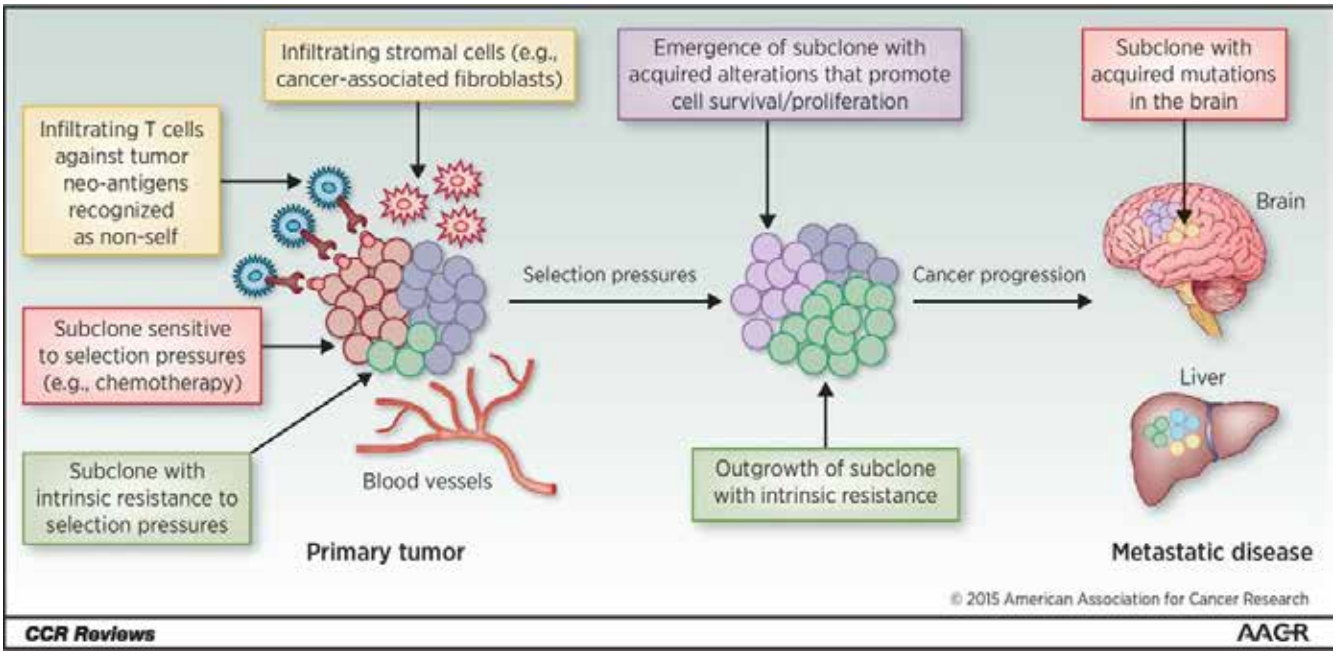


Source: PubMed Query, Quantum Research

What will be key for TumorGenesis to become a leader in the space is to have the NCI recognize their media and PDCLs and buy and/or use them. In this case, NCI adoption of various TG products could result in an inflection in use like that of PDx compared to overall preclinical research, shown above. In this case, sales could eventually reach into the hundreds of millions with over 70% gross margins, though it is too early to speculate.

A Key Problem In Cancer Research and Clinical Practice: Tumor Heterogeneity

One primary problem in cancer treatment is the inherent heterogeneity in cancers, which translates to an inability to destroy all the different types of cancer cells within a tumor and its metastases. Tumor heterogeneity was first identified and proposed as a major issue in clinical practice decades ago (~1980), with the exact mechanisms by which tumors become heterogenous being highly debated. Regardless, the translation into the clinic is simple: clearing only one subset of tumor cells only temporarily provides benefit for the patient, as remaining subsets grow to fill the void and contribute to relapse.



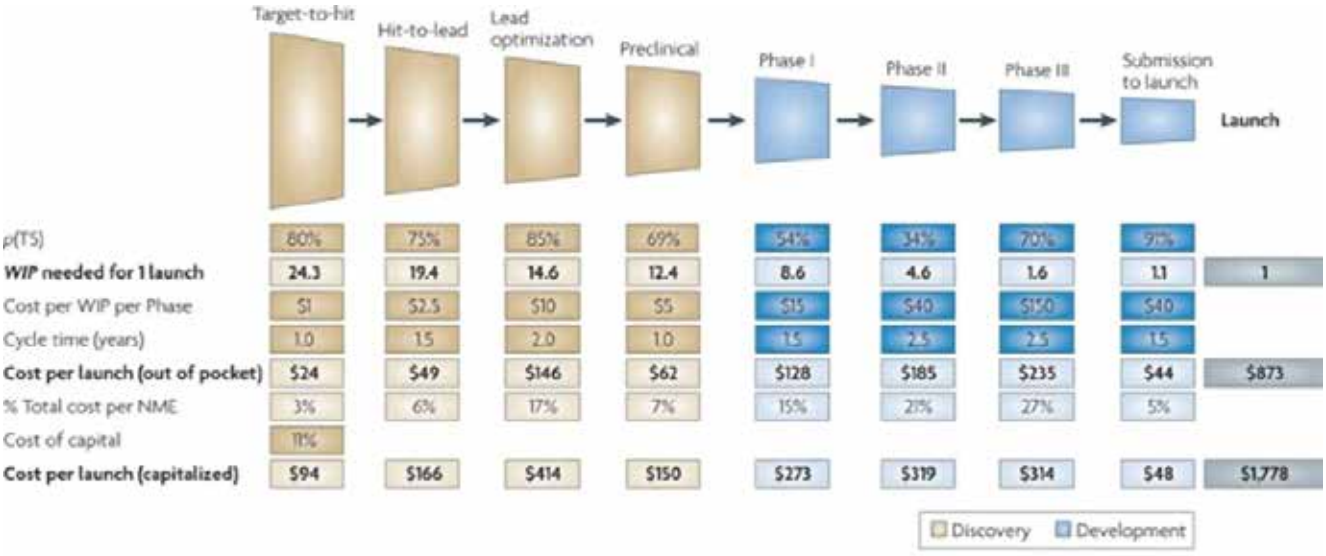
Source: Jamal-Hanjani, M et al. (2015). Translational Implications of Tumor Heterogeneity. *Clinical Cancer Research*, 21(6), 1258-1266.

This is the bane of chemotherapy; many chemotherapies are designed to destroy rapidly dividing cells (which rapidly grow as a tumor), and therefore would stop the cancer in its tracks… but many times only temporarily. Often, the selective pressure of chemotherapy taking out the most aggressive cells would only make way for the same aggressive cells, now resistant to the chemotherapy, or the residual cells, now not outcompeted (for nutrients) by the more aggressive cells, ready for growth. A clinical regimen that could identify all the different cells in a tumor and administer a drug, or multiple drugs, that renders all the cells susceptible could at the least improve clinical outcomes, and at most eradicate the cancer permanently. Thus, preclinical research that can use PDCLs which are heterogeneous and replicate the patient tumor as well as preclinical research that uses AI to identify drugs or drug cocktails that address various kinds of tumor heterogeneity may have much more success when translated into clinical studies, compared to single agents used in conjunction with only a handful of biomarkers.

A Closer Look at Helomics' and TumorGenesis' Opportunity:

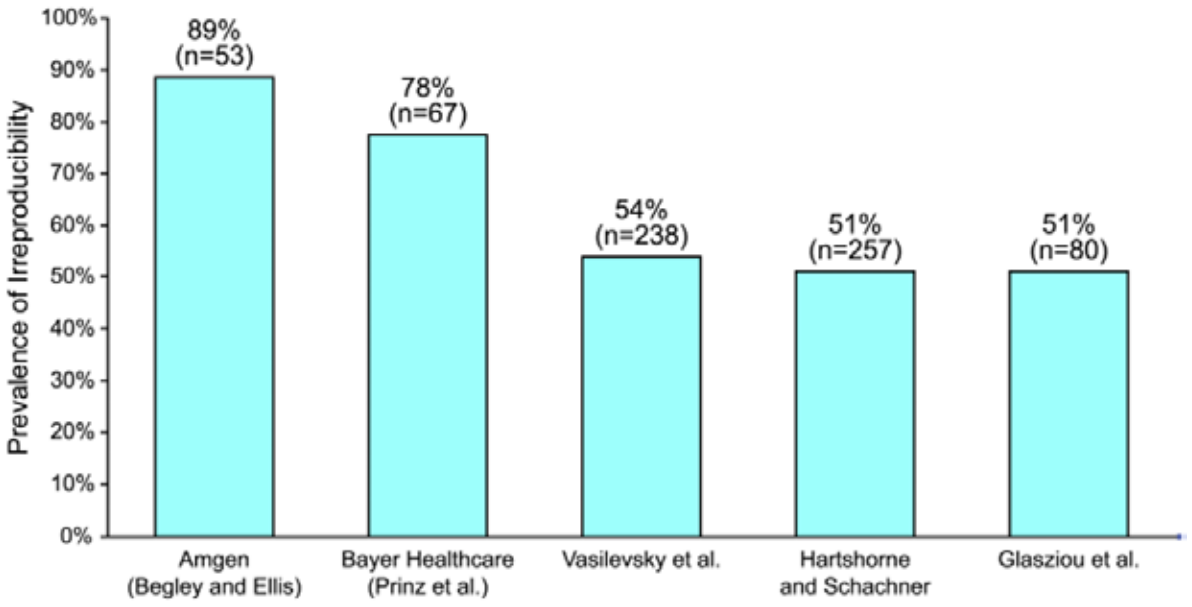
One cited reason for high drug prices is the total cost and failure rates for bringing drugs to market through all of the stages of development: target-to-hit, hit-to-lead, lead optimization, preclinical, and clinical (phase 1 through 3 and regulatory submission). According to various estimates, the cost of preclinical research, that is, finding a target, finding a drug for that target, optimizing the drug, and testing it in animals and ex vivo, can cost $600-700 million per launched (successful) drug, or ~⅓ of the entire cost of a new drug.

Improvements early on in the development process can lower overall costs by reducing failure rates (gaining better insights that translate into clinical trials such as potential hepatotoxicity, biomarkers for the proper patients, etc.), and making the process more efficient (using AI to quickly identify the right drugs for certain biological targets using approaches like PeDAL).



Source: Paul, S., Mytelka, D., Dunwiddie, C. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nat Rev Drug Discov 9*, 203–214 (2010).

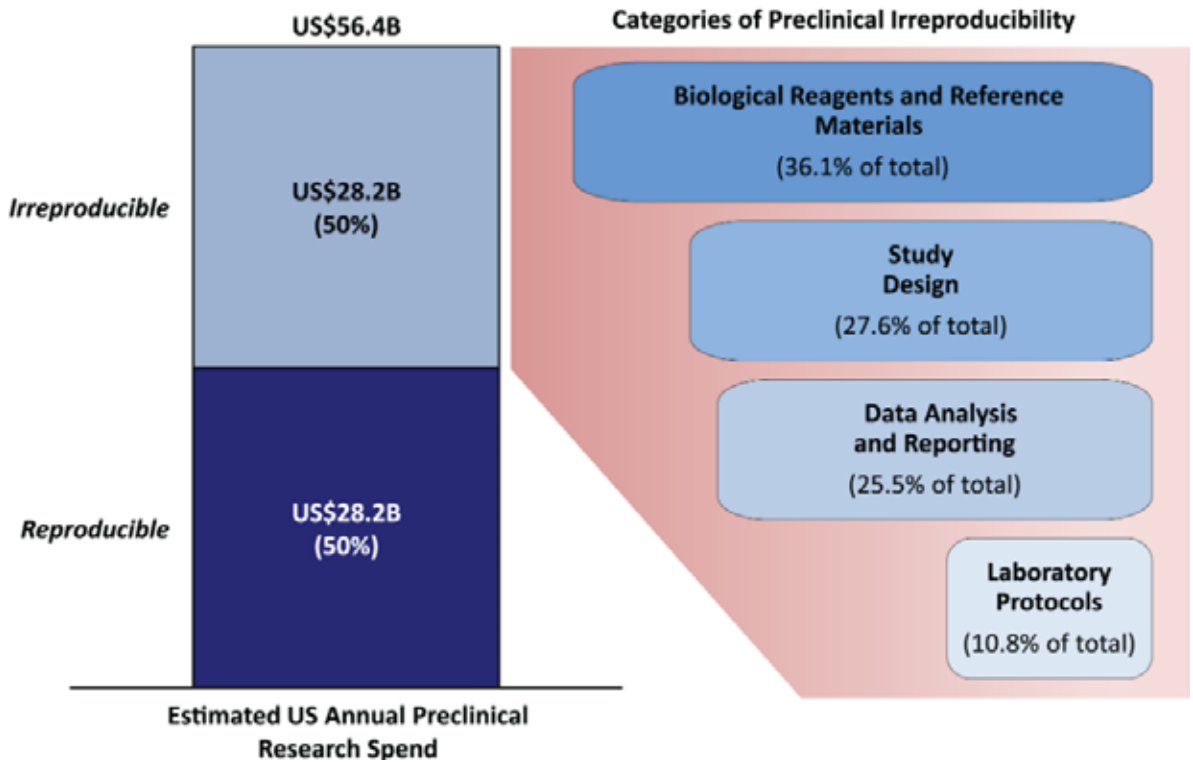
Experiments are the backbone of preclinical research and further development and are used to formally test hypotheses and gain more insight into biomolecular interactions and pathways. According to a study on the economics of reproducibility of preclinical research, Freedman et al. estimated that waste from irreproducibility (i.e., a poor design or wrong conclusions that render parts or the entire experiment flawed) in preclinical research using unvalidated media and reagents costs the pharmaceutical companies over $28 billion in 2015, due to irreproducibility rates in experiments exceeding 50%. This is in preclinical research alone, with irreproducibility rates (i.e., a bad study) conservatively estimated to be 50%. Thus, it is implied that there is extra waste in clinical research as well.



"Fig 1. Studies reporting the prevalence of irreproducibility.
Source: Begley and Ellis [6], Prinz et al. [7], Vasilevsky [8], Hartshorne and Schachner [5], and Glasziou et al. [9]."

Source: Freedman, L. P et al. (2015). The Economics of Reproducibility in Preclinical Research. *PLOS Biology*, 13(6).

Now, this does not mean that flawed studies have no utility, and the author cites that the actual dollar amount wasted could be higher or lower based on the assumptions made. But there is a lot of waste in research regardless of the exact amount, specifically preclinical research, due to issues such as unvalidated or flawed reagents/ materials, study design, data analysis and reporting, and laboratory protocols. Arguably, CoRE and Predictive Oncology's digital (CoRE and patient responses and records database) and physical (TumorGenesis ex-vivo 3D platform, matrices, media, tumor sample bank) assets are applicable to all of these causes of irreproducibility in some sort of manner. In fact, one publication states that **upwards of one third of all cell lines are imposters** (the wrong cell line—i.e., melanoma instead of thyroid cancer). In Nature, it was suggested that more than *half* of biomedical researchers "do not bother to verify the identity of their cell lines." When billions of dollars are wasted every year on flawed preclinical research and this then informs future research (with an additional 10,000 citations each year on false cell lines), the importance of what TumorGenesis and other similar companies are doing to fine-tune and control the quality of future preclinical research is difficult to overestimate.



Source: Freedman, L. P et al. (2015). The Economics of Reproducibility in Preclinical Research. *PLOS Biology*, 13(6).

If one assumes that these promising studies are replicated in the pharma industry before advancing pipeline candidates, an additional $28 billion may be wasted. According to Freedman et al.:

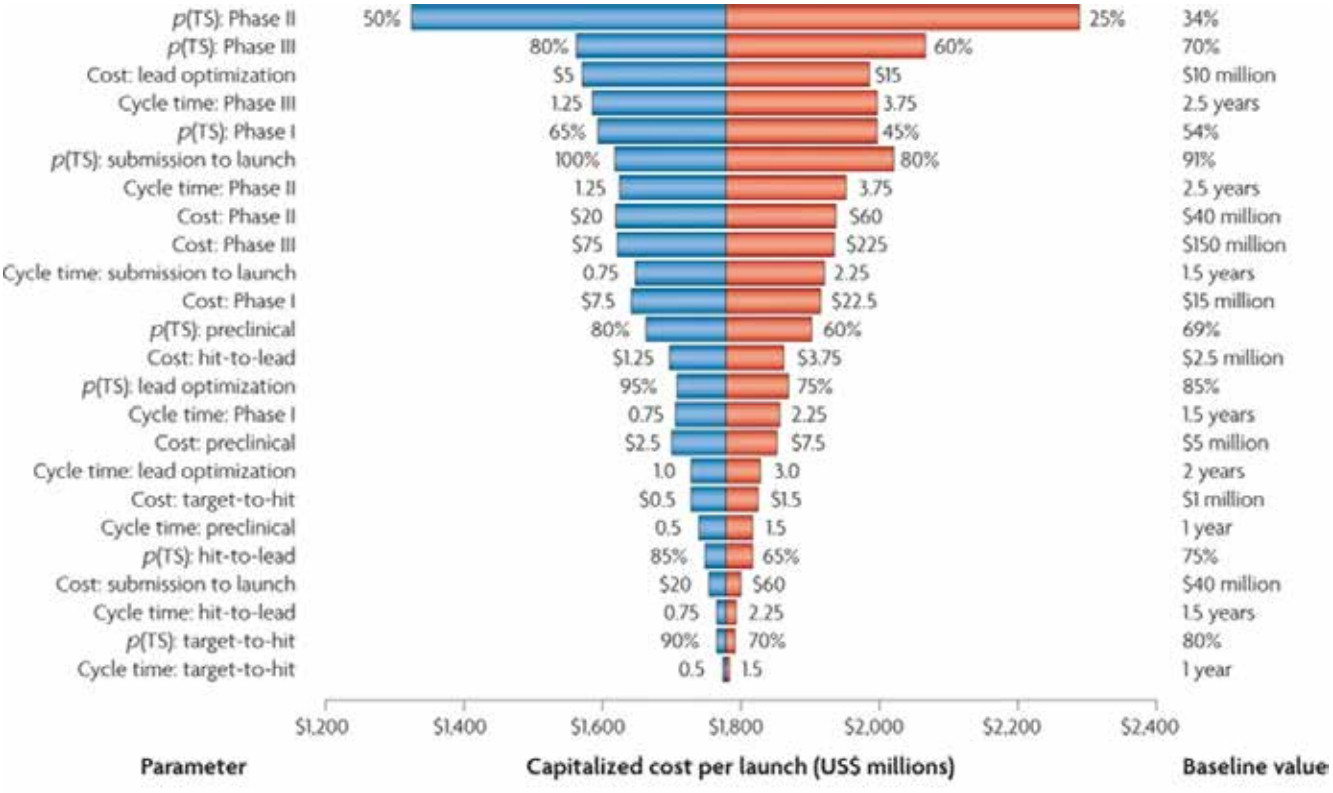
> *"Irreproducibility also has downstream impacts in the drug development pipeline. Academic research studies with potential clinical applications are typically replicated within the pharmaceutical industry before clinical studies are begun, with each study replication requiring between 3 and 24 months and between US$500,000 to US$2,000,000 investment.*

> *While industry will continue to replicate external studies for their own drug discovery process, a substantially improved preclinical reproducibility rate would derisk or result in an increased hit rate on such investments, both increasing the productivity of life science research and improving the speed and efficiency of the therapeutic drug development processes. The annual value added to the return on investment from taxpayer dollars would be in the billions in the US alone."*

These estimations do not account for clinical trial failures in studies downstream, which might be avoided by better study designs, which can be accomplished in several ways, notably using PDCLs or historical patient data, AI and biomarkers for study design, etc, from industry players such as Predictive Oncology.

With industry-standard preclinical oncology research including xenograft models using standard immortal cell lines, referred to as standard cancer cell lines (SCCLs), and a large amount of waste estimated to be *due* to *study design and study reagents and materials*, which includes the manner in which a study is conducted (selection of correct biomarkers and tools) as well as **irrelevant and invalidated cell lines**, there is undoubtedly much waste in preclinical oncology due to the use of these SCCLs. Overall, many aspects of preclinical experimentation may be improved using AI and better cell lines, though that benefit at this time may be difficult to quantify without specific applications or benchmarks. One could estimate the economic benefit of using TG media and PDCLs along with PeDAL AI in preclinical research using estimated costs and failure rates for each stage, per successful launch. Estimated savings per experiment preclinically would be a different calculation, a fraction of a per launch number. The graph below shows a sensitivity analysis of the total cost to launch one drug when varying different assumptions in the model, including the time, cost, and chances of success for each step in the development process. Considering the estimation that CoRE/PeDAL can speed discovery up by 40% while cutting costs by 60%, the savings could be quite substantial per launched drug.

The tornado graph below depicts hypothetical cost swings of a fully capitalized cost of an average new molecular entity (NME) developed by a typical large pharmaceutical company, by varying different parameters while keeping others constant. The Nature publication this graph is taken from notes the importance of reducing late-stage attrition rates for improving overall R&D productivity. For instance, the top bar indicates the incurred cost per NME launch if phase 2 success rates are swung from 34% (average) to 50% or 25%. Phase 3 success rates, according to this publication, have the second highest effect on average cost per NME launched. Shown through the bar's spread, it is implied hundreds of millions of dollars—even billions of dollars—could be saved by significantly increasing the probability of success for phase 2 and 3 trials. Given that traditional preclinical research in oncology poorly translates into the clinic, this implies that preclinical research driven by joint TG/Helomics models could save hundreds of millions or billions of dollars in R&D.



"This parametric sensitivity analysis is created from an R&D model that calculates the capitalized cost per launch based on assumptions for the model's parameters (the probability of technical success (p(TS)), cost and cycle time, all by phase). When baseline values for each of the parameters are applied, the model calculates a capitalized cost per launch of US$1,778 million (see Supplementary information S2 (box) for details). This forms the spine of the sensitivity analysis (tornado diagram). The analysis varies each of the parameters individually to a high and a low value (while holding all other parameters constant at their base value) and calculates a capitalized cost per launch based on those new values for that varied parameter. In this analysis, the values of the parameters are varied from 50% lower and 50% higher relative to the baseline value for cost and cycle time and approximately plus or minus 10 percentage points for p(TS). Once cost per launch is calculated for the high and low values of each parameter, the parameters are ordered from highest to lowest based on the relative magnitude of impact on the overall cost per launch, and the swings in cost per launch are plotted on the graph. At the top of the graph are the parameters that have the greatest effect on the cost per launch, with positive effect in blue (for example, reducing cost) and negative effect in red. Parameters shown lower on the graph have a smaller effect on cost per launch."

Source: Paul, S., Mytelka, D., Dunwiddie, C. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nat Rev Drug Discov 9*, 203–214 (2010).

So, for instance, if one assumes the use of Helomics/TG PDCLs in preclinical research to fully and completely characterize each patient's heterogeneous tumor, as well as the use of PeDAL to provide guidance on patient inclusion criteria, the chances of success for a given drug in trials powered to measure efficacy (phase 2 and phase 3) might hypothetically be much greater as the clinical models being tested during the clinical trial (human tumors) would more closely match the preclinical models developed up to that point in the trial. On a per-launch basis, this could hypothetically save about a billion dollars in R&D costs.

According to the referenced analysis above, the overall impact of better quality and more efficient preclinical research can result in at least hundreds of millions of dollars saved per drug launched. Additionally, ROIs could increase simply due to a more time efficient process.

Pharmaceutical Research Manufacturers Association has followed 10 cancers and tracked their success and failures as shown in the following table. Picking one target for drug development that is present in high measurable quantities, STAT3 (Signal Transducer and Activator of Transcription, 3) and at a cost of $30,000 per patient treatment, a discovery made in STAT3, known as a 'Master Protein Regulator', for Predictive Oncology would be astounding.

Oncology Drugs- Winners & Losers*						The 10 Deadly Cancers**				STAT3 %	$ New Cases	$ Stage 4
Cancer	Failed	Approved	Total	Percent +	Percent -	New Cases	Deaths	Percent +	Percent -	Active	100% Treatment	100% Treatment
Malignant Melanoma	158	12	170	7.1%	92.9%	324,635	57,043	82.4%	17.6%	58%	$9,739,050,000	$1,711,290,000
Brain Cancer	122	3	125	2.4%	97.6%	308,102	251,329	18.4%	81.6%	60%	$9,243,060,000	$7,539,870,000
Acute Myeloid Leukemia	91	7	98	7.1%	92.9%	474,519	311,594	34.3%	65.7%	71%	$14,235,570,000	$9,347,820,000
Kidney Cancer	96	11	107	10.3%	89.7%	431,288	179,368	58.4%	41.6%	50%	$12,938,640,000	$5,381,040,000
Liver Cancer	73	5	78	6.4%	93.6%	905,677	830,000	8.4%	91.6%	49%	$27,170,310,000	$24,900,000,000
Lung Cancer (all)	268	32	300	10.7%	89.3%	2,210,000	1,800,000	18.6%	81.4%	60%	$66,300,000,000	$54,000,000,000
Small-Cell lung Cancer	51	4	55	7.3%	92.7%	331,500	270,000	18.6%	81.4%	100%	$9,945,000,000	$8,100,000,000
Pancreatic Cancer	131	7	138	5.1%	94.9%	495,773	466,033	6.0%	94.0%	80%	$14,873,190,000	$13,980,090,000
Ovarian Cancer	139	13	152	8.6%	91.4%	313,959	207,252	34.0%	66.0%	79%	$9,418,770,000	$6,217,560,000
Prostate Cancer	237	21	258	8.1%	91.9%	1,410,000	375,304	73.4%	26.6%	67%	$42,300,000,000	$11,259,120,000
Totals	1,366	115	1,481	7.8%	92.2%	7,205,453	4,747,893	34.1%	65.9%	67%	$216,163,590,000	$142,436,790,000
											$30,000	
											$ Drug Cost/patient	

From: Exhibit: Oncology winners and losers from 1994 to 2020 of the 10 deadly cancers.
Sources: PhRMA and WHO Cancer Statistics, STAT3 Percent in cancer, and projection of treatment; GLG Pharma.

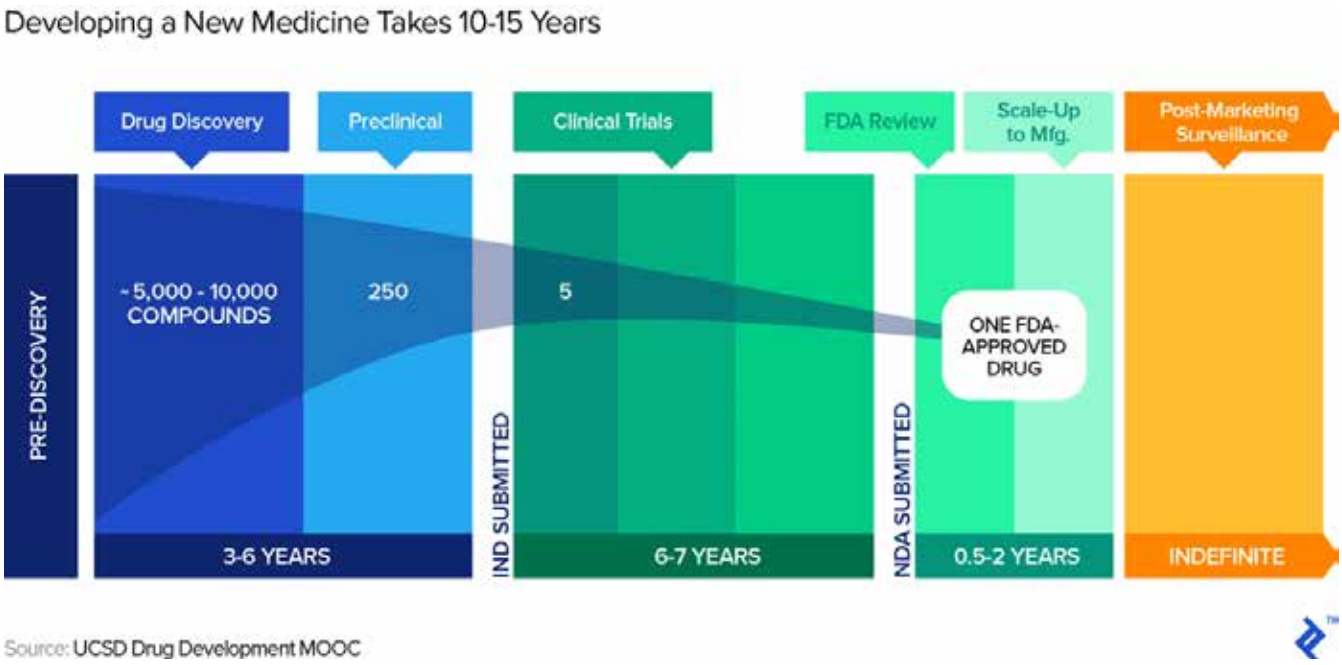
Probability of Success[2] by Clinical Trial Phase and Therapeutic Area

	P1 to P2	P2 to P3	P3 to Approval	Overall
Oncology	57.6	32.7	35.5	3.4
Metabolic/Endocrinology	76.2	59.7	51.6	19.6
Cardiovascular	73.3	65.7	62.2	25.5
Central Nervous System	73.2	51.9	51.1	15.0
Autoimmune/Inflammation	69.8	45.7	63.7	15.1
Genitourinary	68.7	57.1	66.5	21.6
Infectious Disease	70.1	58.3	75.3	25.2
Ophthalmology	87.1	60.7	74.9	32.6
Vaccines (Infectious Disease)	76.8	58.2	85.4	33.4
Overall	66.4	48.6	59.0	13.8
Overall (Excluding Oncology)	73.0	55.7	63.6	20.9

Source: Chi Heem Wong, Kien Wei Siah, Andrew W Lo. "Estimation of clinical trial success rates and related parameters." *Biostatistics* 20(2): April 2019, Pages 273-286. Published online: 31 January 2018. DOI: 10.1093/biostatistics/kxx069

Sources: Berezow, A. (2020, June 12). Clinical Trial Success Rates by Phase and Therapeutic Area.

Failure rates in later stages of oncology research tend to be comparatively high. One could speculate that, since phase 1 trials are often dose-escalation and safety analyses, the 32.7% and 35.5% chances of moving from phase 2 through phase 3, and phase 3 through approval suggests that the preclinical models used to determine efficacy of a drug correlate extremely poorly with real human (often complex and heterogeneous) disease. Other analyses suggest phase 1 trial successes in oncology are higher, while phase 2 success rates are lower (below 30%), further indicating poor translation of preclinical efficacy to clinical efficacy. Thus, Predictive Oncology's assets (database and PDCLs) could be extremely useful in increasing chances of success in mid-and-later stages of research (phases 2 and 3). Overall, only one out of 5,000-10,000 drugs are able to make it to FDA approval—accurate preclinical research could drastically increase chances of success.



From: Toptal Finance

The Contract Research Services Market

Predictive Oncology is betting high on its AI-driven R&D division; The company plans to monetize its research activities through contract research services. If Predictive Oncology strikes even a few meaningful deals with pharma companies, this business segment would likely become the company's major source of revenue.

According to Fortune Business Insights, The Contract Research Organization (CRO) market stood at $38.4 billion as of 2018 and is projected to reach $91 billion by the end of 2026, exhibiting a CAGR of ~11.5% in the forecast period.

Source: Fortune Business Insights

Contract research organizations are the companies that offer research-based services on a contract to many pharmaceutical and biotechnology companies, medical devices industries, and various government research organizations.

These services include four subgroups: drug discovery, preclinical research, clinical trials, and laboratory services. While clinical services (mostly clinical trials) are the largest part of the market by transaction size, it is a crowded space with many competitors. Predictive's services may fall under the drug discovery subgroup, which is also growing and is a less saturated market.

In terms of clinical applications, oncology is the largest segment of contract research, due to the increase in the prevalence of cancer globally, the value of the oncology market, the unmet needs in oncology, and the vast amount of research going on and required to "solve" cancer. Predictive Oncology, for a smaller company, has a positional advantage because it competes in a space that is perhaps less crowded (drug discovery) but is more scalable (oncology).

Contract Research Services: Growth Drivers

We believe that the contract research services market is positioned for growth over time. We support our belief with the following growth drivers:

1. There is growing demand for effective, novel drugs and healthcare devices.
2. There is a high and increasing cost of drug development and increasing regulatory scrutiny.
3. There is a growing patient population globally.
4. Growing strategic collaborations among industry key players make it difficult and expensive to perform in-house research at the same quality.

5. A rising number of drug manufacturers from emerging markets are likely to outsource their research activities or collaborate with companies like Predictive Oncology.

Industry Threats:

The CRO services market is currently a highly fragmented market with the presence of many players; however, most of the market share is owned by a few big players. Mergers, acquisitions, and collaborations witnessed in recent years are likely to result in market consolidation. Therefore, POAI faces threats of competition from big players, as well as potential in-house teams developing AI for drug development. The fact that the AI was essentially acquired from CMU, a highly regarded, top tier university, gives us confidence in the quality of the asset.

In our opinion, the key assets that Predictive Oncology has and that are difficult to replicate are its tumor database and patient response history, as these assets represent 5-15 years and about $180 million dollars in investment of a competitive moat. Predictive Oncology may also use its specialized assets and moat to work with top CROs instead of competing against them.

Listed below are some notable Contract Research Organizations (CROs) and their recent reported revenues.

Company Name	Reported Revenue (2020)
LabCorp (Covance)	$13.9 B
IQVIA	$11.4 B
Syneos Health	$4.6 B
Pharmaceutical Product Development (PPD)	$4.6 B
PAREXEL International Corporation	$3.6 B
PRA Health Sciences	$3.1 B
Charles River Laboratories	$2.9 B
Medspace Holdings	$0.9 B

While all these corporations are big players in CRO services, they are not primarily focusing on AI-driven drug discovery and development, thus they may not pose a major and direct threat to Predictive Oncology. However, many of them are making collaborative agreements in AI for various purposes. For instance, Covance recently teamed up with AI imaging company, Definiens (a subsidiary of AstraZeneca (NASDAQ: AZN), to develop AI for image pathology in the context of clinical trial design and tissue-based testing. This enables a faster and more rigorous approach to validating biomarkers and co-developing companion diagnostics with immunotherapies and a focus on immuno-oncology. In our opinion, this is a relevant competitive threat to Predictive. However, as stated before, the company has historical assets that will be very useful for R&D and simply cannot be quickly or inexpensively reproduced. The pure play AI-driven R&D industry is discussed in the next part of this report, which highlights direct competition.

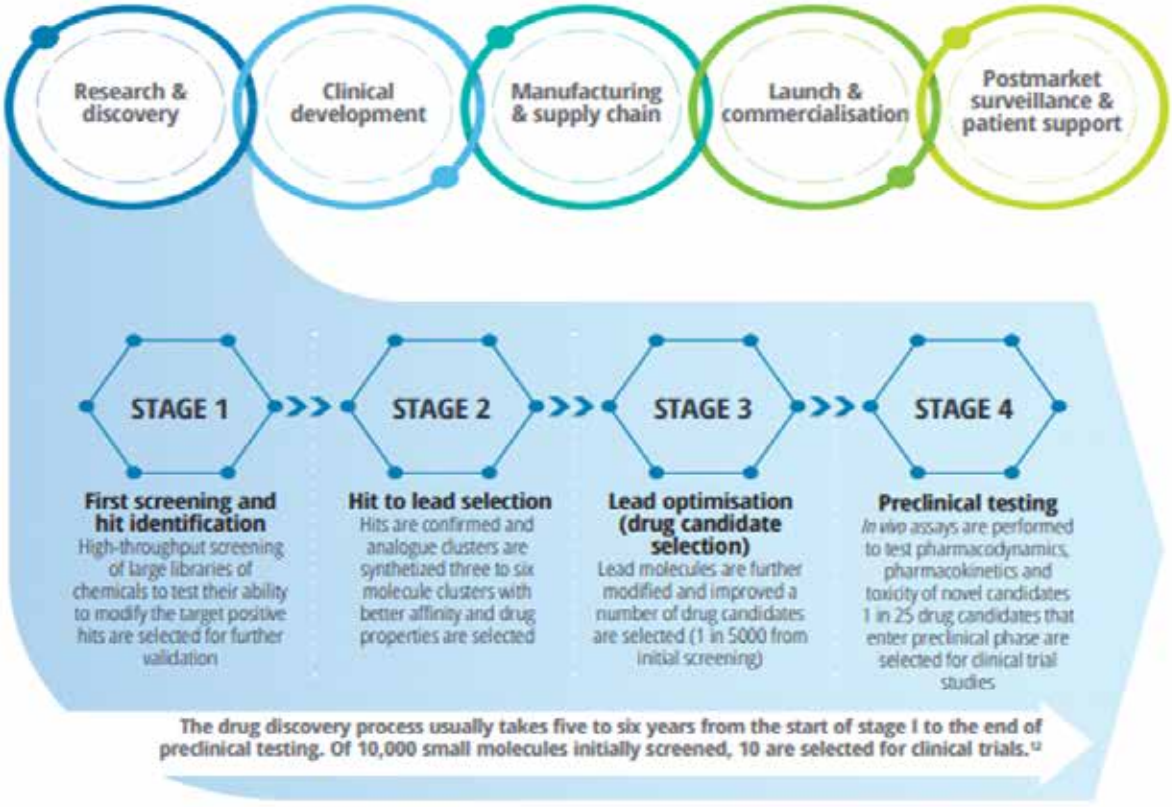
Rapid technological advancement and growing globalization are encouraging many biotech and pharmaceutical companies to outsource their research development to many contract research organizations, and Predictive Oncology is well positioned to take advantage of the trend. It is possible that, in the future, PeDAL could be productized and sold as a software service to CROs for enhancing the insights of their preclinical or clinical studies and saving costs for themselves and their clients.

Artificial Intelligence: Transforming Biopharma R&D

Drug discovery is the first phase of the value chain that identifies new candidates or therapies for treating human disease. It is the initial stage of R&D that involves the identification and optimization of potential new drugs and preclinical in vivo validation through cell assays and animal models. Successful candidates that meet the regulatory requirements move into the clinical trial phase where drugs are tested on humans, typically in three phases.

FIGURE 2

The biopharma value chain for drug discovery



Source: oodlesai

In the past couple of decades, drug discovery has been carried out using a traditional labor-intensive approach, but with the advancement of robotics, artificial intelligence, and machine learning, the paradigm is shifting. Advancement in technology has not only reduced the cost but has also reduced the time required to discover a drug candidate, which is then tested in clinical trials. In a few cases, AI applications have already delivered new candidate therapeutics, in some cases in months rather than years. According to Deloitte, the artificial intelligence R&D market size has increased from $200 million in 2016 to more than $700 million in 2018 and is expected to reach $20 billion in the next five years by 2023. The AI and ML market raised more than $10

billion in investment in one year, fueled by increased demand for digitization in the healthcare sector. There has been a slew of deals in the AI-driven drug discovery phase ranging from $5 million to over $1 billion, and many major pharma companies are exploring AI-driven solutions for drug discovery. Many pharma companies are accomplishing this by outsourcing their research activities to CROs, which helps them stay competitive and flexible with major disruptions in technology.

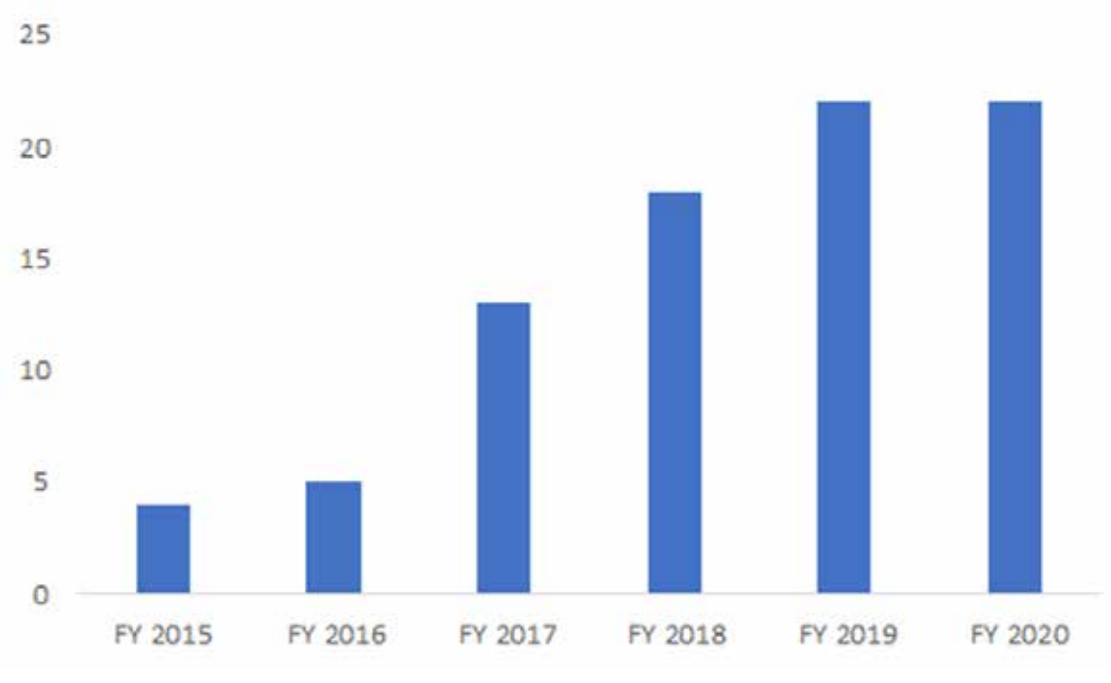


Exhibit: Number of Big Pharma AI partnerships
Source: Global Data Pharmaceutical Intelligence Center

The number of pharma industry AI deals or partnerships with big pharma has been increasing at a rapid rate. Many of the top pharma companies have disclosed multiple deals already.

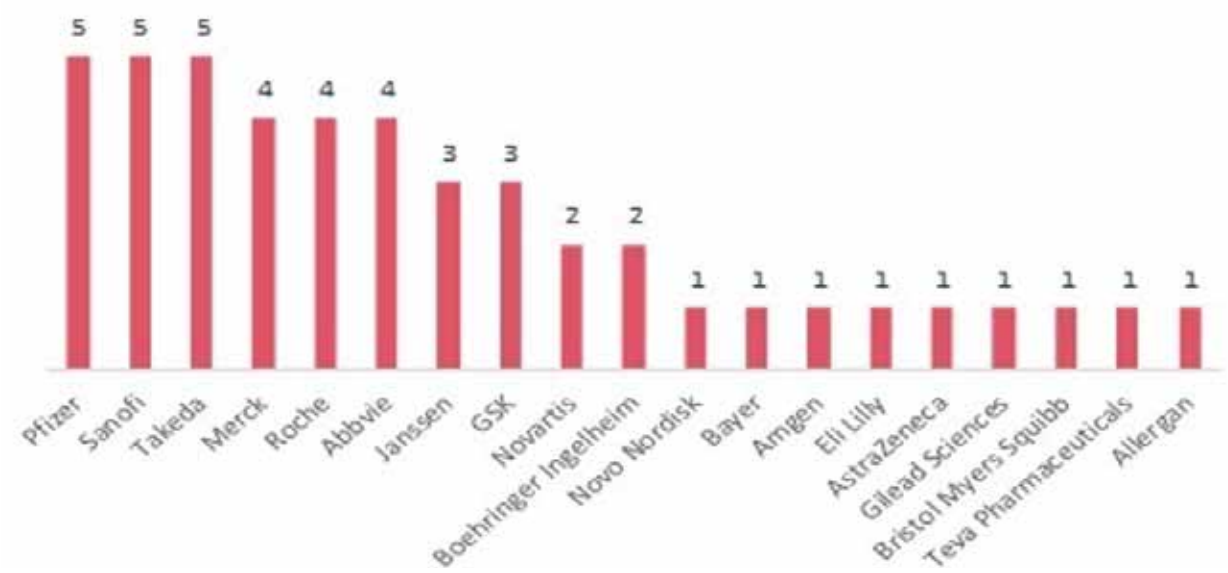


Exhibit: Big Pharma AI Partnerships Disclosed to the Market
Source: Market Future Research

There have been many impressive accomplishments in the field of AI-driven R&D wherein AI algorithms tailor approaches for a more accurate understanding of pathological cellular and molecular mechanisms. An increasing number of startups are targeting major chronic diseases like oncology, cardiovascular and neurodegenerative diseases. Furthermore, AI-driven companies target different interdisciplinary domains:

1. AI for drug target identification and validation
2. AI for target base and phenotypic drug discovery
3. AI for dealing with biomedical, clinical, and patient data
4. AI for polypharmacological discovery
5. AI for drug repurposing programs
6. AI for biomarkers development
7. AI for analyzing research literature, publications, and patents

Many big pharma companies have begun long-term collaborations with AI-driven research companies, providing services ranging from target identification to using AI imagination for drug design.

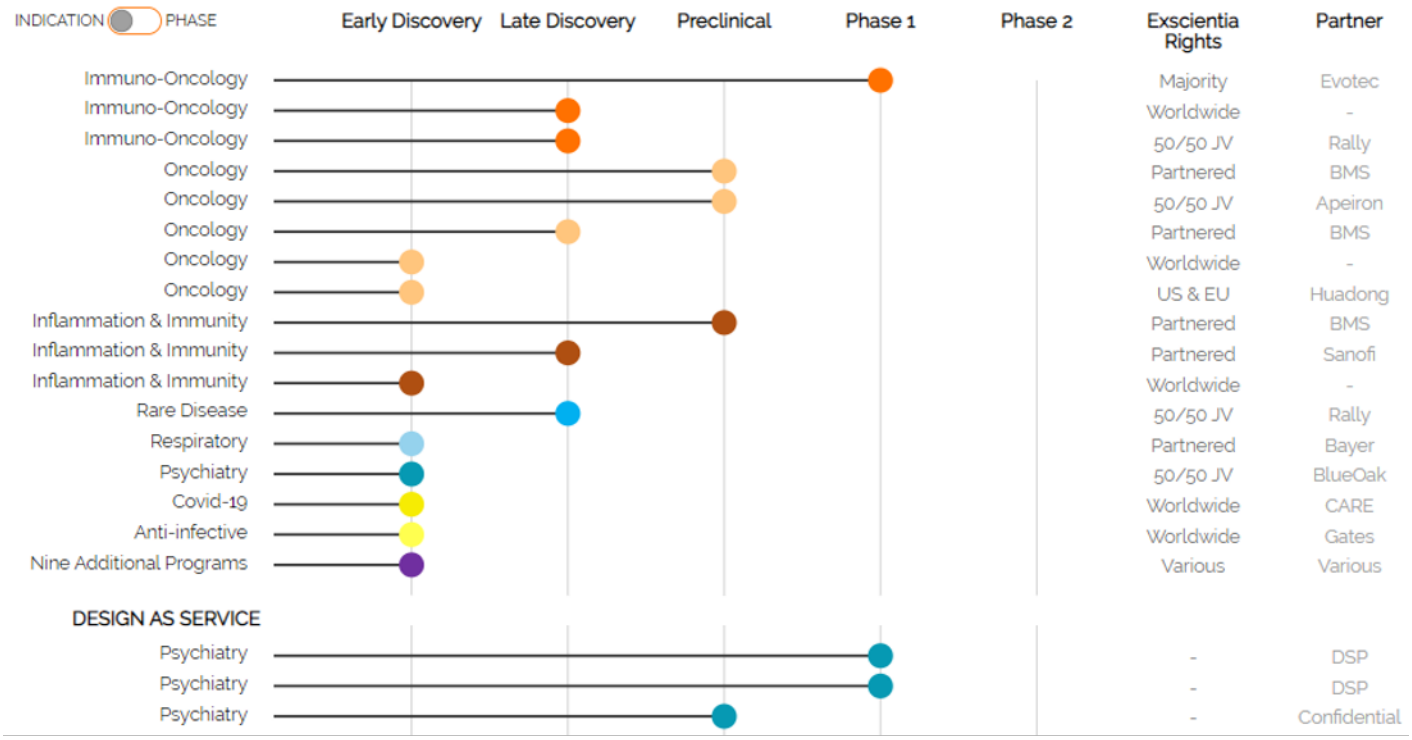
1. **BenevolentAI** is a UK-based company providing AI solutions for drug discovery. The company has collaborations with blue chip pharma companies like AstraZeneca (NASDAQ: AZN) aimed at using AI and machine learning to develop new treatments for chronic kidney disease (CKD) and idiopathic pulmonary fibrosis (IPF). In addition to this, the company has signed a framework collaboration agreement with Novartis (NYSE: NVS), wherein BenevolentAI will use the application of AI and ML to stratify patients with various oncology-related diseases and obtain a better understanding of patient and disease to personalize patient treatment.

2. **AtomWise** is a US Company that uses its proprietary DL AI technology to predict small-molecule protein binding and focuses on identifying potential therapeutics for any disease target. The company has 300 partnerships with major biopharma companies across the globe on drug discovery projects for a variety of diseases including Ebola, multiple sclerosis, and leukemia. In September 2019, Atomwise and a China-based company, Jiangsu Hansoh Pharmaceutical Group, launched an up-to-$1.5 billion (USD) collaboration to design and discover potential drug candidates for up to 11 undisclosed target proteins in cancer and other therapeutic areas.

3. **Insilico** is a US-based Company, headquartered in Hong Kong, that uses ML techniques based on neural networks that produce new data objects. They have developed a platform called generative tensorial reinforcement learning (GENTRL) which has generated new drug hits against fibrosis in 21 days and validated them, selecting one lead in another 25 days. The process from the beginning of the design process took 46 days, 15 times less than traditional biopharma lead times.

4. **Exscientia** is a UK-based company and is at the forefront of the AI-driven drug discovery process. The company has three main AI-based proprietary approaches which include single-target drug discovery projects, bio specific as well as phenotypic drug design. In general, the company focuses on lead generation, given a biological target, which is complementary rather than competitory to what Predictive Oncology does. The company has developed collaborations with several big biopharma companies. Exscientia signed a deal for £33 million in 2017 to deliver a lead molecule aimed at the treatment of chronic obstructive pulmonary disease. In May of 2020, the company entered into a $266 million agreement with Bayer while leveraging Exscientia's AI technology to quicken the drug discovery programs on oncology and cardiovascular diseases. Under the terms, Exscientia is entitled to receive

upfront fees, ongoing research funding as well as clinical milestone payments. The company claims that it can help reduce time required to discover preclinical candidates by up to 75%. Various sources claim that the company is worth between $650 million and $1.42 billion. With 20 programs in its pipeline, each program could be considered to be worth about $50 million. While Exscientia might be considered a competitor, its focus is on designing drugs, not testing specific oncology drugs preclinically using AI and PDCLs. Exscientia's valuation serves as a good proxy for Predictive's future valuation if the company can execute on multiple deals with pharma.



Source: Exscientia Website, July 2021

5. **Tempus** is another AI-driven pharma company that has a different focus. The company has recently raised $200 million, and sources estimate it is worth over $8 billion. Tempus claims to have analyzed data from a third of all cancer patients in the United States, working with thousands of oncologists across hundreds of medical systems, including Northwestern University and the University of Chicago. Tempus also licenses anonymized, de-identified data (including images and clinical information) to pharmaceutical companies, researchers, and the government, which use the information to evaluate potential new treatments before taking them to the lab. The company has raised over $1 billion in venture funding to date. Its services include data licensing as mentioned before, as well as genomic profiling and other tests aimed to help physicians make educated clinical decisions for their patients, like Helomics' legacy business. Interestingly, the company also leverages its data to aid companies and patients in clinical trial matching—linking patients with matching desirable inclusion criteria to respective clinical trials. The company is led by Groupon (NASDAQ: GRPN), founder Eric Lefkofsky. The company's capabilities are somewhat competitive to Predictive Oncology's. Most recently, the company expanded its Cancer Biomarker Alliance with Bristol Myers Squibb (NYSE: BMY) to provide additional terabytes of information for transcriptomic (RNA) data.

With lots of advancement going on in this industry, companies like Helomics and TumorGenesis with well-established data assets and proprietary technology are likely to benefit, given the growing amount of demand for their services. Compared to most companies in this space, Predictive has unique assets with multi-omic and historical data, while much of the competition uses mostly genomic data.

Purely in-silico or purely big data approaches have significant drawbacks that vary by the scope of work. For instance, companies can develop drugs *in silico* to perfectly bind certain targets, but in general there are many variables that must still be tested against; namely, the drug's effects on any other targets, as well as its tolerability in-vivo. Perfect binding is not everything; clinical outcomes and safety are. Other approaches in oncology such as big data-only do not necessarily use human tumors linked to responses and rely on connecting biomarkers to responses, which is valuable, but this approach does not necessarily correctly link correlation and causation. Predictive/Helomics' approach is uniquely valuable since they have a significant number of patient-derived cell lines and live tumors, historical data, and multi-omic data to couple with PeDAL to find drug responses ex-vivo that most closely represent an in-vivo tumor. This enables significant insight into tumor drug responses before ever testing in the clinic. The other key part of the PeDAL platform is its ability to minimize experimentation while maximizing insight.

While their tumor bank and database represent a significant competitive moat, companies can, with enough time and money, acquire or build similar assets, so Predictive must continue to grow their database with more testing and partnerships as well as translating their data and AI into preclinical and clinical applications. Their competition is well capitalized.

Helomics' Current Focus and Future Direction: Ovarian Cancer and More

The tumor types most frequently tested through the Helomics panel are gynecologic cancers, lung cancers, breast cancer, colon cancer, and pancreatic cancer. As mentioned before, the company has a proprietary database of more than 150,000 cancer cases. More than 38,000 of those are specific to ovarian cancer, and ovarian cancer is common, leth al, and devoid of a variety of highly effective treatment options, which is why the current focus is on ovarian cancer.

Ovarian cancer ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. The ACS estimates that in 2021, more than 21,000 women will be diagnosed with ovarian cancer, with more than 13,000 women dying from it.

According to iHealthcareAnalyst, the global ovarian cancer drugs market is expected to reach $10.1 B by 2027, exhibiting a CAGR of ~17.1% during the forecast period, including just PD-1, PARP, and angiogenesis inhibitors. The growing geriatric population of women, increase in ovarian cancer cases, and a rise in healthcare expenditure and increased government funding is expected to drive forward the ovarian cancer drug market.

According to the American Cancer Society, only 40-50% of patients diagnosed with ovarian cancer survive more than five years past their diagnosis. Predictive Oncology believes that through its proprietary tumor modeling, it can provide pharma companies with a newfound ability for more effective and expeditious drug development, and as a result, improve patient outcomes and increase ROI. However, Predictive is not the only company to sequence or model tumors; there are several other companies that pursue the development and offerings of PDCLs, especially for preclinical xenograft models. Many efforts to develop PDCLs in the past have failed; however, Predictive states that "TumorGenesis technology enables cell lines from patients to represent more than 90% of patient tumors; current SCCLs represent merely 1% of ovarian cancer diversity—and this leap is

expected to be transformative for ovarian cancer patient treatments." In fact, TumorGenesis President Richard Gabriel recalled when a researcher the company supplied media to was able to culture a tumor in 3 days that he had been working on, in vain, for about *an entire decade*.

There are also many other companies sequencing tumors for targeted therapy, though "genomics alone" has not yielded impressive results for targeted oncology—the response rates are generally low, and the targeted therapy niches within particular cancers are typically in the single digits as a percent of the entire cancer population. The commercial uptakes for targeted therapies in oncology are also generally lackluster, highlighting the need for a multi-omics approach that better characterizes a patient's tumor and potentially their response to a therapy. Predictive's approach is multi-omic, which much better characterizes the tumors.

The result assists health providers in selecting the most effective drug to treat a specific patient's unique cancer. The personalized medicine approach is the beginning of a new era in the pharmaceuticals industry, and Predictive Oncology is well-positioned to take advantage of it.

However, ovarian cancer is not the only space where Predictive is settling in for the long term. In addition to its partnership with UPMC/Magee (400 patients, multi-omic data, and clinical outcomes) and the UK 100,000 Genomes Project, Predictive has established collaborations with:

1. Interpace Diagnostics Group (OTCMKTS: IDXG) to build AI-driven models of thyroid cancer to enhance diagnosis and identify the best therapeutic options for thyroid cancer,
2. ChemImage, a molecular imaging company, to establish the feasibility of coupling genomics to Raman spectroscopy to better determine disease progression, specifically in prostate cancer,
3. Viome, to study the link between the gut microbiome and ovarian cancer, with a focus on gut microbiome changes during treatment and its potential effects on outcome,
4. SpeciCare, another company that also cryopreserves live tumor specimens and aims to connect patients to better therapies, similarly to Helomics' legacy business, and,
5. The National Alopecia Areata Foundation (NAAF), which serves sufferers of alopecia areata, an autoimmune skin disease that causes hair loss and emotional pain. NAAF aims to use a next generation patient registry to drive research into new treatments for people with this disease.

While we do not currently assign value to these collaborations, they highlight the company's ability to collaborate to acquire data, and to apply PeDAL to other areas of healthcare to gain additional insights and drive innovation.

The next sections of the report will focus on additional Predictive Oncology subsidiaries that do not fall under the oncology umbrella.

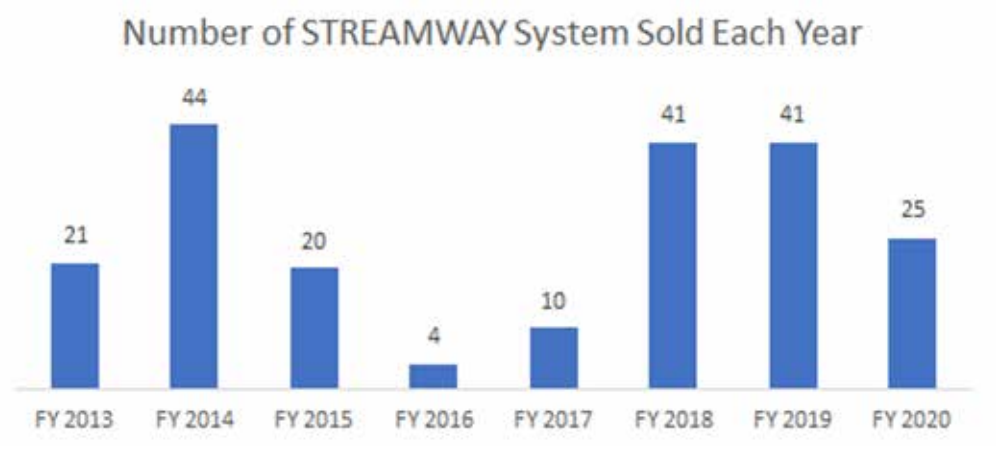
Skyline Medical

Somewhat supporting Predictive Oncology's aspirations in drug discovery, precision medicine, and oncology is the legacy business, Skyline Medical, *which the company may consider selling as it refocuses on AI, drug development, and oncology.* As stated before, this company provides solutions for fluid and waste management for operating room procedures. Most surgical procedures produce some sort of fluid or waste which are potentially infectious materials that are to be stored in disposal plastic suction canisters and disposed of with the lowest possible risk of cross-contamination. Though it is frowned upon, sometimes hospital employees have been known to dispose

of the fluid down the drain. Either way, without an operating room drainage system, these tasks are manual, where human error can lead to life-threatening situations. Studies suggest that suction canisters comprise 25% of regulated medical waste at hospitals and that up to 40% of surgical waste is related to suction canister disposal.

Skyline Medical's product solves these issues. The company has developed a fluid medical waste disposal system known as the STREAMWAY system. It eliminates staff exposure to blood, irrigation fluid, and other potentially infectious fluids found in the healthcare environment. This not only reduces exposure to risk but also reduces overhead cost through reduced manual labor and also increases efficiency by enhancing the surgical team's ability to collect data to accurately assess the patient's status during and after the procedure. Through its patented design, STREAMWAY assists in safer and more profitable surgical procedures. The company has been granted patents for the STREAMWAY System in Canada, the United States, and Europe and has been US FDA cleared and has received its CE mark. The patents cover technology which enables direct-to-drain fluid waste disposal and allows the system to provide continuous suction to the field and unlimited waste fluid capacity.

Source: Skyline Medical Website



Source: Quantum Research, Company Reports

Skyline is working on developing a new third generation STREAMWAY system for direct-to-drain fluid waste management.

- The new system will include:
- A 25% reduction in unit size.
- Modularized subassemblies and drop-down cover to streamline assembly and servicing.
- Upgraded software providing state-of-the-art on-screen graphics.
- New technology for on-screen training as required.
- **An automated dripless system for filter changes between procedures.**
- Reduced electrical and mechanical internal connections increasing vacuum efficiency.
- New integrated PC board providing real-time fluid waste management.
- Eliminated relays and inputs/outputs.

The advantages the STREAMWAY system has over competing options include:

- Uninterrupted services (no pausing to empty canisters).
- No wheeling the disposal system down the hall to drain fluid, as is needed with Stryker's Neptune.
- Takes up very little space.
- Saves money over the long run compared to solidifying fluid and disposing of canisters in biowaste, and having those bags shipped away.
- Safety – infection control; no exposure to waste through the direct-to drain system.
- Interventional Radiology – safe, fast method of ascites fluid draw and disposal. Less expensive per procedure than manual procedures using glass canisters.
- Razor and razor blade theory deriving perpetual annual revenue per machine for the sale of proprietary bifurcated filters and cleaning solution.

The Medical Waste Fluid Management System Market

Predictive's Skyline Medical division currently generates most of the company's revenue. Skyline is primarily engaged in the production and sale of the FDA-approved STREAMWAY System for automated, direct-to-drain medical fluid disposal and associated products.

According to MarketsandMarkets, the fluid management systems and accessories market currently stands at $8.5 billion and is projected to reach $16.1 B by 2025, exhibiting a CAGR of 13.6% during the forecast period.

Medical Waste Fluids Management System: Growth Drivers

The growth of this market is majorly driven by an increasing number of minimally invasive surgeries, technological advancements in fluid management systems, an increase in government funds and grants worldwide for endosurgical procedures, an increasing ESRD patient base, and a rising number of hospitals and investments in endoscopy and laparoscopy facilities.

Emerging markets and single-use disposable devices and accessories are expected to provide significant opportunities for providers of fluid management systems and accessories. Additionally, the rising number of minimally invasive cancer treatment procedures is expected to contribute to the demand for fluid management systems and accessories.

Emerging countries such as China, India, Brazil, Mexico, and South Korea offer significant growth opportunities to players operating in the global fluid management systems. This can be attributed to the increasing public and private initiatives undertaken by market shareholders across these countries, low regulatory barriers for trade, growing patient population, and other factors.

Industry Threats

The high cost of endosurgical procedures, a lack of awareness, and a dearth of qualified surgeons in the future may reduce industry growth.

The COVID-19 pandemic has resulted in a global healthcare crisis, causing a shift in healthcare delivery in most regions. Most nonessential procedures and in-hospital therapies, such as elective surgeries, are deferred to prevent the spread of infection and ease the toll on healthcare infrastructure. This has severely impacted revenues of the fluid management industry and is expected not to ease until 2022. However, we predict that the demand for these surgeries may rapidly return to normal as the global population is vaccinated against SARS-CoV-2. The increased demand for procedures will directly lead to an increase in demand in the waste fluids management industry, both in new systems and disposables.

Skyline: Recent Performance and Competitive Positioning

Skyline Medical currently accounts for the majority of Predictive Oncology's revenue through the sale of the STREAMWAY System. The company's business has been affected due to COVID led events that have not only affected the company's business process but have also put a dent on the company's capital and financial resources, affecting the company's recent year performance.

Apart from traditional medical fluid waste disposal methods, "cap and can", which involves disposing of fluid in canisters as waste, or simply draining the fluid into the sewage system (which can expose a worker to the fluids through aerosolization or splashing), there are automated waste disposal systems that are in direct competition with that of the STREAMWAY system. The competitor's products are well-positioned, having brand recognition and extensive market exposure. Some competing products are bundled with other products which can make it

difficult for Skyline Medical to have sales leverage, though STREAMWAY is generally the superior product. In general, these systems can save hospitals money over time but generally cost money upfront.

There are many companies that are well-positioned, having a diversified array of products in addition to intensive care disposable products. Stryker Corporation (NYSE: SYK), Zimmer Biomet (ZBH), Merit Medical Systems (NASDAQ: MMSI), Bemis Healthcare (acquired by a Kohlberg), Cardinal Health (NYSE: CAH), DeRoyal Industries, and MD Technologies are in direct competition with Skyline Medical, with fluid and waste management systems and products. These products range from additives for canisters to solidify the fluid before it is disposed, to both elaborate and primitive drainage systems. Given the competitiveness of the industry, it might take a great deal of effort to ramp Skyline's sales.

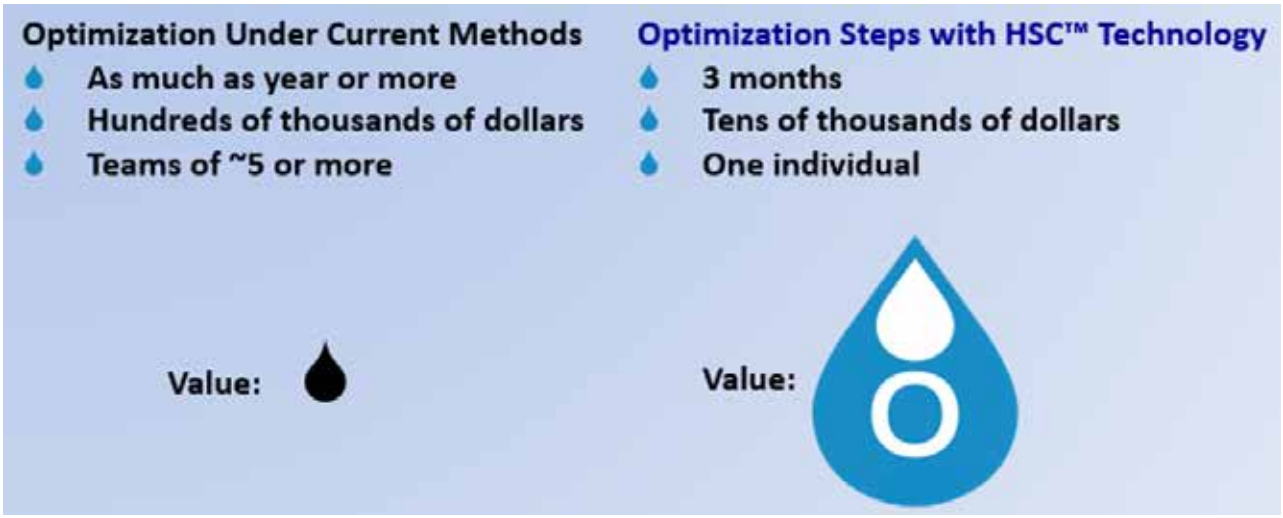
To deal with the fierce competition, Skyline is engaging enthusiastic distributors, increasing awareness at industry events, using trials for the STREAMWAY system before hospitals are required to buy later (the vast majority eventually do, according to Skyline), and targeting certain hospitals where operating rooms are being redone or are being built from the ground up. Alternatively, a sale of the Skyline business to a competitor could build value for both Skyline and the competitor, as bundled product offerings are difficult to compete against.

Soluble Biotech: Rapid Drug Formulation Services

Soluble Biotech, another subsidiary of Predictive Oncology, provides products and services for drug solubility improvements, stability studies, and protein production. Solubility is one of the important parameters in drug development that helps in achieving the desired concentration of drug in-vivo for the intended pharmacological response. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as for generic development. More than 40% NCEs (new chemical entities) developed in the pharmaceutical industry are practically insoluble in water, so solubility is a major challenge for drug formulation. Soluble provides optimized **formulations using FDA-approved additives** for vaccines, antibodies, peptides, and biologics. These services are being provided through the company's proprietary HSC technology.

The High Throughput Self-interaction Chromatography (HSC) is a self-contained automated system that conducts Chromatography screens on FDA-approved excipients for protein formulations. ***Many of the company's clients "have seen ten-fold and hundred-fold increases in their protein solubility while maintaining physical stability."*** This is based on work done for 30 different projects with 23 different companies in the industry, to date.

For biopharmaceutical clients of Soluble, this translates to faster development times and decreased costs. For academic collaborators, the key outcome is aiding in studies necessary to advance fundamental research in areas of unmet medical need.



Source: Soluble Biotech Website

The company's HSC technology helps in decreasing the cost, time, and manpower required to optimize formulations. In addition to this, Soluble also provides comprehensive protein stability analysis as well as protein solubility kits. Soluble Biotech also operates the purchased assets of BioDtech. BioDtech has developed processes and systems to identify and remove endotoxins from aqueous solutions. Last year the subsidiary moved its division to a new research park located in Birmingham, Alabama. This new facility quadruples the company's office as well as research space, with new state-of-the-art equipment in place in addition to its existing equipment, and increases the scope of the business, while adding substantial lines of businesses like protein degradation studies. The company is also planning to begin the development of an FDA-compliant cGMP facility to further support their pharmaceutical needs. The company has inked [1,2] a couple of sizable contracts with large pharmaceutical companies for protein expression, solubility, and stability. These companies remain unnamed as is standard without client approval and joint review of a press release. Management is quite optimistic and expects that Soluble will generate a considerable amount of revenue, *starting in the second half of fiscal year 2021*, using its proprietary, patented [3,4] technology.

Drug Formulation: Additives and Excipients

Different excipients that have been well tested, or for instance, are a modification or combination of excipients, have different testing requirements. This is because excipients, though meant to be "filler" or "inert," actually can have effects on the final formulation's efficacy and toxicity through direct interactions with the API (active pharmaceutical ingredient) or other excipients. Furthermore, excipients can affect drug absorption, distribution, metabolism, and elimination of the API, making carefully designed and well characterized formulations important. In fact, excipients typically make up a large majority of a formulation, up to 90% of a product's mass or volume.

Furthermore, it is estimated that about 40% of current drugs are poorly water soluble, and about 90% of those in development have shown poor aqueous solubility. As such, these drugs are in need of "functional" excipients, which might be referred to as additives, to improve solubility, pharmacokinetics, drug release and bioavailability, and other physico-chemical properties. These "functional excipients" are even used to reformulate existing drugs to produce more efficacious and more cost-effective products. Clearly, the additives and excipients that make up a drug can have profound effects such that a drug's properties are not just a function of the API. This importance

calls for rapid and accurate characterization of formulations, and this is why Soluble's products and services are important.

Soluble's HSC Approach

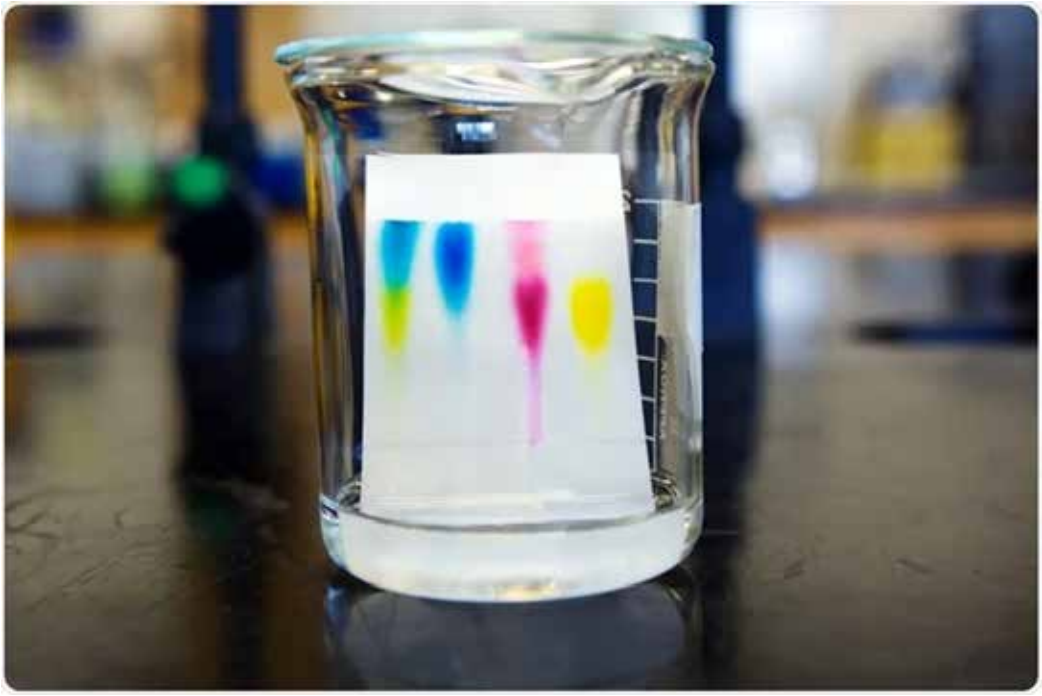
Soluble quickly screens for solubility through a calculable variable, B22 (the second virial coefficient), which describes the attraction or repulsion of pairs of particles, in this case protein-protein interactions. B22 has been shown to correlate well [5,6,7,8] with solubility, and as far as we can tell, no studies contradict these correlations. But what is this second virial coefficient?

Most people are familiar with the ideal gas law, PV=nRT, or PV=kT. The second virial coefficient is typically taught in context of how a fluid, such as a nonideal gas, deviates from the behavior of an ideal gas. In other words, in a fluid where particle interactions (in this case, gases) repel or attract each other, how does this particle interaction affect the relationship of PV=kT for what otherwise would have been an ideas gas (ideal fluid), where P is pressure, V is volume, k is a constant based on the fluid composition, and T is temperature? The math required to derive various coefficients will not be reviewed, but theoretically they are written as a Taylor series, with the second coefficient as the most important, and therefore can be a good approximation. There are other correction factors for deviation from ideal gas behavior, and there are various ways of writing the ideal gas law using correction factors. Basically, correction factors such as virial or van der Waals attempt to adjust the ideal gas relationship for particle interactions. This is relevant in liquid mixtures, too.

The advantage of measuring protein second virial coefficients is that the second virial coefficient value (B22) represents the sum of all of the interactions between protein molecules (i.e. charge, dipole-dipole, and even van der Waals interactions). This is relevant to Soluble Biotech because Soluble uses B22 calculations (second virial coefficients) to determine the protein-protein (particle-particle) attraction or repulsion, or protein-excipient combination interactions, to correlate with solubility. If proteins, or proteins and excipients repulse one another, they will likely be more soluble and not want to stay in an aggregated, solid state—indeed, these parameters correlate well. But how are the B22 values calculated? They require calculations using experiments in a process familiar to chemists called chromatography.

Chromatography

To understand HSC, one must first understand the basic principle of chromatography. There are many forms of chromatography, but the underlying principle is that chromatography is used to separate components in a mixture by passing them through a medium (typically a solid) using solution, whereby the different components of the mixture move at different rates. The classic example is that of black ink on a paper. When the paper is exposed to water and the water moves through it through capillary action, it smudges the ink into various colors, as the pigments in the ink dissolve at different rates.

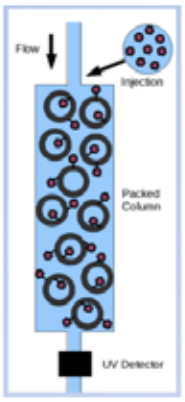


Source: AZO Life Sciences

There are many ways one can set up chromatography experiments, such as by using different mixtures (the ink), solutions (water), and media (paper). Soluble's founders, over the course of two decades of collaboration, created an automated form of column chromatography paired with AI (artificial neural network) for analyzing a massive number of potential interactions between proteins based on varying formulations (different amounts and types of excipients).

So how does this work, in layman's terms? Basically, this is a fancy form of chromatography where the ability of the protein to elute (deadsorb) from itself is determined. The protein itself is randomly bound to the stationary media, so that the unbound protein can be washed from the bound protein. Then, B22 values are calculated from the self-interaction chromatography (SIC) experiment, which correlate well with other approaches to determine B22 values. This whole process is done in an automated machine with several different formulations, and then the AI takes the data of a few experiments to solve a large number of experiments through an interactive process of calculating and comparing to subsequently observed B22 values, similarly to the iterative process of Helomics' PeDAL. Soluble's academic publications show that the AI does an extremely good job of predicting many formulation B22 values using the data of a handful of experiments. Then, the B22 values from in-silico predictions are experimentally validated using the HSC and then used to select optimal formulations for solubility (solubility and B22 values have been shown to be well correlated), and those few "likely" optimized formulations can be empirically tested. This basically means that **Soluble can accurately predict the solubility of a wide variety of formulations it has not yet tested, just based on a handful of automated tests** in an iterative process. This massive amount of data generated can help maximize solubility in a cost-efficient and time-efficient manner.

Self-Interaction Chromatography Method to Determine B22 Values



- Covalently bind protein of interest to chromatography media (stationary phase) and load protein-bound media into a micro-column
- Flow formulation of interest over the column using HSC system
- Inject protein into formulation flow and measure volume required to elute protein (retention volume) as it interacts with the same protein covalently bound to column media
- Calculate retention factors and B22 values of proteins in different formulations
- High B22 values indicate that the formulations promote protein solubility

Source: Soluble Biotech Website

There are a few different reasons the HSC technology has a leg up on other approaches. First, the proprietary AI explores a vast number of formulations just based on a few. Second, the self-interacting chromatography approach lends itself to high throughput experiments, since once set up, the chromatographic column (with covalently bonded protein to the stationary media) can be repeatedly used. Third, the self-interacting chromatography allows for "direct measurement of interactions between different protein molecules, which cannot be accomplished using any conventional characterization methods." This appears to be especially useful for peptides or perhaps other more complex proteins. According to Johnson et al.,

> *"In a recent overview of pharmaceutical drug screening techniques (18), three methods of solubility screening were identified: UV absorption, nephelometry and flow cytometry. These methods, developed for analysis of small molecules, are used to calculate current or potential solubility of a specific drug formulation and can be performed in a high throughput manner. However, they do not directly quantify the protein self-interactions that influence solubility and aggregation of protein therapeutic molecules."*

One key issue in protein therapeutics' efficacy is the fraction of protein that remains stable or is not broken down into a form where it is at best, useless, or worse, allergenic. Protein denaturation is a well understood concept where proteins can twist, break, or be modified and lose their original structure (quaternary structure, tertiary structure, and/or secondary structure). This can be caused by external stress (such as in nano milling), exposure to a solvent, acid, base, heat, or even an organic salt. Denaturation can also occur when a protein in solution is exposed to a solution interface. For instance, a protein might denature as it is exposed on the outside of a droplet as that solution is spray dried to make a fine powder. While HSC may help identify excipients for optimal formulation, work still must be done to ensure protein stability and minimization of denaturation, as well as bioavailability.

From Solubility to Bioavailability

The goal in improving solubility is to increase bioavailability, both for increasing the amount of drug that actually "does its job," as well as decreasing potential side effects due to inactive API/drug (which may have unintended interactions in-vivo) and decreasing costs for manufacturing. The Biopharmaceutics Classification System (BCS) identified two primary factors considered to influence bioavailability: aqueous solubility and membrane permeability. There are many different approaches to improving bioavailability and drug absorption that do not have as much to do with simply choosing excipients; for formulations, there are both excipients as well as the process or technology by which the therapy is manufactured. Industry techniques such as spray drying, spray freeze drying, thin film freezing, nano milling, lipid particle encapsulation, micronization, other complexes, loading onto polymers, and other approaches can accomplish similar goals of improving bioavailability or other related parameters like HSC does. In our opinion, there is not necessarily any "one size fits all" solution.

Other competing platforms may offer better solubility or bioavailability in some cases, depending on the application. However, further complicating the competitive landscape are the costs of these formulation technologies, as these may be licensed, more complicated technologies. In some cases, simpler solutions may be necessary, such as well-known excipients. Some companies may prefer to license their formulation technologies for milestone payments and revenue sharing.

For instance, TFF Pharmaceuticals (NASDAQ: TFFP) uses a process called thin film freezing (TFF) to produce amorphous, tiny particles of drug, where aggregation is dealt with as the proteins or molecules are not crystallized or oriented in an orderly manner. The process basically freezes the formulation liquid while it is dripping onto a surface such that the order of the formulation is being broken just as it is freezing. Then, the thin films that are frozen are lyophilized. TFF has shown that this process can even be used to lyophilize and aerosolize therapies like solid lipid nanoparticle (SLN) siRNA, with improved stability and passing through to the deep lung, compared with spray drying. This process is optimal for inhalable formulations for drug dosing directly to the deep lung, where the fine powder, amorphous state allows for much better transportation to the alveoli, adsorption to the alveoli barrier, and absorption and dissolving at the air-lung interface. The process is also optimal for lyophilizing complex proteins and other complicated, delicate therapies that would benefit in elimination of the (very) cold supply and distribution chain, such as vaccines or bacteriophages.

Other competing solubility-improving technologies include Mountain Valley MD Holdings, Inc. (OTCMKTS: MVMDF), which has a few patents for desiccated liposomal technology for encapsulating and drying drugs in a lipid particle, for oral or intramuscular delivery, though there seems to be less information on this process than what TFF has provided with their technology, in patents and peer-reviewed journal articles. Regardless, there are many bioavailability process technologies that can be developed and pursued.

For vaccines, an example of a proprietary formulation includes Novavax, Inc.'s (NASDAQ: NVAX) recombinant nanoparticle vaccine technology, which basically uses genetic engineering and a proprietary cell line to produce antigens for a virus that have the correct glycosylation as well as quaternary and tertiary structures. This means that the antigens, the immunogenic proteins, more closely resemble the proteins encountered during viral infection. Those proteins/antigens are then put together in a nanoparticle resembling the size of a virus. While this application is probably best suited for the vaccines Novavax is working on and no other types of drugs, and therefore does not really compete with Soluble's HSC technology, it serves as a good example of the creativity that can take place in formulations.

Overall, our view is that different approaches to optimizing formulations of therapies will have strengths and weaknesses depending on the application. As Soluble's approach can decrease costs and time while improving low-cost formulations' solubility and stability using common excipients, we are fairly confident that there will be reasonable demand for the company's services.

Competition Profiles

Competition in AI-Driven Pharmaceutical and Biotechnology Oncology Research

1. Turbine.AI

   Turbine is a Europe-based simulation-driven drug discovery company. It has built cell models that depict how cancer works on a molecular level and tests millions of potential drugs using its AI technology.

   Turbine uses in-silico experiments to test an infinite number of interventions on simulated cells that reflect the molecular diversity of cancer cells accurately. In the past, the company has secured partnerships with various big pharma like Bayer building their own stream of targets with a special focus on overcoming DDR (DNA damage repair) Inhibitors resistance by working to create PARP inhibitors.

   Predictive Oncology, on the other hand, uses an in-vivo in addition to an in-silico approach to testing various drugs against a panel of tumors, which is most likely a more efficient and accurate process and reduces the chances of errors. Given the company's assets in ovarian cancer, we believe that the extent of competition between the two companies is quite limited.

2. Lantern Pharma (NASDAQ: LTRN)

   Lantern Pharma is a US-based oncology pharma company that leverages AI and machine learning to develop personalized and targeted therapies. Lantern uses its RADR platform (Response Algorithm for Drug Positioning & Rescue) to enable more efficient drug positioning and repurposing. RADR "uses transcriptome data, genomic data and drug sensitivity data from a wide range of curated sources that are continually being analyzed, monitored and updated," through "(i) publicly available databases (ii) data from commercial clinical studies and trials and (iii) our proprietary data generated from ex vivo 3D tumor models specific to drug-tumor interactions." The company has a healthy pipeline with a few drug candidates in clinical trials and has established a partnership with the Developmental Therapies Branch of the NCI to analyze gene signatures in preclinical and clinical research to help predict patient responses. It is somewhat concerning that Lantern uses data from the NCI60 cell lines to inform its RADR platform, though gathering multi-omic data in clinical trials should help guide each of its therapeutic candidates forward and better tailor the machine learning models. Even though Lantern Pharma's strategy is quite similar to that of Helomics and might pose a direct competition to Predictive Oncology, the database that Predictive has developed over the years acts as a moat for the company and will enable it to leverage its assets in drug discovery. In addition, the issue of tumor heterogeneity and the difficulty obtaining patient tumors as opposed to using standard cell lines poses a problem for Lantern's data generation abilities. Publicly available sources are also available to Predictive Oncology.

3. Indivumed

   Indivumed is an integrated global oncology company engaged in precision medicine as well as contract research services. The company uses its "Indivutype" multi-omic database and AI data analytics platform to discover novel targets. The database includes genomic, transcriptomic, proteomic, and phosphoproteomic data, which is an approach that more closely mirrors Predictive's approach, compared with other competition. The company is a new entrant in AI-driven R&D and drug discovery and possesses only data and FFPE samples, not any live cells; Indivumed uses an in-silico approach as compared to the iterative, live sample machine learning approach used by Predictive Oncology. The company recently launched the nRavel AI platform for cancer research and drug development, which currently includes six "toolboxes," including immuno-oncology, pathways and signaling, biomarkers, genomics, signatures, clinical analytics.

4. Insilico Medicine

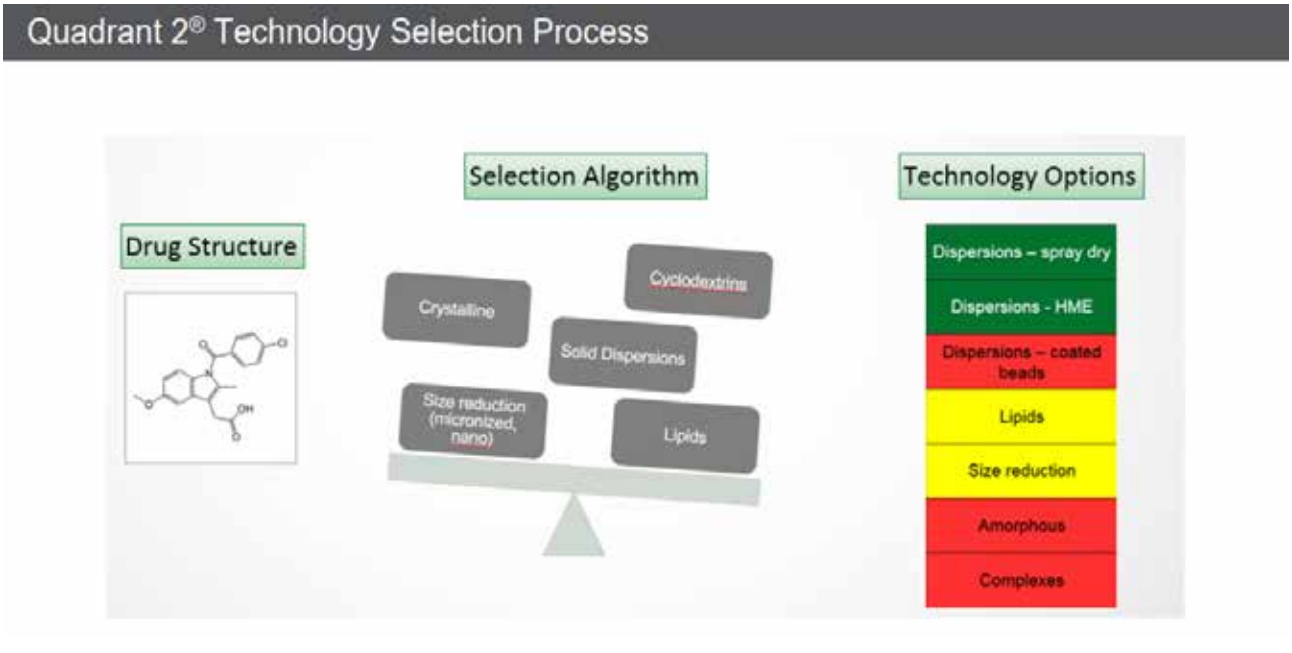
   Insilico is a biotechnology company combining genomics, artificial intelligence, and machine learning for in-silico drug discovery. Insilico has developed partnerships for various indications spanning from oncology to fibrosis, anti-infectives, and immunology. The company has over 150 academic and industry collaborations worldwide. Their approach uses AI platforms that discover and identify novel targets, generate novel molecules, and design and predict clinical trials. Given the vast array of services with success in drug discovery and development, Insilico holds a prominent position in the AI-driven R&D industry.

There are various other companies that focus on AI-driven R&D to improve and guide development of therapies in oncology such as immunotherapy, which is substantially different than what Predictive Oncology appears to be focusing on. Even though there are well-established players like Insilico and BenevolentAI, there is a large playing field for Predictive Oncology to position themselves in, given their unique assets, the size of the overall industry, the complexity of biology and clinical research, and the industry's rapid growth rate.

Competition in Formulation and Solubility of Drugs

1. Thermo Fisher (Pantheon)

   Thermo Fisher, through Pantheon, has an offering called Quadrant 2 that uses proprietary algorithms incorporating a variety of different computational methods including Quantum mechanics, Molecular Dynamics, QSAR, ADMET, statistical analysis, and internally developed models. This program also uses the compound's molecular structure and chemical characteristics as well as the clinical and biological target to advise on optimized formulations, including the process technology selection (i.e., spray drying) and excipient selection. This technology has been used to help formulate over 200 drugs.



Source: DDF Summit

2. Emerson Resources (Pace Analytical Life Sciences)

   Emerson Resources, through its subsidiary, Pace Analytical Life Sciences, provides specialty excipients, MarCoat and PlasACRYL for improved enteric release, as well as formulation optimization, including drug-excipient compatibility studies, differential scanning calorimetry (DSC), powder x-ray diffraction (XRD) polarized light microscopy (PLM), scanning electron microscopy (SEM), particle size analysis (LLS), forced-degradation studies, solubility determination (aqueous/solvents), intrinsic dissolution (paddle over disk), texture analysis, bulk powder characterization, stability studies, as well as various process technology optimization services including but not limited to spray drying, milling, blending, and encapsulation.

3. TFF Pharmaceuticals as well as Mountain Valley MD were described in prior sections and in some cases would be considered competition. Our opinion is that these solutions will mostly be used in inhalable therapies and in cases where complex therapies or therapies requiring cold-chain transportation and storage would otherwise be necessary, whereas HSC technology potentially would be less expensive and worthwhile for more "typical" solutions. There are several other competitors in this space, and it appears that Soluble's low-cost solutions and rapid turnaround time will be key in driving industry adoption.

Management Profile

Predictive Oncology has an experienced management and board team with years of experience working in the pharmaceutical and biotechnology industry. The industry experience of the management team is essential for the company's long-term goal of becoming a leader in precision medicine.

J. Melville ("Mel") Engle **Chief Executive Officer and Chairman of the Board**	Mr. Engle joined POAI's Board of Directors in October 2016 and was appointed Chairman of the Board in January 2020. In March 2021, Mr. Engle replaced Dr. Carl Schwartz (retired) as the CEO of the company. Mr. Engle has over 20 years of experience in leadership roles in both the biotechnology and healthcare industries. He has extensive experience in turning companies around and driving sales. He has served in top-level capacities, e.g., President, CEO, Director, Chairman of the Board, CFO, Regional Director (North America), Managing Director (Canada), and Senior VP of Sales (US) and has launched hundreds of products. Mr. Engle holds a BS in Accounting from the University of Colorado and an MBA in Finance from the University of Southern California. Mr. Engle previously served as an SVP, Director of Financial Planning, Controller, and CFO at Allergan before his tenure as CEO, Chairman, and President at Anika Therapeutics. Mr. Engle then served as CEO and Chairman at DEY L.P., a $600 million respiratory pharmaceuticals company previously owned by Merck Generics Group, which was sold to Mylan. Mr. Engle's later served as CEO of Raydiance Inc., before his tenure as CEO and Chairman of Thermogenesis (NASDAQ: THMO). Since 2012, Mr. Engle consulted for CEOs and business owners, which included coaching, development, problem solving, decision making, strategic leadership, succession planning, among other areas. Mr. Engle currently also serves as a Director at WindGap Medical.
Bob Myers **Chief Financial Officer**	Mr. Myers was appointed as the company's Chief Financial Officer in 2012. He has over 40 years of experience in multiple industries focusing on medical devices, service, and manufacturing, and prior to joining the company was a financial contractor represented by various contracting firms in the Minneapolis area. He has spent much of his career as a Chief Financial Officer and/or Controller. Mr. Myers was a contract CFO at Disetronic Medical, contract Corporate Controller for Diametric Medical Devices, and contract CFO for Cannon Equipment. Previously he held executive positions with American Express, Capitol Distributors, and International Creative Management and was a public accountant with the international firm of Laventhol & Horwath. Mr. Myers has an MBA in Finance from Adelphi University and a BBA in Public Accounting from Hofstra University.
Nancy Chung-Welch, Ph.D **Director**	Dr. Chung-Welch was appointed to the Board on July 9, 2020. Dr. Chung-Welch is currently an independent consultant advising life science companies and their institutional investors on life science companies, technologies, and industries with an emphasis on the research product/tools market. Previously she was a Director, Business Development at Cell Signaling Technology and was Director, Business Development at Thermo Fisher Scientific and Technical Marketing Manager for Fisher Scientific. She has over 25 years of marketing and business development experience in the life sciences market. She received her Ph.D. in Vascular Physiology and Cell Biology from Boston University.
Christina Jenkins, M.D. **Director**	Dr. Jenkins was appointed to the Board in April of 2021. She also serves as a Director for Independence Health Group, a Board Observer for Madorra, and an advisory board member to multiple value-generating healthcare companies. Dr. Jenkins is also a Venture Partner at Portfolia and at Phoenix Venture Partners Seed Fund, where she leads investments and provides post-investment advisory support to seed-to-revenue stage digital health and medical device companies focused on women's health as well as other underserved markets. She is a member of the Kauffman Fellows, a global leadership development program for venture capitalists. Prior to her investing roles, Dr. Jenkins was the the founder and CEO of OneCity Health Services, a subsidiary of NYC Health + Hospitals (H+H). There, she set the vision and strategy to reimagine care delivery and accelerate population health and value-based payment (financial risk) capabilities for 1 million lives. During her tenure, she built a high-performing team from 2 to 130, earned $350M in revenues over her tenure, formed 200+ new organizational partnerships, designed and scaled new integrated care models and technology platforms, and drove sustained improvements in health outcomes.
Daniel E. Handley M.S., Ph.D. **Director**	Dr. Handley was appointed to the Board on February 19, 2020. He serves as a Professor and the Director of the Clinical and Translational Genome Research Institute of Southern California University of Health Sciences. Previously, he was the Chief Scientific Officer of the Clinical and Translational Genome Research Institute. He holds a B.A. in Biophysics from Johns Hopkins University, an M.S. in Logic and Computation from Carnegie Mellon University, and a Ph.D. in Human Genetics from the University of Pittsburgh.

Chuck Nuzum **Director**	Mr. Nuzum was appointed to the Board on July 9, 2020. Mr. Nuzum has extensive experience as a CFO that ranges from private start-ups to large publicly-traded companies. Mr. Nuzum presently provides financial consulting services on a project basis to companies such as McKesson, BioMarin, AutoDesk and Squire Patton Boggs, mentors start-up companies and serves on the Board of Directors of several companies. Previously he was co-founder and CFO of the Tyburn Group, a financial services company that creates and delivers prepaid payroll and general-purpose card programs for customers. For the four years prior, Mr. Nuzum served as the Controller of Dey, L.P., a large pharmaceutical manufacturing subsidiary of Merck KGaA. Prior to that he was co-founder, Executive Vice President and CFO of SVC Financials Services, one of the first companies in the field to integrate a mobile money solution for global distribution, Vice President of Finance and Administration at Tiburon, Inc., a leader in public safety and justice information systems, and CFO of Winebid.com the world's leading e-commerce wine auction company. For more than two decades, Mr. Nuzum was CFO of Loomis Fargo & Co., the well-known international provider of ATM systems, armored cars, and other security services. Mr. Nuzum, a Certified Public Accountant, earned his BA at the University of Washington at Seattle.
Gregory S. St. Clair **Director**	Mr. St. Clair was appointed to the Board on July 9, 2020. Mr. St. Clair is the Founder and Managing Member of SunStone Consulting, LLC, a healthcare consulting firm that serves healthcare providers throughout the United States since 2002. As frequently sought experts on issues related to compliance, reimbursement and revenue integrity, Mr. St. Clair and his team are constantly on-call to assist clients as they address financial challenges through creative solutions to the nation's health systems. Previously, Mr. St. Clair worked as a national vice president for CGI, ImrGlobal, and Orion Consulting and as national director for Coopers & Lybrand. He holds a B.S. in both Accounting and Finance from Juniata College in Huntington, Pennsylvania.

Future Outlook

- AI-driven R&D companies have to go through a long incubation period to develop their technology and/or establish a knowledge base, if applicable. Predictive Oncology is nearing the end of that phase of the business cycle, and with a unique set of assets at their disposal, it seems the company is in a sweet spot to monetize their assets, but exactly when and how is still somewhat unclear.

- The company has collaborated with UPMC-Magee to establish robust data for their AI-driven approach in treating ovarian cancer. The company recently announced that it has successfully generated high-quality genomic and transcriptomic data while gathering historical outcome data from UPMC-Magee. Additional sequencing and data generation milestones will help the company's drug repurposing/repositioning program which it recently initiated, as well as other potential programs for potential contracts with pharma.

- Skyline Medical subsidiary is the only division that generates significant revenue, cushioning the company's cash burn rate. It still is generating operating losses close to its revenue. A sale of the business to a competitor could monetize this asset and provide Predictive with additional resources to drive its internal programs in oncology and AI. Additionally, Soluble Biotech is expected to generate significant revenues later this year, which will help offset Predictive's losses.

- The company's internal drug repurposing program may require additional resources. However, this will prove the platform's potential to the industry and make way for partnerships and contract revenue, using PeDAL.

- In the long term, if the company is successful in driving a robust pipeline and becoming a full-fledged AI drug discovery incubating platform, Predictive Oncology could demand a valuation more like Schrödinger or Exscientia.

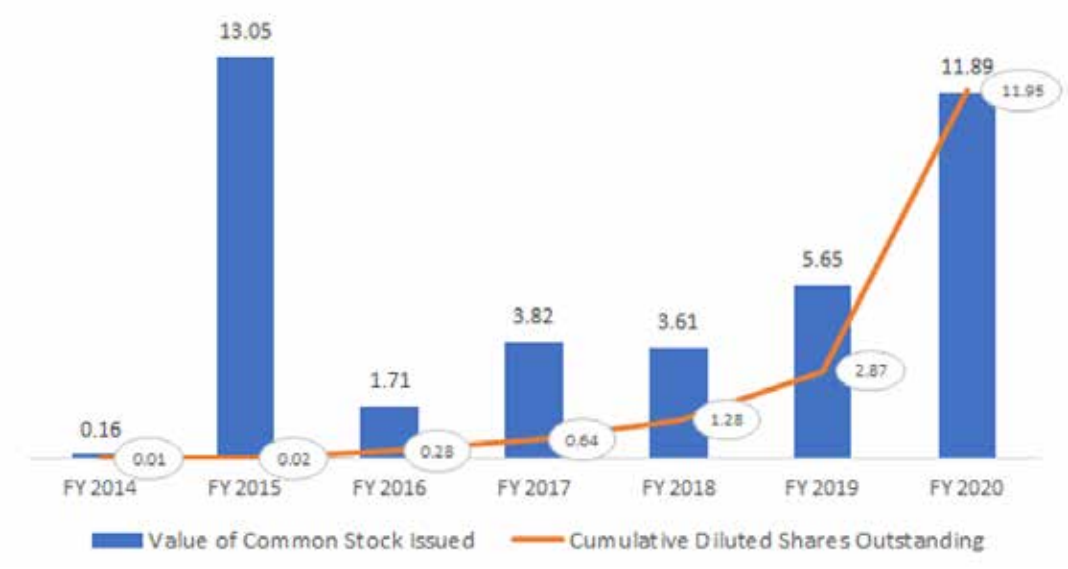


Exhibit: Total number and value ($ millions) of shares issued, Source: Quantum Research

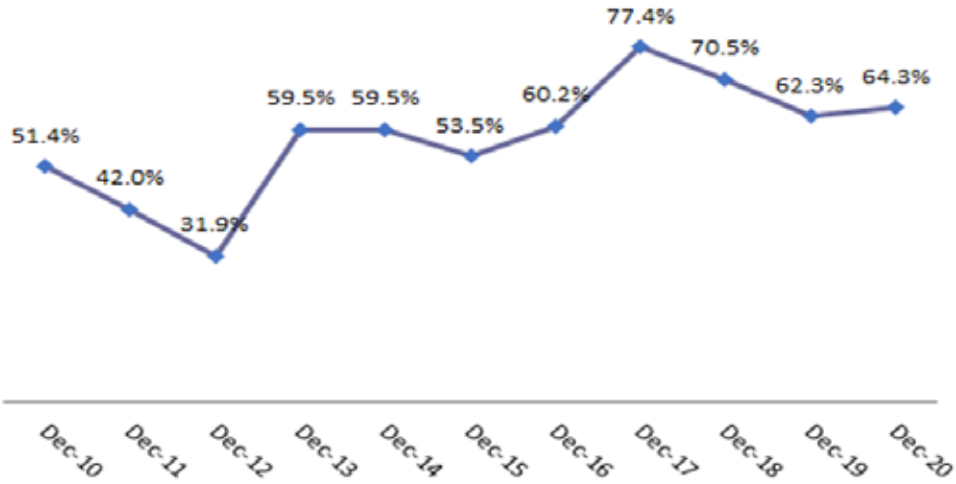


Exhibit: Gross Margins, Source: Quantum Research

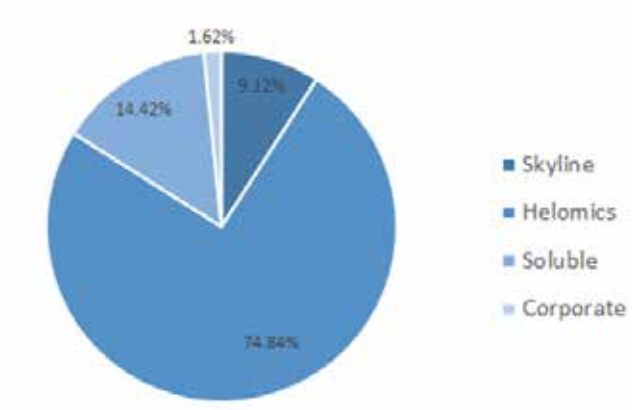


Exhibit: Distribution of assets among different subsidiaries, Source: Quantum Research Group, LLC

Risk Factors

Predictive Oncology faces a number of common industry risks that must be taken into consideration, though being somewhat of a pick-and-shovel for the pharma R&D industry ameliorates some of the risks of preclinical, clinical, and regulatory risks. Risks include, but are not limited to:

1. **Industry, regulatory, and technological Risks:** Predictive Oncology operates in an industry that is characterized by intense competition, high regulatory oversight, and rapid technological changes. These risks can majorly affect the business and can often lead to business failure. POAI faces uncertainty whether it would:
    - Succeed in uncertain markets.
    - Respond effectively to competitive pressures.
    - Continue to develop and upgrade its products.

2. **Limited experience in precision medicine services:** Predictive Oncology has been in operation for only two years with respect to experience in precision medicine, and the company has not generated any significant revenue in this area yet. Their limited corporate experience makes their ability to implement a successful business plan in precision medicine unproven.

3. **Cash flow negative:** As Predictive has limited revenue and is performing significant R&D, it requires outside sources of cash to fund its operations. It has committed and will likely continue to commit significant capital to R&D or acquiring other synergistic early-stage companies, etc. It is possible that all its cash and revenues may be spent, and the company may be required to raise additional capital to continue its operations. Failure to obtain funding may also lead to failure of the business.

4. **High litigation costs:** Companies such as Predictive Oncology face the risk being sued for product liability, or errors and omissions liability. The company could face substantial liabilities that could exceed its resources and potentially lead to the ceasing of its operations.

5. **COVID-19 impact:** COVID-19 pandemic affected businesses all over the world. It has negatively affected Predictive on both fronts, i.e., research and products. Factors such as reduced staff, disruption of the supply chain, and reduced production may have adversely affected both the research and product divisions of Predictive Oncology. The revenue-generating Skyline business was also affected significantly because the demand for their STREAMWAY systems was impacted; hospitals all over the world shifted their focus and resources to treating COVID patients and preventing the spread of the virus. In addition, COVID may have also impacted the company's capital and financial resources, including its overall liquidity position and outlook.

6. **Nasdaq delisting risk:** Currently, POAI shares trade near $1.00. Nasdaq has a $1 minimum closing bid requirement that states "If a company trades for 30 consecutive business days below the $1.00 minimum closing bid price requirement, Nasdaq will send a deficiency notice to the company…" If the company is delisted, it will adversely affect the liquidity of the shares. Although Nasdaq accepts reverse stock splits as a method to regain compliance, this method may undermine investor confidence in the stock. As of the date hereof, POAI shares remain listed on Nasdaq.

Valuation and Scenario Analysis

Amid the growing trend in the pharmaceutical industry to use AI during the R&D process, Predictive Oncology is well-positioned to make its mark, especially with a focus on oncology, and in particular ovarian cancer, where there are fewer competitors, and none that we are aware of that can boast comparable assets in both ovarian cancer and AI.

As POAI is engaged in two business segments, i.e., research and products, we have used a hybrid sum-of-the-parts valuation method to arrive at our calculated valuation.

For the research division, we have used a relative valuation methodology to estimate the value of its R&D/AI business. Predictive's research business currently does not generate any revenues, though it does include somewhat tangible assets in the lab with equipment, personnel, database, and tumor bank. As research, and in the future, contract research, is its primary activity, we have used a P/R&D multiple for estimating its fair value compared with certain competitors. We also use a P/(database of patient data samples) along with a conservative factor (0.5) to value the tangible data and sample assets when compared with Foundation Medicine, using the size of Foundation's/Roche's database 5 years into the future given the current sampling rate.

We used Lantern Pharma, BioXcel (NASDAQ: BTAI), Schrödinger (NASDAQ: SDGR), Foundation Medicine, and Exscientia as the closest comparable to estimate a hybrid comparison of value.

The relative valuation model is shown below:

Company Comparables

Comparable Companies (P/R&D)	Market Cap	R&D Exp.	P/R&D ($mm)	Weight	Weighted Expected Value ($mm)
Lantern Pharma	$172.2	$2.2	76.8	0.25	40.3
BioXcel	$860.4	$57.7	14.9	0.10	3.1
Schrödinger	$5,070.0	64.70	78.37	0.20	32.91
Comparable Companies (P/program)	**Market Cap**	**Programs**	**P/Program ($mm)**	**Weight**	**Weighted Expected Value ($mm)**
Exscientia* (assumes 1 program, 50% chance)	$650.0	20	32.50	0.25	4.06
Comparable Companies (P/patient samples)	**Market Cap**	**Sample # (5yr)**	**P/Sample ($mm)**	**Weight**	**Weighted Expected Value ($mm)**
Foundation Medicine (40,000 FFPE currently)	$5,300.0	920,000	0.006	0.20	115.22
Total Expected Value (P/R&D)	-	-	-	1.00	195.63

Source: Quantum Research Estimates, Company Reports, Other Reported Information
**some sources estimate that Exscientia is valued up to $2 billion*

P/R&D Summary:

Multiples Analysis:	
FY2023E R&D Expense ($mm)	2.10
P/R&D	66.11
FY 2023E Market Cap ($mm)	**138.82**
Equity Value ($mm)	**104.97**

The total relative value for Predictive's TumorGenesis and PeDAL assets is calculated to be $195.63 million.

On comparing with its closest peers using P/R&D and taking informed estimates about the weight of various comparables, we arrived at a P/R&D multiple of 66.11. In our model, we conservatively estimated that Predictive Oncology will need to spend $2.1 million as an R&D expense in 2023. Applying the P/R&D multiple of 66.11 to the R&D expense of $2.1 million, we get a 2023E market cap of $138.82 million. We then used a discount rate of 15% to arrive at the 2021 intrinsic market value of the research division at $104.97 million.

For comparing with peers with similar types of future pipelines and data/tangible assets, we assumed Predictive oncology would have a 50% chance of inking one R&D drug discovery contract with another pharma company within the near future, and we valued that R&D contract on par with 1/20th of Exscientia's lowest reported market capitalization, $650 million. For the database and tangible lab and tumor sample assets, we valued the samples proportionally to Foundation Medicine's total samples in 5 years, expected to be 920,000 samples. We used 40,000 samples (of FFPE) for Predictive's total instead of the 150,000 longitudinal patient data. This is somewhat an apples-to-oranges comparison as Helomics is selling actionable models, not data, and their data is in general more robust than Foundation's data. Helomics is arguably more advanced than Foundation was when Roche acquired it. The company has a similarly sized library of samples with deeper, more robust data. Furthermore, it is important to note that we conservatively assume Helomics will not increase its database within the next 5 years, though the company has a network of 1400 clinicians that have validated the ChemoFX platform and continue to use it. Using this proportional comparison, we also assign a factor of 0.5 to further remain conservative in our estimates of Predictive Oncology's database.

For valuing the company's product sales, i.e., the "products" division, we have used a more traditional discounted cash flow (DCF) approach to determine the NPV of projected unlevered FCF using a discount rate of 15.3%. The rate reflects the relative risk associated with these cash flows, as well as the rates that security holders could expect to realize from alternative investment opportunities. We took a long-term growth rate of 3% which is similar to the overall economy and the biotechnology industry.

Below is the snapshot of the DCF analysis that we performed for the medical products division. It is a four-staged DCF valuation model with varying growth rates that determines the equity value of products division using projected Free Cash Flows.

	Actual Period		First Stage of Valuation			Second Stage of Valuation					
	FY2019 A	FY2020 A	FY2021 E	FY2022 E	FY2023 E	FY2024 E	FY2025 E	FY2026 E	FY2027 E	FY2028 E	FY2029 E
Revenues	1.363	1.188	3.484	4.363	5.261	6.496	7.930	9.666	11.676	14.116	16.738
EBITDA	(3.087)	(1.581)	(2.990)	(2.437)	(1.360)	(0.380)	0.555	1.643	4.320	5.223	6.193
EBIT	(3.135)	(1.804)	(3.213)	(2.659)	(1.582)	(0.602)	0.333	1.421	4.098	5.001	5.971
Tax Rate	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210
Net Operating Profit After Tax	(3.135)	(1.804)	(3.213)	(2.659)	(1.582)	(0.602)	0.263	1.122	3.237	3.951	4.717
Depreciation & Amortisation	0.048	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222
Working Capital Change	-	-	-	-	-	-	-	-	-	-	-
Operating Cash Flow	(3.087)	(1.581)	(2.990)	(2.437)	(1.360)	(0.380)	0.485	1.345	3.460	4.173	4.939
Capex	-	-	-	-	-	-	-	-	-	-	-
FCF	(3.087)	(1.581)	(2.990)	(2.437)	(1.360)	(0.380)	0.485	1.345	3.460	4.173	4.939

Terminal Value	
Sum of PV of FCF for explicit forecast	9
WACC	15.3%
Long term growth in EBIT	3%
Present Value of terminal value	13
Terminal Value as % of Total Value	59%

Calculated Equity Value	
Enterprise Value	23
- Debt	-
+ Cash	67
Net Debt	(67)
Equity Value	90

Intrinsic Value	
Equity Value	90
Diluted Shares	89
Intrinsic Value	$1.01

Intrinsic Value	LTGR					
	1.01	2.00%	2.5%	3.00%	3.5%	4.00%
WACC	10.00%	1.4580355	1.4955899	1.5385357	1.5881169	1.6459925
	12%	1.2128879	1.2312661	1.2517017	1.2745578	1.3002882
	15.00%	1.0120348	1.0194183	1.0274247	1.0361353	1.0456459
	18%	0.9045560	0.9079098	0.9114912	0.9153238	0.9194344
	20.00%	0.8593758	0.8614537	0.8636565	0.8659956	0.8684838

CAPM Assumptions	
Ke	15.3%
RFR	1.6%
Beta	1.96
Mkt Rp	7.0%

Using the DCF approach, we arrived at an intrinsic market **value of the devices division at $89.6 M**. We also performed a sensitivity analysis for different WACC and long-term growth rates (LTGR) to provide a sensitivity analysis of the equity value.

Sum of the Parts

To estimate the intrinsic value of POAI shares, we then combined both the "divisions." The summary of both divisions is shown below.

R&D (Helomics and TumorGenesis)	
Valuation Approach Used	Relative Valuation
Relative Multiple Used	P/R&D, P/Program, P/Sample
Discount Rate	15.00%

Multiples Analysis:	
FY2023E R&D Expense ($mm)	2.10
P/R&D	66.11
FY 2023E Market Cap, 55% weight ($mm)	138.82
Discounted Equity Value, 55% weight ($mm)	57.73
Market Cap, 45% weight, Database/Pipeline	119.28
Equity Value (weighted average, $mm)	177.01

Products/Services (Skyline and Soluble and Helomics Testing)	
Valuation Approach Used	Absolute/NPV
WACC	15.30%
Long term Growth rate	3.00%

Net Present Value	
Sum of PV of FCF for explicit forecast	9.27
Present Value of Terminal Value	13.43
Enterprise Value of NPV ($mm)	22.70
Net Debt ($mm)	0.00
Cash ($mm)	66.94
Equity Value	89.64

$POAI Intrinsic Value	
Equity Value	266.65
Diluted Shares	88.63
Intrinsic Value	$3.01

Source: Quantum Research Estimates, Company Report

Valuation Breakdown Summary:

	Business Segment	Equity Value ($mm)	Value Per Share ($)	% of Total	Rationale
Helomics	(R&D)	177.01	2.00	67%	Relative Valuation Methodology: P/R&D multiple of 66, comparisons to Exscientia's pipeline and Foundation's database (with significant conservative factor)
Tumor Genesis					
Skyline Medical	(Products)	50.00	1.01	33%	DCF Methodology: terminal growth rate of 3% and WAAC of 15.3%. Variable short term growth rates (10-20%).
Soluble Biotech					
Total		**227.01**	**$3.01**	**100%**	

Thus, the **base case intrinsic value for POAI shares is $3.01. We performed a similar analysis for the bull case as well as the bear case.**

The bull case scenario incorporates a more optimistic value of its research division, where we expect that Soluble and Helomics will strike CRO deals with pharma companies. The bull case also incorporates a more optimistic revenue projection for its devices division. **The bull case value for POAI arrived at $5.30.**

In the bear case scenario, we assume that POAI would not be able to secure any meaningful CRO contracts from pharma companies. We also assumed a sluggish growth rate for its medical division, as competition will take over it. **The bear case value for POAI arrived at $0.85.**

	Intrinsic Value	Probability	Expected Value
Bull Case	$5.30	40%	$2.12
Base Case	$3.01	40%	$1.20
Bear Case	$0.85	20%	$0.17
		Price Target	**$3.49**

Considering the base case, bull case, and the bear case scenario, and making informed estimates of expected value, **we are initiating coverage on POAI with a 12-month price target of $3.49 per share**, using a hybrid SOTP valuation as our preferred methodology for valuing the stock. It incorporates a long-term view of the company's operations and will be highly dependent upon the contracts the company inks with potential partners and will be adjusted accordingly based upon future contracts, which will validate the company's strategy.

Helomics and Tumor Genesis Contributes ~67% of SOTP Value.

Even though both Helomics and TumorGenesis have minimal book value currently, we believe that the companies'

AI-driven R&D segment will play an important role in creation of shareholder value going forward. It has gathered a specialized set of assets with proven applicability which may garner the attention of big pharma names. We expect that management could ink research agreements with pharma companies later this year or early next year. The company's recently initiated drug repurposing program in ovarian cancer might prove to be a major asset, potentially out-licensable, for the company.

Skyline Medical and Soluble Biotech Contributes ~ 33% of SOTP Value.

Skyline's business has been generating close to ~95% of the company's revenue. On a gross basis, Skyline is generating profit but is affected by large operating expenses. Due to COVID-19, there has been a decrease in the company's operating expenses and we expect that the savings, due to decrease in expenses, would persist to an extent, increasing the margins of the company. Soluble Biotech's drug stability and endotoxin removing solutions should start generating considerable revenue starting this year, as well as drug stability studies and evaluations, and potentially additional NIH/SBIR grants.

Financial Statements

Income Statement

Particulars	Dec-16	Dec-17	Dec-18	Dec-19	Dec-20
Revenues	**0.456**	**0.655**	**1.412**	**1.412**	**1.252**
Revenue Growth YoY		43.45 %	115.57 %	(0.01) %	(11.28) %
Cost of Revenues	0.182	0.148	0.416	0.532	0.447
Gross Profit (Loss)	**0.275**	**0.507**	**0.996**	**0.88**	**0.805**
Gross Profit Growth YoY		84.37 %	96.51 %	(11.66) %	(8.49) %
Operating Income & Expenses					
Selling General & Admin Expenses	5.782	6.56	8.857	13.998	13.289
Depreciation & Amortization	0.082	0.072	0.148	0.705	1.025
Operating Income	**(5.507)**	**(6.054)**	**(7.861)**	**(13.118)**	**(12.484)**
Other Non-Operating Expenses	-	0.051	(1.915)	(3.619)	(0.36)
EBT Excluding Unusual Items	**(5.507)**	**(6.003)**	**(9.776)**	**(16.737)**	**(12.843)**
Merger & Restructuring Charges	-	-	-	(0.657)	-
Impairment of Goodwill	-	-	-	(8.1)	(12.876)
Gain (Loss) On Sale of Investments	-	-	-	6.164	1.29
Other Unusual Items Total	(1.019)	-	(0.31)	(0.061)	(1.455)
EBT Including Unusual Items	**(6.526)**	**(6.003)**	**(10.086)**	**(19.391)**	**(25.884)**
Income Tax Expense	-	-	-	-	-

Earnings from Continuing Operations	**(6.526)**	**(6.003)**	**(10.086)**	**(19.391)**	**(25.884)**
Earnings Growth YoY		(8.01) %	68.02 %	92.25 %	33.49 %

Balance Sheet

Particulars	Dec-16	Dec-17	Dec-18	Dec-19	Dec-20
Current Assets					
Cash and Equivalents	1.764	0.766	0.162	0.151	0.678
Short Term Investments	0.384	0.245	-	-	-
Accounts Receivable	0.039	0.137	0.233	0.297	0.257
Notes Receivable	-	0.668	0.497	-	-
Inventory	0.272	0.265	0.241	0.19	0.29
Prepaid Expenses	0.149	0.29	0.318	0.16	0.289
Total Current Assets	2.608	2.371	1.452	0.798	1.514
Non-Current Assets					
Net Property Plant & Equipment	0.101	0.088	0.18	2.238	5.218
Goodwill	-	-	-	15.69	2.814
Other Intangibles	0.098	0.095	0.964	3.649	3.398
Other Assets	-	1.07	1.113	-	0.116
Total Assets	2.808	3.624	3.709	22.376	13.06
Current Liabilities					
Accounts Payable	0.22	0.14	0.446	3.156	1.372
Accrued Expenses	1.346	0.785	1.279	2.372	2.588
Short-term Borrowings	-	-	1.635	4.796	4.432
Current Portion of LT Debt / Leases	-	-	-	0.459	0.597
Other Current Liabilities Total	0.008	0.007	0.296	0.091	0.347
Total Current Liabilities	1.574	0.932	3.656	10.874	9.337
Long-term Liabilities					
Long-Term Leases	-	-	-	0.27	0.845
Other Long-Term Liabilities	0.31	-	-	-	0.236
Total Liabilities	1.884	0.932	3.656	11.144	10.418
Shareholder Equity					
Total Preferred Equity	0.001	0.007	0.001	0.036	0.001
Common Stock & APIC	47.94	55.706	63.161	93.694	111.025

Retained Earnings	(47.018)	(53.021)	(63.108)	(82.499)	(108.383)
Treasury Stock & Other	0.002	-	-	-	-
Total Common Equity	0.923	2.685	0.053	11.196	2.642
Minority Interest	-	-	-	-	-
Total Equity	0.924	2.692	0.053	11.231	2.643
Total Liabilities and Equity	2.808	3.624	3.709	22.376	13.06

Important Research Disclosures

Karl Egeland, MBA, and Nikhil Bhauwala, CFA, each certify that (1) the views expressed in this report accurately reflect our personal views about all of the subject companies and securities and (2) no part of our compensation was, is, or will be directly or indirectly related to the specific recommendations or views expressed in this report.

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