

Market Assessment Study of Precision Medicine in Oncology (in USA)

By

Neha Sarda

*Dissertation submitted in partial fulfillment of the requirements of the degree
MBA Hospital and Health Management*

Academic year, 2018-2020



The IIHMR University, Jaipur

1, Prabhu Dayal Marg, Sanganer, Airport
Jaipur 302029, Rajasthan
Ph: 0141 3924700, Fax: 3924738
Website: www.iihmr.edu.in

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Ph: 0141 3924700, Fax: 3924738
Website: www.iihmr.edu.in



SALES + MARKETING

June 17, 2020

EXPERIENCE CERTIFICATE

This is to certify that Neha Sarda (Employee ID – 23480) was interning in our organization from February 3, 2020 to May 29, 2020. At the time of leaving she was working in the capacity of Knowledge Management Associate – Intern based at the New Delhi office.

We wish you all the success in future endeavors.

For ZS Associates India Pvt Ltd

Mohit Sood
Office Managing Principal

ZS Associates India Private Limited

A Subsidiary of ZS Associates International, Inc. CIN - U72900IN200647C00001

Registered Office:
World Trade Center, Tower 3, Khiradi,
Pune - 411004, Maharashtra, India

T | +91 20 6734 5000 F | +91 20 6734 5001

www.zsassociates.com

Branch Office:
Block AA, IT Park BSG of OLF Limited
Village - Badliwala, Sector-34, Gurgaon (Haryana) 122002 India

T | +91 124 679 3990 F | +91 124 679 3991

Impact where it matters.

Acknowledgment

On the very outset of this report, I would like to extend my sincere and heartfelt obligation towards all the personages who have helped me in this endeavor . The internship opportunity I had with ZS Associates was a great chance for learning and development .

I am also grateful for having a chance to meet so many wonderful people and professionals who led me through this internship period .

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At this juncture I feel deeply honored in expressing my sincere thanks to **Ms. Isha Makkar** (Associate consultant) who despite being extra ordinarily busy with her duties, took time out to hear, guide and keep me on correct path and providing valuable insights leading to the successful completion of my project .

I would also like to thank all my teammates for their critical advice and guidance without which this project would not have been possible .

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I perceive this opportunity as a big milestone in my career development. I will strive to use gained skills and knowledge in best possible way and I will continue to work on their improvement in order to attain desired career objectives .

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ABSTRACT

Cancer is a collection of rare diseases wherein body cells begin to divide uncontrollably and further invading into surrounding tissues.¹ Even though science has advanced to such great heights, yet not all causes are identified. Various factors can contribute to its occurrence which can be classified as modifiable and non-modifiable factors. Modifiable - tobacco consumption and obesity, Non-modifiable - inherited genetic mutations and immune conditions. All these risk factors might work together to promote the disease or in a sequence.²

According to American Cancer Society, United states could witness 1,806,590 incidence cases and 606,520 mortality value in year 2020. It is well known that cancer is a major public health issue worldwide and with the increasing number it is becoming the second leading cause of mortality in US.³ With the increasing cancer burden, finding a cure to it has certainly become the biggest challenge of 21st century and the continuous struggle has led to several advancements in the field of medicine. New approaches to cure these deadly diseases have made it possible to a future where cancer becomes a curable disease. Personalized vaccines, cell therapy, gene editing and microbiome treatments are amongst them.

This secondary research analysis has helped in understanding the market dynamics of the Precision Medicine in the area of Oncology and how over the time it is gaining popularity in the market. The study explains the mechanism of action of the treatment. Market assessment research also helps us in gaining insights about the US market and its key players. It has highlighted the growth drivers and the challenges for the acceptance of the new approach and showed how over the time the treatment has moved into different therapy areas besides oncology. Due to the recent COVID-19 situation, how it has affected the development and sales in the present scenario has been also captured in this study.

SECTION 1

Organization Profile

ZS Associates is a sales and marketing outsourcing, staff augmentation, and technology firm headquartered in Evanston, Illinois that provides services for clients primarily in the pharmaceutical industry . Andris Zoltners and Prabha Sinha, who worked together as professors of marketing at the Kellogg School of Management at Northwestern University, founded ZS in 1983 .



Figure 1: ZS Associates Gurgaon

The firm employs approximately 3,400 employees in 20 offices in North America, Asia and Europe . Most of the workforce is located in large outsourcing hubs in Pune and New Delhi, India . ZS works with 49 of the 50 largest drug-makers and 17 of the 20 largest medical device makers and also serves consumer products, financial services, industrial products, telecommunications, and transportation and logistics industries .

ZS Associates offers integrated sales and marketing services ranging from customer insights and strategy to companies that need specialized expertise in areas ranging from analytics, operations and technology.

The firm serves clients in the consumer products, energy, financial services, high tech, industrial products, telecommunications, transportation and logistics sectors, although a large number of the firm's clients work in the pharmaceuticals, biotechnology, and medical products and services space.

ZS Associates developed the first personal computer-aided sales territory mapping system in 1985 . In 2008, ZS created 12 software products focused on incentives, call planning, promotion, strategy, forecasting and account management, and integrated them as one unified sales and marketing software platform: The Javelin™ software suite .

ZS in Sales:

For nearly 30 years, ZS's sales consulting services have helped companies around the world excel at critical sales activities such as: designing sales channels that leverage both direct and indirect paths to market; creating the best sales force structure, territory plan, size, allocation and incentive approach; and integrating sales and marketing programs with extraordinary results and levels of efficiency. ZS Associates offers the following solutions:

Business Intelligence and Technology

- **Maximize profit at a fraction of current costs**

ZS delivers superior business intelligence solutions that transform data into insight . Business Intelligence practice gives a specialized analytical monitoring and diagnostic solutions that improve sales and marketing and help cut costs .

Business Process Improvement

- **Streamline sales and marketing operations**

When struggling to uncover operational roadblocks and inefficiencies in sales and marketing departments, ZS helps to reengineer sales and marketing processes and facilitate successful change management within organization . The unique mix of analytics, operations and technology identify and implement the right solutions to improve your organization's commercial operations .

Customer Targeting and Activity Planning

- **Increase Sales Success and ROI on Field Force Investment**

The sales field force remains one of the most effective channels to engage the customer. But it is also one of the most expensive . And in a market in which one has to achieve more with less, companies must maximize the return on their sales force. ZS helps sales organization identify the best opportunities and field force tactics .

Go-to-Market Strategy and Transformation

- **Achieving Step-Function Increase in Sales and Profitability**

ZS helps sales and marketing executives identify critical growth opportunities, determine sales and marketing strategy, and implement the necessary changes – changes that regularly boost the clients' revenue 2-10% or more . ZS knows how to transform sales and marketing strategies and capabilities while minimizing transition risks and driving sustained adoption of new approaches .

Sales Channel Strategy and Management

- **Develop and Manage Channel Partner Programs to Meet Evolving Customer Needs**

ZS creates winning channel strategies . It aligns go-to-market strategy with overall business strategy by helping clients develop and manage a channel program with the right mix of direct and indirect (partner) channels to meet business goals and customer engagement requirements .

Sales Compensation

- **Compensation that boosts sales force retention and market share**

An effective sales compensation plan helps retain the top sales people, increase market share, make selling costs predictable and reduce the cost of plan administration . An inferior plan does the opposite. ZS helps to create plans and quotas that support your strategy and streamline administration .

Sales Force Design

- **Design a customer-centric sales Force**

The sales force is one of an organization's most valuable and expensive marketing resources . Unlike other marketing tactics, building or reshaping a sales force can take considerable time, money, and attention . ZS has designed sales forces for organizations across more than 25 industries and in over 70 countries .

Sales Force Effectiveness

- **Maximize the return on your sales force**

Over the past 30 years, ZS has conducted thousands of sales force effectiveness engagements with over 700 companies in more than 70 countries and 25 industries . ZS has helped clients' salespeople achieve longer face time with their customers, more topics discussed during customer visits, significantly improved customer satisfaction ratings—and most important, up to 30% higher sales performance

ZS in Marketing

Leading companies turn to ZS marketing consulting services because they excel at helping them accomplish marketing mandates such as: creating tailored and practical strategies to capitalize on their market opportunities; sorting through myriad options for creating demand to determine the optimal marketing mix; and evaluating marketing programs to dramatically improve their performance .

Customer Insights

- **Increase Customer Insight to Make Better Sales and Marketing Decisions**

A clear understanding of customer needs, buying processes, buying preferences, perceptions, and potential is essential to sales and marketing success . ZS uses qualitative and quantitative methods spanning both primary and secondary data-based approaches to provide clients with customer insights .

Customer Segmentation

- **Enable Sales and Marketing Strategy and Execution through Actionable Customer Segmentation**

ZS combines marketing science expertise with decades of experience to help companies around the world develop highly actionable segmentation strategies that drive brand strategy through to tactical execution .

Forecasting

- **Create Robust and Transparent Forecasts for Your Products**

Understanding fundamental market drivers and their influence in shaping product demand is integral to good business planning and full utilization of company resources . ZS has developed customized forecasting processes to serve the clients . It merges forecasting knowledge and experience with the industry expertise of clients to produce collaborative results

Marketing Mix

- **Maximize the Return on Sales and Marketing Investments**

Sales and marketing organizations face unrelenting cost pressures . ZS helps sales, marketing and brand executives substantially increase the return on their investments and gives them confidence that they are making the optimal promotional spending decisions .

Marketing Performance Measurement and Optimization

- **Improve In-Market Effectiveness Through Timely Insight into Marketing Performance**

Accurate and timely feedback on marketing program performance is critical to the real-time fine tuning and course corrections necessary to maximize marketing results and return on investment . ZS has extensive experience helping clients maximize the value realized from their investments in marketing programs .

Pipeline Strategy

- **Optimize Return on New Pharmaceutical and Medical Products**

Pharmaceutical brands and medical products may not be generating returns that maximize your company's substantial R&D and marketing investments . With market conditions creating higher barriers to commercial success, the pressures on R&D and marketing executives are becoming only more acute . ZS helps life science companies increase the commercial success of their product pipelines .

RESPONSIBILITIES AS A KNOWLEDGE MANAGEMENT ASSOCIATE

- Assess the knowledge needs and requirements (short-term or long-term) of the firm
- Deliver targeted insights using internal knowledge and external sources
- Help the firm prepare materials for Summits and Conferences
- Support the creation and update of knowledge assets including client updates, competitive intelligence, industry research etc
- Maintain, manage and develop the firm's knowledge infrastructure
- Share best practices and tactical knowledge across offices, practice areas and teams

SECTION 2

Dissertation report

Market Assessment Study of Precision Medicine in Oncology (in USA)

➤ **INTRODUCTION**

Cancer has become an alarming issue as its burden is increasing exponentially and giving great economic concerns. With over 18 million cases in 2018 and continuously growing and aging population, health experts expect to have 29 million cases by 2040. Since the cancer burden is increasing in such an exponential phase there are various other factors shaping the new oncology market: Increasing pace of development and increase in competition amongst the biopharma companies has made us witness a major number of approvals than the preceding years which also led to various mergers and acquisitions, boom of biosimilars and increasing focus for value among the payers and providers, enabling the patient voice and understanding his/her need, new regulations governing the onco-specific market and at last digitalization of healthcare giving seamless decision making along with better customer experience and optimizing the patient adherence.

Researchers have established the fact through various studies that behavior of cancer in person differs from that in another and with the upcoming personalized healthcare initiative, it has made possible for doctors to give tailored treatments according to the person's tumor. Each tumor has its unique genomic change, or "mutations", which helps doctors to decide the best treatment will help the doctors to decide which treatment works best for them. This further helps them to deliver targeted therapies specific to the patients giving more successful results.⁴ Thus Precision medicine today is the new face of the treatment to cancer. A market assessment study is a detailed investigation of the new product or any new business idea. It is a comprehensive analysis of market trends, entry barriers, environment forces, competition, risks, opportunities and the company's resources and constraints and so considering the available literature and scope of furthering research, this study will help the researcher investigate the in-depth coverage of Precision Medicine drugs market in Oncology including its drivers, restraints and opportunities thus giving a better understanding of market behavior.

➤ **OBJECTIVE:** To investigate the Precision Medicine (in oncology) and Companion Diagnostics market w.r.t its market size in US and assess its scope in other therapeutic areas.

➤ **MATERIAL AND METHODS:**

- **STUDY DESIGN:** Observational
- **SETTING:** ZS Associates, Gurgaon
- **DURATION OF STUDY:** 3 Months
- **DATA COLLECTION PROCEDURE:** Data was collected through secondary resources using various combinations of relevant strings and keywords
- **DATA ANALYSIS TOOL:** Following data collection tools were used to derive key information using relevant keywords:
 - Research papers

- Reports
- Articles
- Journal
- Internet
- Other databases

➤ RESEARCH FINDINGS

1. *What is Precision Medicine?*

A rapid shift in the healthcare industry towards Precision Medicine is being witnessed owing to its advantages which is offering a deeper understanding of human using its genomic data and advancements in technology. Currently, medicines are effective only to subset of patients and there might be chances that patients with similar symptoms don't respond similarly to the given treatment. This might further outweigh the benefits of the treatment due to unintended side effects as a result of the current one-size-fits-all approach.

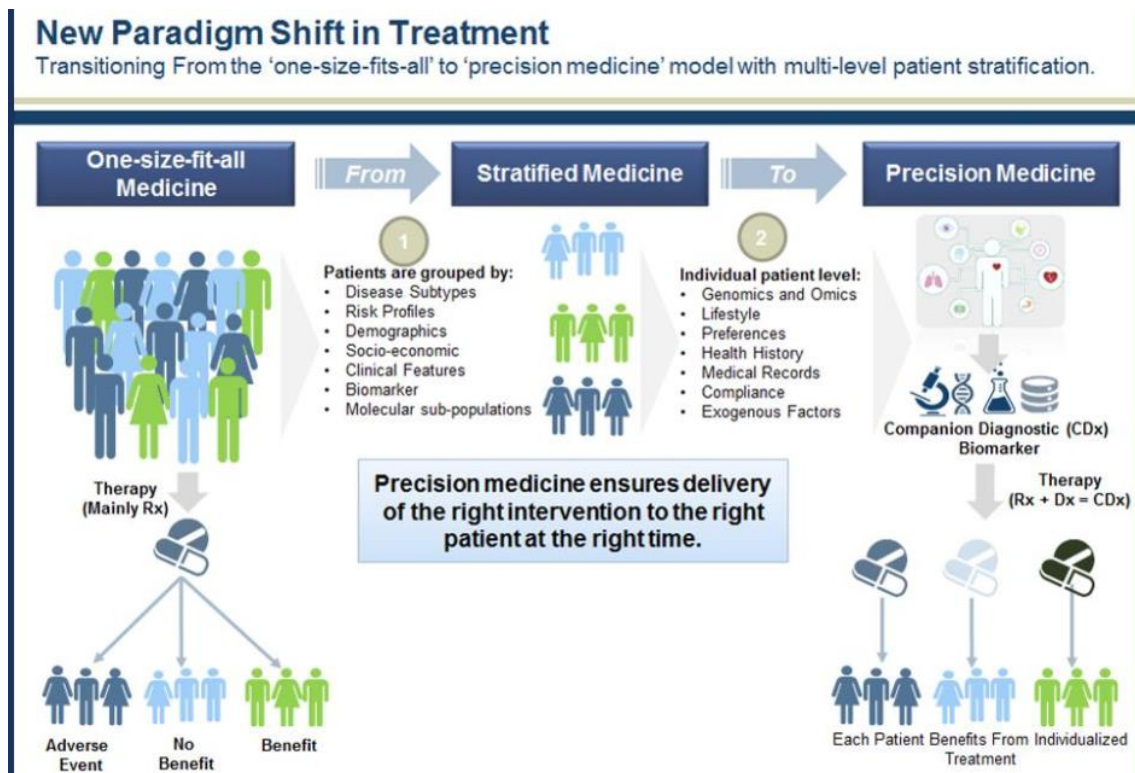
Precision Medicine is now being looked at from a broader perspective which is getting the right therapy for the right patient at the right time, using any one or more of a multitude of tools and technologies, be they molecular, digital, imaging, or other, simple or complex.⁵ It allows for getting a better idea about the patient's condition, his needs and about lifestyle so that the treatment could be designed in a much more specific and effective manner.

Not all diseases are linked to genetic mutations like the chronic conditions: Cardiovascular diseases or Diabetes etc. They are affected mostly from the combination of environmental, lifestyle, and behavioral factors, alongside biology and physiology. And so Lyold Minor, managing director and dean of Stanford Medicine brings the concept of precision health wherein the focus from curing the disease shifts towards preventing the inception of by promoting healthy lifestyle and importance of wellness further having a meaningful impact on reducing the healthcare costs.⁶

The foundation of Precision Medicine exists upon the robust data infrastructure. Large genomic data about the normal as well as disease-associated mutations are not enough, rather one should be able to meaningfully interpret this data to translate it into clinical decisions and better outcomes. To create a better understanding this requires an integration between the data sources pertaining to electronic health records which have the information about the diseased patients and their outcomes with the IT support systems. Further all this data should also feed into research databases and biobanks to support discovery, ultimately creating a system that continuously learns.⁷ Clinical care decisions and outcomes based on today's genomics data and knowledge base will contribute

to improving future decision-making. “Rich and highly credible information will be the primary catalyst for the broad adoption of precision medicine, particularly in oncology,” said Michael Pellini, CEO of genomic profiling group Foundation Medicine, in his announcement of a 2015 tie-up with information and services firm IMS Health to create a new cancer diagnostics tool.⁸

Figure 2: New Paradigm Shift in Treatment



Source: Frost & Sullivan⁴⁴

2. Precision Medicine in Oncology

Each person has its own unique genome, which consists of large changes in DNA sequences or named as mutations and can even include small single nucleotide polymorphisms (SNPs). These changes could be either hereditary or can be introduced through various external agents such as carcinogenic chemicals or radiation. It has been observed that depending upon these changes an individual's body response could be different to another's may be due to difference in the drug target, or through ADMET considerations (i.e. absorption, distribution, metabolism, excretion and toxicology).⁹

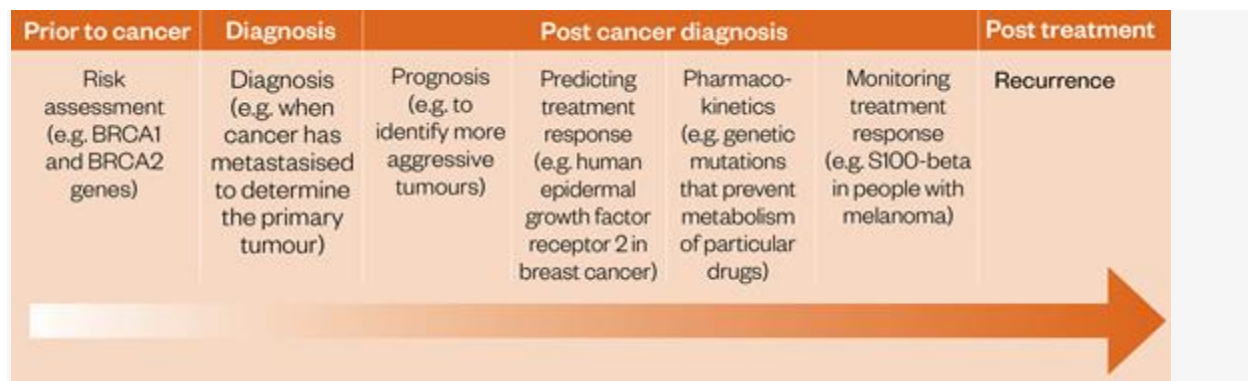
Recent advancements in technology have shown that there is tremendous heterogeneity in cancer. These findings have opened a new era for the therapy area which now focuses on the concept that each tumor has its own way and functions differently and thus should be treated in a specific way depending upon its molecular structure.¹⁰

Precision medicine, or also known as ‘personalized medicine’ or ‘PM’^{[11],[12]}, is a term used to describe a set of treatments or therapeutic agents which can be tailored according to the individual patient’s needs^[13]. The overall goal of this is to match the treatment or the therapy according to the individual so that he/she receives the maximum output with minimal toxicity. This has become important particularly in the area of oncology where patients have minimal life expectancy. Further, the decreasing cost of human genome sequencing has further led to adoption of PM approach for the treatment of cancer^[14].

US National research council introduced the Precision medicine concept first in 2011, which had an aim of providing the customized treatments specifically for a patient sub-group on the basis of their genomics study^[15]. The concept of PM in oncology further gained importance due to launch of PM initiative in US in 2015, which increased the pace of the development of biomarker-driven therapeutic strategies^[16].

Within oncology, PM approach uses mostly the identification of biomarkers involved or associated with a cancer type. A biomarker is a unique mutated nucleic acid sequence, protein, glycoprotein or group of proteins, expressed by the tumour cells but not normally by healthy cells^[11]. There are four main types of biomarkers: pre-disposition (indicating the likelihood of developing the disease), diagnostic (used to confirm the patient has a particular cancer), predictive (determining which cohort of patients may benefit from a particular drug therapy) and prognostic (suggesting how the cancer may develop in the individual)^[17]. Each biomarker type is relevant at different stages of the disease (see Figure 2)^[11].

Figure 3: Role of biomarkers in oncology



Source: The precision medicine approach to cancer therapy: part 1 – solid tumors, the Pharmaceutical Journal⁹

3. Precision Medicine in US: Market Scenario

Advancements in medical sciences has facilitated in the prediction for an individual its personal risk factors and how individual might behave differently in various treatments.²⁰

Evidence suggests that governments around the globe are building large genomic repositories and biobanks to push forward the precision medicine approach as they have realized its importance. This also led to launch of the Precision Medicine Initiative by Former US President Barack

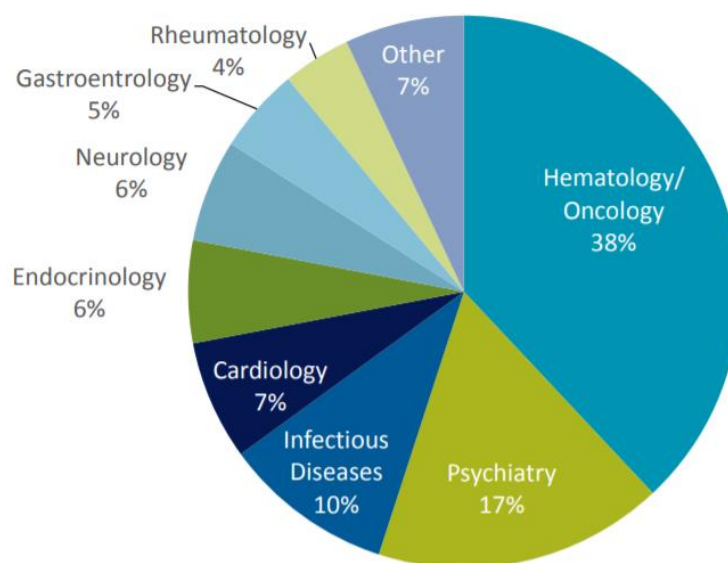
Obama to great fanfare in 2015²⁰. The initiative has the following mission statement: *“To enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized care.”*²¹

The Precision Medicine Initiative has its own set of goals. The short-term goal – to bring more precision medicine treatments in cancers for which scientists aim to use the cancer knowledge data banks to find effective treatments for various cancer types. The long-term goals – to expand the approach of precision medicine in other therapeutic areas beyond oncology and for this purpose, NIH launched the All of Us Research Program (involving 1 million volunteers’ cohort from US). Participants in this program are required to provide their genetic data and samples. To maintain transparency, participants will even have access to the information about the usage of their given data. They can see where their data has been used i.e. in which studies. These large data banks will facilitate the researchers to study about various diseases, their prognosis and hence will help in finding improved treatment strategies.²³

According to Worldometer report, US current population is 330,605,277 and is estimated to grow at **331,002,651** people at mid-year 2020.¹⁸ The American cancer society estimates 1,806,590 new cancer cases and 606,520 cancer deaths in 2020 and out of this approximately 89,500 cancer cases and about 9,270 cancer deaths will occur in adolescents and young adults aged 15 to 39 years¹⁹. This leaves with a great market opportunity for the upcoming PM driven projects especially in the field of oncology.

Precision Medicine Market has exceeded USD 57 billion in 2019 globally and is estimated to grow over 11% CAGR between 2020 and 2026, this increase is attributed to the rising prevalence of cancer rendering a positive impact on the market.²⁴

Figure 4: Precision Medicine Market Share by therapeutic area



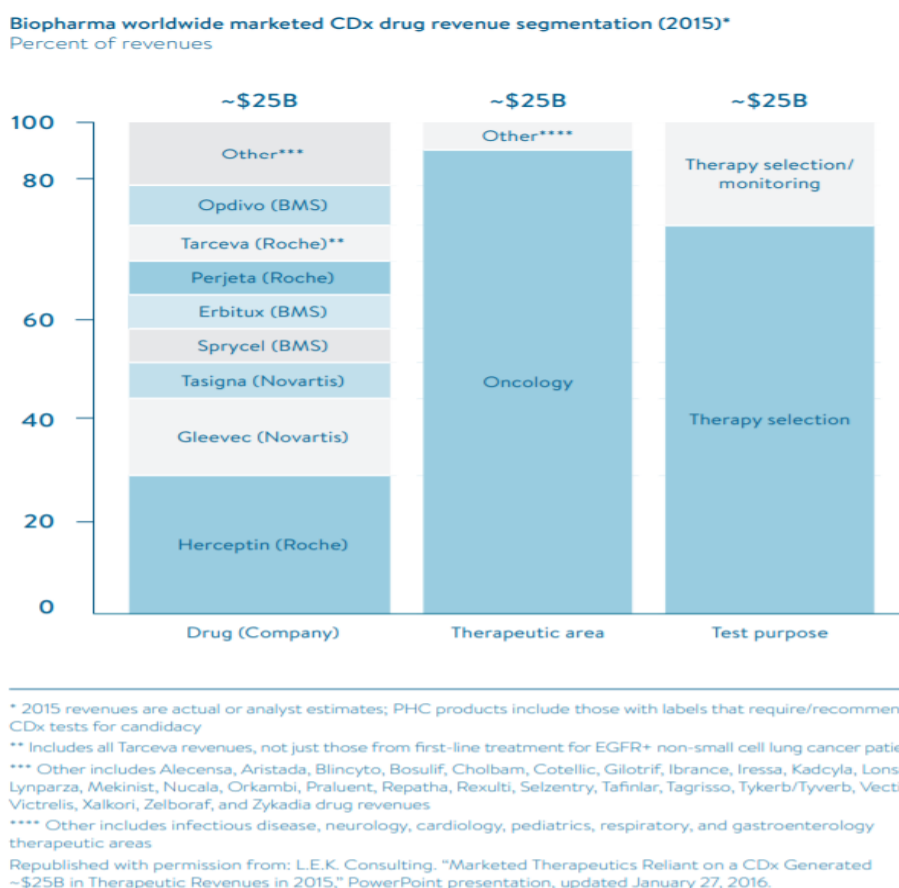
Source: U.S. FDA, “Paving the Way for Personalized Medicine,” Oct 2013²⁷

According to market data forecast report in the North America, Precision Medicine market was estimated to be USD 16.62 Bn in 2019 and is projected to reach at 28.13 Bn in 2024, at a CAGR of 11.10% . North America is the biggest market in terms of share across the globe. Its growth drivers are the higher acceptance rate amongst people and patient affordability. The improved understanding of cancers has also led to discovery of new therapeutic targets in North America, due to which wider range of opportunities for market growth.²⁵

Some of the prominent companies leading in North America in Precision Medicine are: Pfizer, Roche, Covance, Novartis, Qiagen, Biocrates Lifesciences, Teva pharmaceuticals, Nanostring technologies, Laboratory corporation of America holdings, Tepnel pharma services, Intomics, Ferrer InCode, Silicon Biosystems, Eagle genomics, Medtronic, and Quest diagnostics .²⁵

Personalized Medicine Coalition has listed 132 personalized medicines with specific biomarkers and are currently on the market (Appendix). Also, according to the analysts the market value for drugs reliant on companion diagnostics (CDx) was over \$25 billion in 2015 (Figure 4). These numbers are likely to grow way more.²⁶

Figure 5: Marketed Therapeutics Reliant on a Companion diagnostic



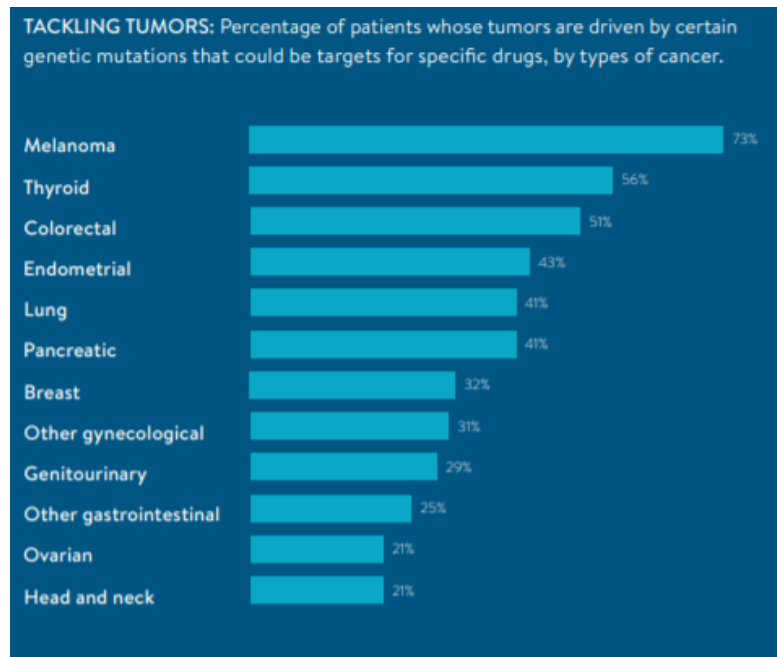
Source: The Personalized Medicine Report 2017, Personalized Medicine Coalition²⁶

A recent survey report by the Tufts Center for the Study of Drug Development demonstrated that 42 percent of the drugs in the pipeline have now included biomarkers in their research studies and

development design.²⁶ A biomarker is an identifiable factor that acts as an indicator of normal biologic processes, disease processes, or biological responses to a therapeutic intervention . They are detected through various diagnostics: Blood draw, microscopic analysis, gene sequencing, biopsy and protein analysis .²⁷

Further, we are moving towards an era where we can treat all the cancers with personalized course of treatment. Following figure shows the percentage of cancer patients whose treatments could be driven by personalized drugs:

Figure 6: Percentage of patients with cancer whose treatments could be personalized with specific drugs



Source: The Personalized Medicine Report 2017, Personalized Medicine Coalition²⁶

4. Companion Diagnostics

According to FDA, “a companion diagnostic is an in vitro diagnostic or an imaging tool that provides information that is essential for the safe and effective use of a corresponding therapeutic product.”²⁸ There has always been a need of regulatory path for the use of companion diagnostics in precision medicine. FDA released the first In Vitro Companion Diagnostics Devices Guidelines which states the methods of conducting reviews of a drug along with its companion diagnostic.²⁹ It describes the conditions under which a targeted drug will get approved along with its corresponding diagnostic test. Besides this FDA, health Canada and EMA had also mandated the biomarker testing prior to prescribing any of the drug. Since the use of companion diagnostics/therapeutics is growing, FDA has also started to publish the list of genomic biomarkers that are considered valid for drug approval.³⁰

Advantages of using a companion diagnostic is that it can identify the patients and thus tell who will get benefitted from the treatment the most and tells about the serious side effects a person could have from any treatment. In addition, these tests are designed in such a manner that they can even monitor the response of a patient to a certain treatment and thus gives improved safety or

effectiveness.³¹ Companion diagnostic helps in simplifying the drug discovery process, they make the clinical trials more informative and efficient and majorly helps in giving the personalized treatment to the cancer patients.³¹

The global companion diagnostics market is estimated to be worth USD 7.3 billion by 2024 from USD 3.5 billion in 2019, at 15.7% CAGR. The major drivers of the growing companion diagnostics industry are the advantages of companion diagnostics along with the rising importance of precision medicine, the increasing number of cancer cases across the globe and so the growing need for targeted therapy.³²

Pharmaceutical & biopharmaceutical companies are the ones holding the largest share of the CDx market in 2019 because of the extensive use of these tests owing to the growth of drug market as well as companion diagnostics biomarkers. Besides this increase in the personalized healthcare approach and the high demand for targeted therapies for various diseases have also driven the CDx market up.³²

Differentiating the CDx market according to the disease indication: Lung cancer is projected to grow at more than 18.5% CAGR up to 2025. This is due to the growing number of cancers across the globe. It is important to give effective treatment at an early stage to curb the disease and so CDx enables to tailor the treatment according to the patient needs. Not only this, it also monitors any adverse reaction to the treatment and so helps in avoiding it. Then comes the skin cancer which accounted for over 13% of overall CDx market revenue in 2018. It is estimated that skin cancer cases would go up due to increasing adverse reactions by cosmetics and damage because of harmful sun rays, which will surge the demand for CDx tests as they play pivotal role in helping doctors to treat skin cancers. As per CDC US had reported 82,476 incidences of melanomas in 2016.³³

Differentiating the CDx market by region: North America companion diagnostics market size is estimated to grow more than 18% CAGR through 2025 owing to the increasing number of cases of chronic diseases and the aging population. Further, high disposable income of the people increases affordability for companion diagnostics tests amongst people which are the growth drivers for the market. Asia Pacific will see up to 20.5% growth up to 2025 as there are various government initiatives supporting the approach plus growing patient pool are the acting boosters for the APAC market. Besides, companies are also demonstrating the usefulness of CDx by taking initiatives and doing necessary alliances, for curbing overall healthcare expenditure.³³

The prominent players operating in the global companion diagnostics market are F. Hoffmann-La Roche AG (Switzerland), Agilent Technologies, Inc. (US), QIAGEN N.V. (Germany), Abbott Laboratories, Inc. (US), Almac Group (UK), Danaher Corporation (US), Illumina, Inc. (US), bioMérieux SA (France), Myriad Genetics, Inc., (US), Sysmex Corporation (Japan), Thermo Fisher Scientific Inc. (US), Abnova Corporation (Taiwan), and Guardant Health, Inc. (US)³²

5. Precision Medicine Beyond Oncology

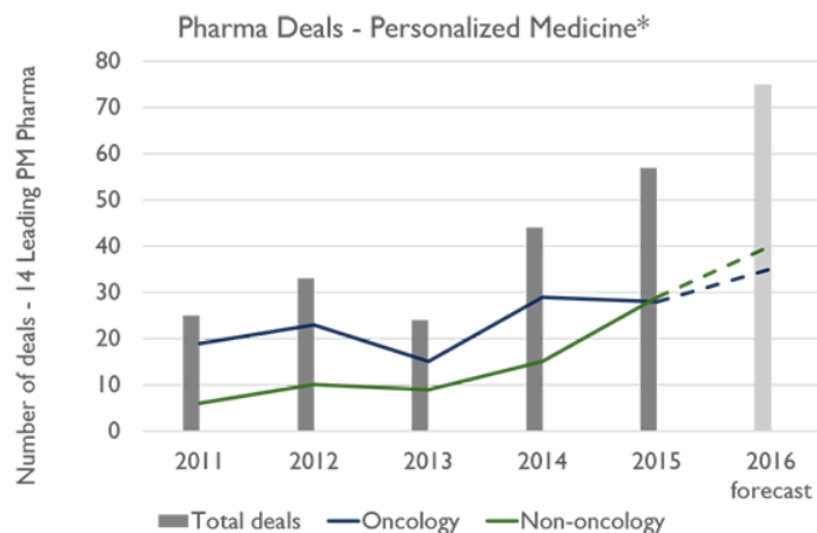
Oncology has always been the most focused area in precision medicine and one can find most of targeted therapies and diagnostics in this therapy area. However, now comes the time when we can

witness the targeted biomarkers and targeted approaches in other areas as well.³⁵ Now, there are targeted biomarker therapies for the diseases like diabetes and inflammatory diseases (such as asthma and rheumatoid arthritis) and neurological diseases (such as Alzheimer's, Parkinson's and multiple sclerosis). In past five years the development in these areas have increased exponentially however, oncology remains the dominated and most important therapy area of all.³⁵

In oncology, single analyte detection-based diagnostics are seen for eg- PCR, FISH, IHC, etc. which are taken from tumors and blood samples and outside oncology, there are multiple entry points, not limited to blood samples. Depending upon the disease, there are a lot of diagnostics which can be used either alone or in a combination with others (e.g. wearables) thus creating a competitive market for non-oncology area. These tools will not only improve the value proposition to the payers but also drive the regulatory approvals faster.³⁵ Even the pharma sector is already preparing itself and moving towards deals in personalized medicine beyond oncology area since 2011 (figure 6).³⁴

In cardiology, precision medicine has advanced to measure the gene variants which increases the risk of diseases. Companies like Roche are developing the CDx for the appropriate selection of the treatment for disease like acute coronary syndrome. But as of now, in cardiology measurements are not significant as the variants are quite small to be considered as actionable.³⁶

Figure 7: "Deals among leading pharma companies for biomarker discovery and companion/ complementary diagnostic development"



Source: Great Expectations for Personalized Medicine Outside Oncology, Diurectics.com³⁵

Research has been also going on in the neurology area with diseases having genetic ties such as “depression, schizophrenia, Parkinson's and Alzheimer's disease”. Many companies are working towards developing a drug which acts against the amyloid deposits of amyloid β -peptide deposits in plaques in brain tissue, hypothesized to cause neurodegeneration in Alzheimer's. Two drugs in

late stage phase III of clinical trials for the same are- Biogen's aducanumab and Roche's crenezumab.³⁶

Even though there are a lot of challenges, companies have increased their efforts towards discovery of biomarkers in non-oncology areas. Many big pharma giants are now focusing on areas such as infectious diseases (eg, hepatitis), rheumatology, and cardiovascular diseases. In rheumatology field, scientists have begun the genetic profiling to assess which all drugs will work for rheumatoid arthritis patients.³⁶

Thus, as more and more companion diagnostics will be developed along with the precision medicines, more personalization would be achieved in the non-oncology space.³⁶

6. Impact of COVID-19

Worldwide restrictions and orders to stay-at-home is helping across everyone to control the spread of virus as much as possible. But these steps have resulted in economic repercussions as well and even the pharmaceutical industry is facing the light. Existing clinical trials have come to a halt and it has become difficult to perform them as well as start the new ones. Hence there is an urgent need to use some advanced options to successfully implement these trials as they are essential to finding treatments for myriads of diseases.

According to Medidata, who has been conducting analyses of a number of clinical trials enrollment data (approx. 4600) and have studied 182,000 study sites worldwide, a significant reduction has been observed recently in participation of clinical trials activity:

- A 65% overall average reduction is observed in the enrollment of new patients for trials during March.³⁷
- Japan has witnessed 43% reduction and India 84%, and these are one of the major markets across. US saw a reduction of 67%³⁷
- However, in countries where situation has started to become normal, there has been a marked improvement from February to March.³⁷
- China observed a 68% in the new patient's enrollment in trials year-over-year in March but saw improvement in March which may suggest beginnings of a recovery.³⁷

The impact of COVID-19 is also not uniform across the various therapeutic areas. Enrollment in studies have decreased in following manner:

- Respiratory Diseases: 34%
- Endocrine Diseases: 80%
- Infectious Disease: 47%
- Oncology Diseases: 48%
- Dermatology Diseases: 64%
- Central Nervous System Diseases: 68%
- Cardiovascular Diseases: 70%

Although things have started to return to normal, the dramatic decline in the participation have during the pandemic shows the vulnerable as well as the fragile position our healthcare system and indicate towards the long-term implications across the board.

However, the era of COVID-19 has led the science to move forth with advanced options, technologies and appreciate the principles of precision medicine. The key opinion leaders across the healthcare domain are now focusing on how to make the health systems stronger and equip it to respond to the increasing medical challenges. And the use of personalized medicines could be an answer to all these discussions.

The pioneers are now discussing the value of diagnostic tools which can help in developing targeted strategies for the prevention of disease amongst the most-at risk population without subjecting the whole population to the devastating social and financial consequences. Michael Pellini, M.D. Managing Partner, Precision Medicine Coalition Board Member points out that ‘despite the fact of breathtaking progress in science and technology, people have been forced to sit at home which directly points out at the malpractice at the national level’. The need for more diagnostic testing is also supported by the former Food and Drug Administration commissioner Scott Gottlieb, M.D., and Lauren Silvis, who served as Gottlieb’s chief of staff at FDA before becoming a Senior Vice President at Tempus , a “data-driven precision medicine” company.

The importance of real-world data and diagnostic testing gives a good outlook for the precision medicine future. Also, the variable effects of this new virus amongst the patient population with similar characteristics is also giving a push to additional research on its molecular structure and how disease reflects in every individual patient.³⁹ Besides, the way virus is causing illness amongst some patients having no risk factors reflects that the disease might have progressed due to some genetic characteristics.³⁸ These studies are opening new opportunities for personalized medicine.

PrecisionLife, UK-headquartered AI precision medicine company, is using this current platform to identify 13 high risk genes for COVID-19, and 59 repurposing drug candidates which further could be used to identify the targeted therapies to treat sepsis which is developed from severe COVID-19. Sepsis is seen in amongst 60% of COVID-19 patients and is a fatal condition with 20% rate of mortality.⁴¹

This disease also has an impact on the cancer patients as well as people involved in providing care to them. According to PhD scholar Wenhua Liang and her colleagues, cancer patients have a much higher risk of getting infected from COVID-19 than any other person.⁴³

However, Precision Medicine can change the face of treatment for the oncology patients in the time of this pandemic. There are different targeted treatments approved for different form of cancers from acute myeloid, non-small cell lung cancer, lymphoid leukemia to stage IV melanoma. These options offer the opportunity for the treatment therapies with better response rate and at same time give increased dose density without increasing the toxicity profile. One of the greatest advantages of precision medicines targeted therapies is that it helps in identifying patients who need the treatment, and in this case is the cancer treatment. Mostly the targeted therapies are administered orally, and it is observed that toxicity and adverse event profiles of these drugs is

significantly different from chemotherapy. The higher rate of complications from the cytotoxic chemotherapy exposes the patients to a much higher risk of COVID-19 infections.⁴³

➤ CONCLUSION

The stage may be set for Precision Medicine to significantly change general wellbeing, yet not many in the clinical field would not deny the fact we are not prepared at this point. Changing from the conventional one-cure-fits-all treatment model to new procedures that involves patients' genetics, ways of life and environmental treatment factors is a massive errand that presents difficulties in both the research facility and the clinic.

Oncology is one area which has been impacted most from the advancements in precision medicine field as 90% of the top products in the market for precision medicine were for cancer. However, the therapies are not tailored specifically for the individuals, they are defined for different patient strata based on the oncogenic mutations in their tumors which is driving the growth of the cancer. Some of the common examples of drugs targeting the mutations are: Roche's monoclonal antibody Herceptin (trastuzumab) for HER-2 in certain breast and stomach cancers, Genentech's Zelboraf (vemurafenib) for BRAF in melanoma and Roche's Tagrisso (osimertinib) for EGFR in lung cancer. Regulatory bodies, FDA and EMA have even approved the 'tumor-agonistic' treatments such as Merck's immunotherapy Keytruda (pembrolizumab) – which target specific biomarkers regardless of tumor location.

But despite having such large number of therapies, matching the patients to right therapy is difficult. According to a survey conducted by Definitive healthcare, 'there are only 20% established precision medicine programmes'.⁴⁵ Advancements in genetic testing is essential to get the patients the best treatment. However, there are certain barriers mainly at the financial and operational side: the cost associated with genomic testing and companion diagnostics is the biggest challenge for the schemes. Besides this, lack of expertise is another challenge as many physicians find it difficult to interpret the results without any specialist which further increases the cost of clinics. Over 60% of physicians don't use genomic data as they find it difficult to interpret it.

In clinical research and development, moving the drug pipeline forward also becomes a problem as cost of manufacturing cell and gene therapies and incorporating new processes into innovative trials is not easy. Also, providing the safety and efficacy details for these therapies becomes an issue as the current regulations do not accommodate these innovations yet. However, pioneers have understood the advantage of creating the precision medicines and believe that it will yield economic returns in the future. Treating the patient with the right therapy modified according to their genetic profile and thus preventing the disease at the first place would lead to huge financial gain over the system. But still, there is a long way before we take over the traditional drug development as it has dominated the modern pharma for decades and even in the field of cancer. Thus, for changing the face of medicines we need a holistic push from regulators, drug developers, clinicians, governments and others which will be enough to bring us over the line.

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➤ APPENDIX

Selected Personalized Medicine Drugs and Relevant Biomarkers (as of September 2016)

Source: The Personalized Medicine Report 2017, The Personalized Medicine Coalition

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Adjuvant Therapy			
1	Cevimeline (Evoxac®)	CYP2D6	Dry mouth
2	Rasburicase (Elitek®)	G6PD; CYB5R1-4	Hyperuricemia, hemolysis, and methemoglobinemia
3	Sodium phenylacetate and sodium benzoate (Ammonul®)	NAGS; CPS1; ASS1; OTC; ASL; ARG	Urea cycle disorders
4	Sodium phenylbutyrate (Buphenyl®)	CPS1; OTC; ASS1	Urea cycle disorders
Analgesia & Anesthesiology			
5	Celecoxib (Celebrex®)	CYP2C9	Pain
6	Codeine	CYP2D6; CYP3A4; UGT2B7	Pain
7	Mivacurium (Mivacron®)	Cholinesterase gene	Anesthesia adjunct
8	Tramadol (Ultram®)	CYP2D6	Pain
Cardiovascular			
9	Carvedilol (Coreg®)	CYP2D6	Cardiovascular disease
10	Clopidogrel (Plavix®)	CYP2C19	Antiplatelet response
11	Isosorbide and hydralazine (Bidil®)	NAT1; NAT2	Heart failure
12	Lomitapide	LDLR	Familial hypercholesterolemia
13	Metoprolol (Toprol-XL®)	CYP2D6	Cardiovascular disease
14	Mipomersen sodium (Kynamro®)	LDLR	Familial hypercholesterolemia
15	Pravastatin	LDR	High cholesterol
16	Propafenone (Rythmol SR®)	CYP2D6	Cardiac arrhythmia
17	Quinidine	CYP2D6	Cardiac arrhythmia, malaria
18	Simvastatin (Zocor®)	SLCO1B1	High cholesterol
19	Warfarin (Coumadin®)	CYP2C9; VKORC1; protein C or S deficiencies	Anti-blood clotting, stroke prevention
Endocrinology			
20	Glyburide	G6PD	Diabetes
21	Chlorpropamide	G6PD	Diabetes
22	Glimepiride	G6PD; CYP2C9	Diabetes
23	Glipizide	G6PD	Diabetes

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Gastroenterology			
24	Dexlansoprazole (Dexilant®)	CYP2C19	Heartburn, gastroesophageal reflux disease, and esophageal damage
25	Esomeprazole (Nexium®)	CYP2C19	Acid indigestion, peptic ulcer disease, and gastroesophageal reflux disease
26	Lansoprazole (Prevacid®)	CYP2C19	Peptic ulcer disease, gastroesophageal reflux disease
27	PEG-3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate, and ascorbic acid (Moviprep®)	G6PD	Laxative
28	Rabeprazole (Aciphex®)	CYP2C19	Gastroesophageal reflux disease
Hematology			
29	Eltrombopag (Promacta®)	F5; SERPINC1	Thrombocytopenia, aplastic anemia
30	Methylene blue (Provayblue)	G6PD	Methemoglobinemia
Immunology			
31	Indacaterol (Arcapta®)	UGT1A1	COPD
Infectious Disease			
32	Abacavir (Ziagen®)	HLA-B*57:01	HIV
33	Atazanavir (Reyataz®)	UGT1A1	HIV
34	Boceprevir (Victrelis®)	IFNL3	Hepatitis C
35	Chloroquine (Aralen®)	G6PD	Malaria
36	Dapsone	G6PD	Leprosy
37	Isoniazid (Nydrazid®)	NAT1; NAT2	Tuberculosis
38	Mafenide (Sulfamylon®)	G6PD	Burns
39	Maraviroc (Selzentry®)	CCR5 receptor	HIV
40	Nitrofurantoin (Furadantin®)	G6PD	Urinary tract infections
41	Peginterferon alfa-2b (Pegasys®)	IL28B	Hepatitis B, hepatitis C
42	Primaquine	G6PD	Malaria
43	Pyrazinamide (Rifater®)	NAT1; NAT2	Tuberculosis
44	Quinine sulfate	G6PD; CYP2D6; CYP3A4	Malaria
45	Rifampin (Rifadin®)	NAT1; NAT2	Tuberculosis
46	Sulfamethoxazole and trimethoprim (Bactrim®)	G6PD	Bacterial infections
47	Telaprevir (Incivek®)	IFNL3	Hepatitis C
48	Voriconazole (Vfend®)	CYP2C19	Fungal infections

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Metabolic			
49	Allopurinol	HLA-B*58:01	High blood uric acid levels, gout
Neurology			
50	Carbamazepine (Tegretol®)	HLA-B*15:02; HLA-A*31:01	Epilepsy, bipolar disorder
51	Carisoprodol (Soma®)	CYP2C19	Musculoskeletal pain
52	Clobazam (Onfi®)	CYP2C19	Lennox-Gastaut syndrome
53	Dextrometorphan and quinidine (Nuedexta®)	CYP2D6	Pseudobulbar affect
54	Divalproex (Depakote®)	UCD (NAGS; CPS; ASS; OTC; ASL; ARG)	Bipolar disorder (antiepileptic drug)
55	Phenytoin (Dilantin®)	HLA-B; CYP2C9	Prevention of seizures
56	Tetrabenazine (Xenazine®)	CYP2D6	Huntington's disease
57	Valproic acid (Depakene®)	OTC; POLG; NAGS; CPS1; ASS1; ASL; ABL2	Epilepsy
58	Vortioxetine (Trintellix™)	CYP2D6	Depression
Oncology			
59	Ado-trastuzumab emtansine (Kadcyla®)	ERBB2	Breast cancer
60	Afatinib (Gilotrif®)	EGFR	Metastatic non-small cell lung cancer
61	Anastrozole (Arimidex®)	ESR1; PGR	Breast cancer
62	Arsenic trioxide (Trisenox®)	PML-RARA	Acute promyelocytic leukemia
63	Busulfan (Busulfex® & Myleran®)	BCR-ABL1	Leukemia
64	Bosutinib (Bosulif®)	BCR-ABL1	Leukemia
65	Brentuximab vedotin (Adcetris™)	CD30	Hodgkin's lymphoma, anaplastic large cell lymphoma
66	Capecitabine (Xeloda®)	DPYD	Multiple cancers
67	Cetuximab (Erbix®)	EGFR; KRAS	Colon cancer
68	Crizotinib (Xalkori®)	ALK	Lung cancer
69	Dabrafenib (Tafinlar®)	BRAF; G6PD	Melanoma
70	Dasatinib (Sprycel®)	BCR-ABL	Leukemia
71	Denileukin diftitox (Ontak®)	IL2RA	Lymphoma
72	Erlotinib (Tarceva®)	EGFR	Non-small cell lung cancer
73	Everolimus (Afinitor®)	ERBB2; ESR1	Breast cancer

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Oncology (cont.)			
74	Exemestane (Aromasin®)	ESR1; PGR	Breast cancer
75	5-Fluorouracil (5-FU) (Efudex®)	DPYD	Multiple cancers
76	Fulvestrant (Faslodex®)	ESR1; PGR	Breast cancer
77	Gefitinib (Iressa®)	EGFR	Non-small cell lung cancer
78	Imatinib (Gleevec®)	BCR-ABL; PDGFRB; KIT; FIPIL1-PDGFR	Multiple cancers, myelodysplastic syndrome
79	Irinotecan (Camptosar®)	UGT1A1	Colon cancer, small cell lung cancer
80	Lapatinib (Tykerb®)	ERBB2; HLA-DQA1; HLA-DRB1	Breast cancer
81	Lenalidomide (Revlimid®)	Del (5q)	Multiple myeloma, mantle cell lymphoma, myelodysplastic syndrome
82	Letrozole (Femara®)	ESR1; PGR	Breast cancer
83	Mercaptopurine (Purinethol®)	TPMT	Acute lymphocytic leukemia, chronic myeloid leukemia, Crohn's disease, and ulcerative colitis
84	Nilotinib (Tasigna®)	UGT1A1; BCR-ABL1	Chronic myelogenous leukemia
85	Obinutuzumab (Gazyva®)	MS4A1	Chronic lymphocytic leukemia, follicular lymphoma
86	Omacetaxine mepesuccinate (Synribo®)	BCR-ABL1	Chronic myeloid leukemia
87	Panitumumab (Vectibix®)	EGFR; KRAS	Colon cancer
88	Pemetrexed (Alimta®)	TS	Lung cancer
89	Pertuzumab (Perjeta®)	ERBB2	Breast cancer
Platinum Therapies			
90	Carboplatin	ERCC1	Ovarian cancer
91	Cisplatin	TPMT	Multiple cancers
92	Oxaliplatin	ERCC1	Colorectal cancer
93	Nedaplatin	ERCC1	Multiple cancers
94	Triplatin tetranitrate	ERCC1	Multiple cancers
95	Satraplatin	ERCC1	Multiple cancers

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Oncology (cont.)			
96	Ponatinib (Iclusig®)	BCR-ABL1	Chronic lymphocytic leukemia, acute lymphocytic leukemia
97	Rituximab (Rituxan®)	MS4A1	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and autoimmune diseases
98	Tamoxifen (Nolvadex®)	ESR1; ESR2; PGR; F5; F2; CYP2D6	Breast cancer
99	Thioguanine (Tabloid®)	TPMT	Acute myeloid leukemia, acute lymphocytic leukemia, and chronic myeloid leukemia
100	Tositumomab (Bexxar®)	MS4A1	Non-Hodgkin's lymphoma
101	Trametinib (Mekinist®)	BRAF	Melanoma
102	Trastuzumab (Herceptin®)	ERBB2	Breast cancer
103	Tretinoin (Vesanoid®)	PML / RAR α	Acute promyelocytic leukemia
104	Vemurafenib (Zelboraf™)	BRAF; NRAS	Melanoma
Psychiatry			
105	Aripiprazole (Abilify®)	CYP2D6	Schizophrenia, bipolar disorder
106	Amitriptyline (Elavil®)	CYP2D6; CYP2C19	Depression
107	Atomoxetine (Strattera®)	CYP2D6	ADHD
108	Citalopram (Celexa®)	CYP2C19	Depression
109	Clomipramine (Anafranil®)	CYP2D6	Depression
110	Clozapine (Clozaril®)	CYP2D6	Schizophrenia
111	Desipramine (Norpramin®)	CYP2D6	Depression
112	Doxepin (Silenor®)	CYP2D6; CYP2C19	Insomnia, depression
113	Fluoxetine (Prozac®)	CYP2D6	Depression
114	Fluvoxamine (Luvox CR®)	CYP2D6	Obsessive compulsive disorders
115	Iloperidone (Fanapt®)	CYP2D6	Schizophrenia
116	Imipramine (Tofranil-PM®)	CYP2D6; CYP2C19	Depression
117	Nortriptyline (Pamelor®)	CYP2D6	Depression
118	Paroxetine (Pexeva®)	CYP2D6	Major depressive disorder, obsessive compulsive disorder, panic disorder, and generalized anxiety disorder
119	Perphenazine (Trilafon®)	CYP2D6	Schizophrenia
120	Pimozide (Orap®)	CYP2D6	Tourette's syndrome

	Drug Name (Brand Name)	Biomarker(s)	Indication(s)
Psychiatry (cont.)			
121	Protriptyline (Vivactil®)	CYP2D6	Depression
122	Risperidone	CYP2D6	Schizophrenia, bipolar mania, irritability with autistic disorder
123	Thioridazine (Mellaril®)	CYP2D6	Schizophrenia
124	Trimipramine (Surmontil®)	CYP2D6; CYP2C19	Depression
Pulmonary			
125	Ivacaftor (Kalydeco®)	CFTR	Cystic fibrosis
Rheumatology			
126	Azathioprine (Imuran®)	TPMT	Rheumatoid arthritis, organ transplant
127	Flurbiprofen (Ansaid®)	CYP2C9	Arthritis
128	Pegloticase (Krystexxa®)	G6PD	Uric acid management, gout
Toxicology			
129	Sodium nitrite	G6PD	Cyanide poisoning
Transplantation			
130	Mycophenolic acid (Myfortic®)	HPRT1	Kidney transplant
131	Tacrolimus	CYP3A5	Organ transplant
Urology			
132	Tolterodine (Detrol®)	CYP2D6	Overactive bladder