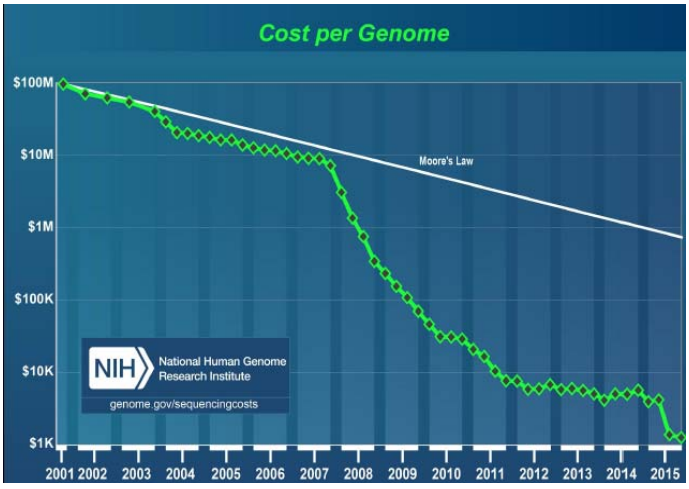
Personalized Medicine Whitepaper

"Currently, most medicine is prescribed with a "one size fits all" approach, meaning that the same medicines are typically prescribed to any individual who is diagnosed with a particular disease." The insight into genomic sequencing is starting to allow predictions and modification targeting of medicine.

The field of personalized medicine, the medical procedure that classifies patients into different groups based on numerous metrics and tailors care to the individual, is primed to see continued growth in the upcoming years. Further development of personalized medicine has the potential to change the face of clinical practice as we know it. Currently, most medicine is prescribed with a "one size fits all" approach, meaning that the same medicines are typically prescribed to any individual who is diagnosed with a particular disease. This approach can lead to multiple rounds of trial and error in prescribing patients, inevitably delaying the healing process. By focusing on DNA structure, what fundamentally determines how humans react to medicinal treatment, preventative medicine drastically improves the probability of prescribing the patient with the optimal medication the first time through.

Huge Drop in Cost Since 2007

As the advances in laboratory technologies have markedly reduced the cost of obtaining patient's genetic information, personalized medicine started to catch attention from the stakeholders in the healthcare industry. These technologies have enabled clinical research that has dramatically improved knowledge regarding gene-drug interactions.



PPGS Overview

Predispositional personal genome sequencing (PPGS) is a technique that identifies risk for health problems such as cancer and heart disease by looking at genetic sequencing of currently healthy patients. The cost of sequencing is rapidly dropping, and as a result it is becoming more pragmatic to conduct widespread PPGS projects. If a patient is aware of his/her risks, it provides them with the opportunity to adjust their lifestyle choice accordingly, whereas in the past this was not an option until it was ultimately too late. For example, someone informed that they are genetically predisposed to becoming a diabetic would be given the opportunity to abstain from sugary foods in order to mitigate some of that risk. From a health insurance standpoint, this is great news as the patient may avoid the expensive diabetes treatment that may have ensued otherwise.

Wanting to Know

Apparently healthy adults gave these reasons for taking part in programs offering genomic sequencing

Personal interest in genetics in general	99%
Curiosity about my genetic make-up	98%
Desire to participate in research to help others	92%
Interest in finding out things to do to improve my health	81%
To learn about my personal response to medications	81%
It seemed fun and entertaining	77%
Desire to plan for the future	69%
Interest in my ancestry	66%
Interest in finding out about personal disease risk	41%
Concern about possible/confirmed family genetic condition	21%

Note: Percentages are the total saying very or somewhat important.

Source: PeopleSeq study of 258 adults from the Harvard Personal Genome Project, Illumina Understand Your Genome program and Mount Sinai HealthSeq study

THE WALL STREET JOURNAL.

Case Study: Prostate Cancer

According to The Institute of Cancer Research, genetic testing in men with advanced prostate cancer can be very useful for men with a certain DNA repair gene mutation. BRCA2, the most commonly defective gene was mutated in 5% of men. Men suffering from these mutations could benefit from new drugs referred to as "PARP inhibitors", which focus on weaknesses in the methods of DNA repair in cancerous cells. This discovery is significant because of the implications it has for men currently diagnosed with advanced prostate cancer. Because a large portion of this group are born with DNA repair mutations (12% in this study, which was the largest of its kind to this date), these patients could be treated with PARP inhibitors, which are showing anti-tumor activity in ongoing clinical trials. This therapy would work in conjunction with already ongoing treatment options and likely improve survival chances.

Source: Institute of Cancer Research

Reimbursement Environment

The ideal targets for personalized medicine providers are self insured companies and third party healthcare plan adminstrators as they are often quicker to adopt genomic testing than large insurance companies. Medicare currently offers specific CPT codes with set reimbursement rates to personalized medicine providers. Each code has a certain dollar value attached to it that the provider will be reimbursed for. With insurance companies this can become more convoluted as it's common practice to not pay the full reimbursable value. From the payer perspective, there are both pros and cons to pharmacogenomics. On a positive note pharmacogenomics would lead to a reduced number needed to treat, the reduced waste of expensive drugs on individuals who do not respond to the treatment and improved treatment outcomes as a result of the more precise

diagnosing method. However risks include additional costs associated with false positive test results, the cost that the inevitable privacy regulatory implications that mass DNA databases will have, and paying for the increased diagnostic budgets associated with increased testing. While there is significant variation in the private insurance space, Medicare has seen quite a few difficulties in the acceptance of personalized medicine reimbursement. Highly impactful policy decisions face CMS in the upcoming years. For traditional diagnostic tests, Medicare lowered its payments between 2012 and 2013. It is very important that reimbursement levels will both ensure access to high quality tests but also offer support for the development of innovative research. Providers need to cover both the cost of testing and any research and development costs that go into developing the tests. Furthermore, there is disagreement about the clinical utility assessments. Clinical utility refers to "the relevance and usefulness of an intervention in patient care". The most important question with diagnostic tests such as personalized medicine is that when the results are acted upon, will the result be more favorable than if the test had not been conducted? If the answer is yes, than the procedure possesses clinical utility and is considered "worth" reimbursing.

Recent Transactions:

Nanthealth IPO

On June 2nd NantHealth, a healthcare company focused on information technology and personalized medicine, went public. Nanthealth, which will trade under the ticker "NH", issued 6.5 million shares at an issue price of $14 per share. NantHealth is currently working to establish a database of patient genetic information to be used for predictive medicine. GPS Cancer, its molecular diagnostic tool uses this data to predict the response patients will have to different treatments. The shares were issued to raise additional working capital for the company, which will likely go towards research and development, marketing and administration expenses.

GE Healthcare

On July 13th GE Healthcare acquired Biosafe Group SA, a Swiss company that supplies integrated cell bioprocessing sytems for the cell therapy and regenerative medicine industry. The purchase price was undisclosed. Biosafe's founder Claude Fell expressed confidence in the move, saying: "Together with GE we will have the combination of biological, engineering and industrial capabilities to help accelerate the fields of cell therapy and cellurar immunotherapy into the mainstream, benefitting patients globally, and bringing the vision of personalized medicine to realtiy." A major driver behind the deal is the synergies to be recognized between the two companies. GE Healthcare's global infrastructure combined with Biosafe's unique technology will hopefully lead to improved opportunities for customers. GE's goal is to develop a digitally driven system of tools for cell therapy in order to expedite the process of standardizing personalized medicine into mainstream practice.

Source: StreetInsider

IGENOMIX

Headquartered in Valencia, Spain, IGENOMIX, a leading provider of genetic testing services for reproductive health patients and clinics, was created in 2011 when it was spun-out from Instituto Valenciano de Infertilidad (IVI). Today it is one of the world's leading providers of advanced services in reproductive genetics, operating from eight laboratories worldwide.
IGENOMIX was sold in Sept 2016 to and investor group: Charme Capital Partners, Amadeus Capital Partners, Aleph Capital, and Graham Snudden. Terms of the transaction were not disclosed. Dresner Partners along with Arcano Group of Madrid (Spain) represented the Seller.

Myriad Genetics

Myriad Genetics, Inc. (NASDAQ: MYGN), a leader in molecular dianostics and personalized medicine, has announced that it has signed a definitive agreement to acquire Assurex Health, a global leader in genetic testing for psychotropic medince selection, for a down payment of $ 225 million with an addition of $185 million to compensate future performance. Assurex had revenue of more than $60 million and served more than 150,000 patients in Myriad's fiscal year of 2016. The transaction is expected to close at the end of Myriad's first quarter of fiscal year 2017.

Notable Company in the Industry

23 and Me

23 and Me is a consumer genetics company that analyzes its customers' DNA and reports back on their health and ancestry. So far, the company has collected data from more than one million of its customers, 850,000 of whom have given the company permission to utilize their genetic information for research.

Recently, the company conducted a research with pharmaceutical giant Pfizer and found 15 new DNA regions associated with mutations that could predispose individuals to major depression. Researches took the DNA of over 75,000 people who reported being clinically diagnosed with depression and compared it with more than 230,000 customers who reported no such diagnosis. The 15 regions in the scrutinized DNA are the first to be linked to major depression in people of European descent. This finding is more significant than the previous study looking at over 10,000 people of Han Chinese ancestry, which found two such regions. Depression is very complicated genetically, so the discovery is unlikely to prove useful as a predictive tool; however, the finding will give scientists a deeper understanding of how major depression works. This is becoming a common theme in genetic studies of complex diseases like major depression, type 2 diabetes and heart disease. Rather than leading to predictive genetic tests, the studies are bringing a better understanding of what causes the illness, leading to new approaches of treatment.

Ancestry.com

AncestryDNA is the world's largest consumer DNA database with more than 2 million samples. Ancestry uses industry standard security system to maintain the DNA samples and DNA test results. Its customers can choose to download raw DNA data, request the company to delelte the DNA test results or destroy the physical DNA saliva sample at any time.

With a price tag of $99, the company will help its customers to uncover their ethnic mix, discover distant relative, and find new details about their unqiue family history with a simple DNA test. The process is quite simple.

Source: Ancestry.com

Improved Patient Outcomes, Inc.

Improved patient Outcomes, Inc. (IPO) is a joint venture between the private sector and Duke University's School of Medcine. IPO applies hundreds of predictive indicators to EHR, Claims, Pharmacy and other data to deploy multi-channel, targeted and tailored behavior changing patient interventions across 90 different disease states or conditions.

This personalized care (a subset of personalized medicine) approach, combined with population health management and patient engagement delivers patient outcomes imporvements of 25% or more on average.

IPO Population Health Management 2.0

Healthcare System Collaboration on Personalized medicine

The high level of complexity of implementing and progressing personalized medicine requires high level of collaboration between different players in the healthcare system.

Most molecular causes of diseases are not simply a single dysfunctional process in the cell, but often combinations of different defects that lead to diseases such as cancer, leukemia, diabetes and inflammatory diseases. This implies that a combinations of long-term treatment and cures may be required to effectively fix these diseases. This means that different pharmaceutical companies, academic groups and regulators will need to be able to work together on combinations of these agents in clinical trials.

The fact that personalized medicine can more accurately define molecular subtypes of diseases, which is leading to smaller sub groups of patients with specific molecular diagnosis. To find the appropriate group of patients for a clinical study, collaboration across many hospitals and even across countries is required. Working with these smaller sub-groups of patients raises challenges comparable to those of orphan diseases, where the traditional model of industry-sponsored clinical studies is often difficult to implement. Instead, collaboration with academic and patient groups will be necessary to identify suitable patients. E-health records would also help to identify patients with rare biomarkers more effectively for the recruitment to clinical trials.

Source:ebe European biopharmaceutical enterprises

Potential Risk Factors

While personalized medicine is an exciting, potentially revolutionary healthcare field, it does come with a myriad of ethical and logistical issues surrounding it. While the research end of the field is rapidly expanding, doctors need to be trained on how to handle questions and concerns of patients who are exposed to personalized medicine. Furthermore, privacy concerns arise as it is likely that with large databases containing people's personal health information there will be hacks and/or leaks. As a patient, the fear of having your health risks becoming public information may act as a deterrent for agreeing to DNA testing. Finally one of the biggest issues involved with personalized medicine is the inconvenient truths that will inevitably arise during patient consultations. Genetic tests will tell doctors things that patients do not ask about, such as incidentally finding out the patient's parent is not really their parent while attempting to find a personalized solution for their diabetes. While it is unlikely that these issues will derail progress in personalized medicine, these are potentially convoluted concerns that healthcare providers and regulators will need to address in the not so distant future.

Future Outlook

Investment in personalized medicine is likely to grow dramatically over the next few years as the cost savings and improvements in patient outcomes are likely to be substantial. A report published by KellySciPub indicates that the personalized medicine market with be worth over $149 billion by 2020. Gene sequences are not an 100% accurate predictor of what a patient's future health history will entail, but it is a key piece of information for doctors to make medication decisions on. In some cases, such as cancer, conducting genetic examinations could lead to a favorable drug treatment as opposed to a major surgery intended to have a similar outcome. If the FDA explicitly ties a genetic mutation to a specific treatment type or drug, insurance providers tend to cover the testing and treatment costs. A hurdle that exists for reimbursement through insurance companies is the burden of proof: insurers want to know for certain that personalized medicine is worth the extra up-front expense. With sequencing costs becoming more and more affordable; however, insurance companies will be taking less risk by laying out money for a genome sequencing scan.

Selected Terminologies

Personalized Medicine: Personalized Medicine is the concept that managing a patient's health should be based on the individual patient's specific characteristics, including age, gender, height/weight, diet, environment, etc. Potential applications of personalized medicine Personalized medicine aims to identify individuals at risk for common diseases such as cancer, heart disease, and diabetes.
Source: ScienceDaily

Precision Medicine: Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. While some advances in precision medicine have been made, the practice is not currently in use for most diseases.
Source: National Institutes of Health

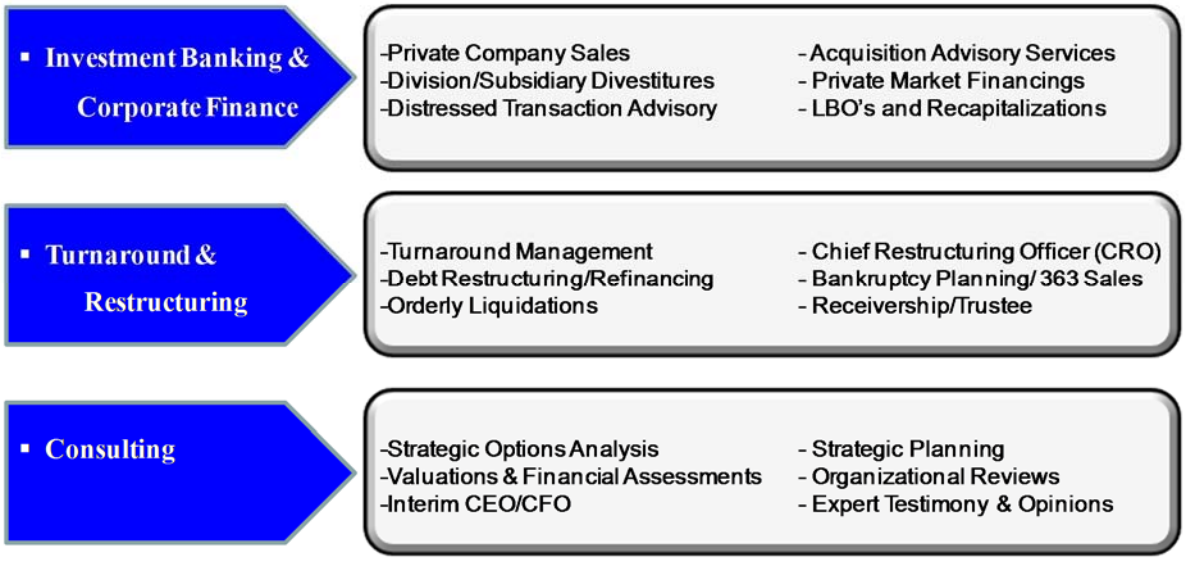
Pharmacogenomics: Pharmacogenomics is the study of genetic variations that influence individual response to drugs. Knowing whether a patient carries any of these genetic variations can help prescribers individualize drug therapy, decrease the chance for adverse drug events, and increase the effectiveness of drugs.
Source: American Medical Association

Pharmacogenetics: The study of how people respond differently to medicines due to their genetic inheritance is called pharmacogenetics. The term has been pieced together from the words pharmacology (the study of how drugs work in the body) and genetics (the study of how traits are inherited). An ultimate goal of pharmacogenetics is to understand how someone's genetic make-up determines how well a medicine works in his or her body, as well as what side effects are likely to occur.
Source: Dartmouth University

Vaccinomics: Vaccinomics is a term which has been defined by Poland and colleagues as "predictive or individualized vaccinology". This describes the production of prophylactic or therapeutic vaccines which are tailor-made for a specific individual.
Source:http://www.forbes.com/sites/brucelee/2016/09/04/designing-vaccines-just-for-you/#5ee0997b2c92

Lawrence, Evans & Co., LLC *provides investment banking, finance, and consulting services for small and middle market healthcare providers and services companies. We are very active on the buy-side and the sell-side of Revenue Cycle Management and related transactions.*

SERVICES



REPRESENTED TRANSACTIONS

Lawrence, Evans & Co., LLC

Contact: Neil L. Johnson
Managing Partner
614-448-1304/614-598-8905
njohnson@lawrenceevans.com

Weian Ye
Analyst
614-448-1304
wye@lawrenceevans.com