A Framework for Demonstrating the Value of Medical Innovation

A White Paper Presented by BioNJ

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Introduction and Acknowledgements

Dear New Jersey Life Sciences Community,

BioNJ, the life sciences trade association for New Jersey, is delighted to release the white paper, "***A Framework for Demonstrating the Value of Medical Innovation***." This white paper came to fruition as a result of ***BioNJ's Beyond Value Frameworks: Defining the Value of Medical Innovation*** workshops.

With nearly 3,300 life sciences establishments, including 12 of the world's largest biopharmaceutical companies, having a headquarters or significant presence in the Garden State, New Jersey's life sciences ecosystem was responsible for more than 40% of all new novel FDA drug approvals over the last two years – more than anyplace else in the world.

It is crucial for patients to have access to this life-changing medical innovation. However, under current benefit designs, patients often don't have access to the right medicines at the right time. The current paradigm frequently assumes a "one size fits all" approach.

As a result, innovator companies need to provide more information and insights to overcome these barriers to access. This white paper, authored by **Shailja Dixit, M.D., M.S., M.P.H.**, President & Founder, ApexBio and **Robert Goldberg, Ph.D.**, Vice President & Founder, Center for Medicine in the Public Interest, outlines a **framework** for assessing the true value of the innovation and identifies steps that innovator companies can take to demonstrate **Differential Value** of their innovation.

We have many people to thank for their contributions to moving this initiative forward, starting with Drs. Shailja Dixit and Robert Goldberg for their expertise and leadership; as well as our advisors **Robert Epstein, M.D., M.S.**, Director of Fate Therapeutics, Inc. and Veracyte, Inc. and past President of United BioSource Corporation at Medco Health Solutions; **Brian Gill**, Founder and President, Gill Communications; **Steven Peskin, M.D., MBA, FACP**, Executive Medical Director, Population Management, Horizon Blue Cross Blue Shield of New Jersey; **Kevin Rigby**, Principal, KRigby Consulting and **Robert Tufts**, Founder of My Life Is Worth it, an organization that advocates for patient and physician access and choice in medical care.

Our hope is that innovator companies find this white paper to be a useful resource and guide as they develop and bring new medical innovation to market. Because, as we say at BioNJ, Patients Can't Wait®.

Sincerely,

Debbie Hart
President and CEO
BioNJ

Executive Summary

Prescription drugs play an important role in the U.S. healthcare system. Innovative breakthrough drugs are providing cures for diseases such as Hepatitis C and helping individuals with chronic conditions lead fuller, more productive lives.

Many more innovative medicines are in the pipeline. This new generation of precision medicine can be used to develop targeted preventive strategies and disease-specific therapies. This approach can improve quality of care, enhance the patient experience and allow more efficient healthcare expenditures.

However, the current approach of providing access and drug benefits is at odds with this goal.

In current benefit design, higher cost-sharing levels and step therapy do not reflect the variations in clinical conditions and patient response. It assumes an approach of "one size fits all". Such policies may increase spending on low value care and discourage and reduce the use of more innovative and effective medicines. In addition, there is a lot of waste in the system since innovator companies must pay at least 15-20 percent of the price of a product directly to wholesalers, specialty pharmacies and other intermediaries; as well as subsidize the out-of-pocket costs of many consumers while maintaining programs to negotiate with Pharmacy Benefits Managers (PBMs) and insurance companies to allow and approve the use of new medicines.

Even if rebates and prior authorization are eliminated altogether, innovator companies will still struggle to differentiate their products and demonstrate effectiveness due to lack of data and the right analytical framework. Just as current drug benefit designs ignore patient variation and preferences, traditional analytical approaches used to measure value are often limited to population-averaged approaches. As Dr. Mark Fendrick, Director of the Center for Value-Based Insurance Design, has observed, the model that we currently use to pay for and price new medicines and other healthcare services is unsuited to covering groundbreaking, one-time treatments, particularly those with clinical benefits that are incurred in the near and distant future.

The facts are:

- **Payers want evidence that new treatments will improve well-being, clinical outcomes and reduce costs at a patient level.**
- **Patients lack the information and support required to overcome barriers to access and find the treatments that can best help them.**
- **Value or outcomes-based contracts where reimbursement is linked to better patient outcomes is increasingly being proposed as a solution.**
- **The current paradigm struggles to answer a few basic questions by stakeholders.**

At the same time, most innovator companies need more information and insights to overcome barriers to access. In particular, innovators suffer from a lack of evidence:

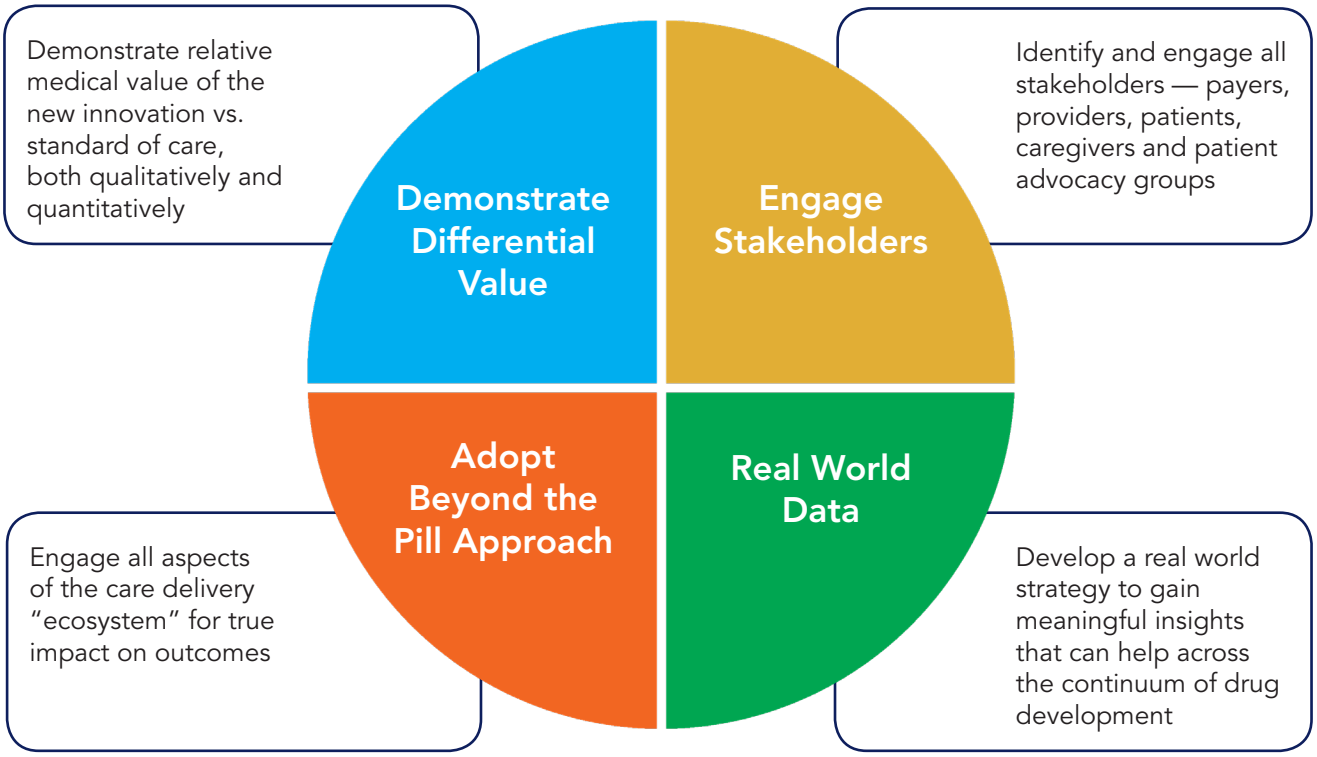
- For predicting or measuring real world product performance for specific patient groups.
- For assessing financial impact of improved outcomes.
- To help caregivers and patients improve activation and adherence.
- To align incentives with specific contract performance goals.

To be successful under the current reimbursement model, innovators must begin to evaluate the relative value of their new innovation early in the drug development process. In particular, they must invest more time and effort into demonstrating that their treatments improve health compared to existing treatments and tailor the delivery and price of products to allow patients, physicians and health systems to capture the full value of these innovations. Such an approach can help bring much needed innovation to patients and contribute to the sustainability of individual innovator companies.

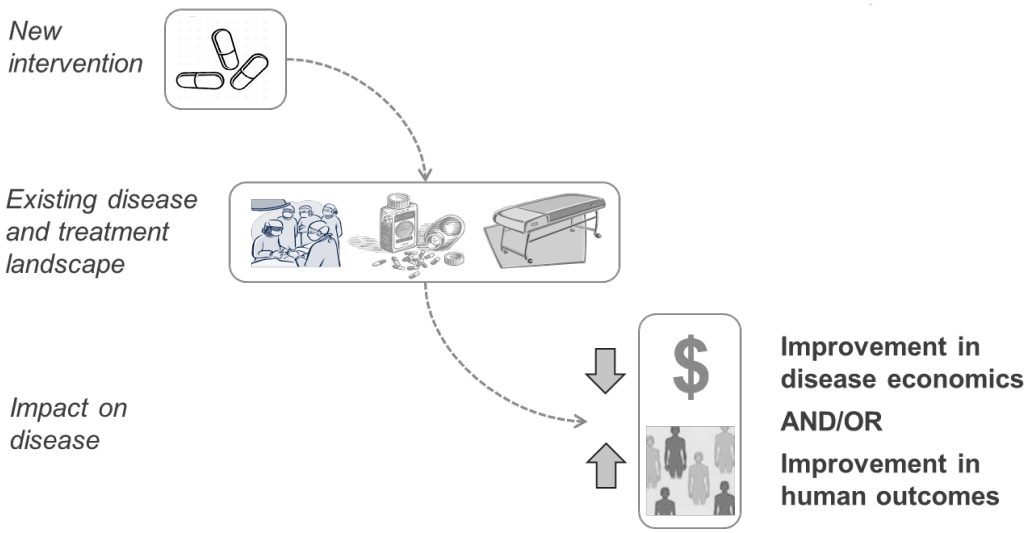
This white paper outlines a framework for assessing the true value of the innovation and identifying steps that innovator companies need to take to demonstrate **Differential Value** of their innovation. It outlines a stepwise process with an inventory of important tools, as well as a recommendation on when the time is right to adopt this framework during the drug development process.

A Four-Pronged Approach

We are outlining a four-pronged approach that can help innovator companies understand the unmet need, assist in product development and help capture and demonstrate the value of the innovation.



Value Framework: How to Measure Value of New Innovation and Focus on Differential Value of the Innovation



To demonstrate medical or relative medical value of any innovation, it is important to ***Identify***, ***Define***, ***Demonstrate*** and ***Capture*** the value of the new innovation as compared to the existing treatment landscape.

Identifying the Value of the Innovation: The first step is to identify the potential impact of the innovation on the disease and treatment pathway. The questions to be asked are: Is this innovation going to delay the natural pathway of disease progression as compared to the standard of care; is this innovation going to have an impact on clinical parameters/outcomes that are clinically meaningful or is it going to have an impact on a patient's quality of life. Last, but not least, an innovation might have an impact on economics, i.e. may drastically impact length of stay or may change the IV infusion to oral ambulatory thereby impacting cost per patient and the overall cost to the healthcare system.

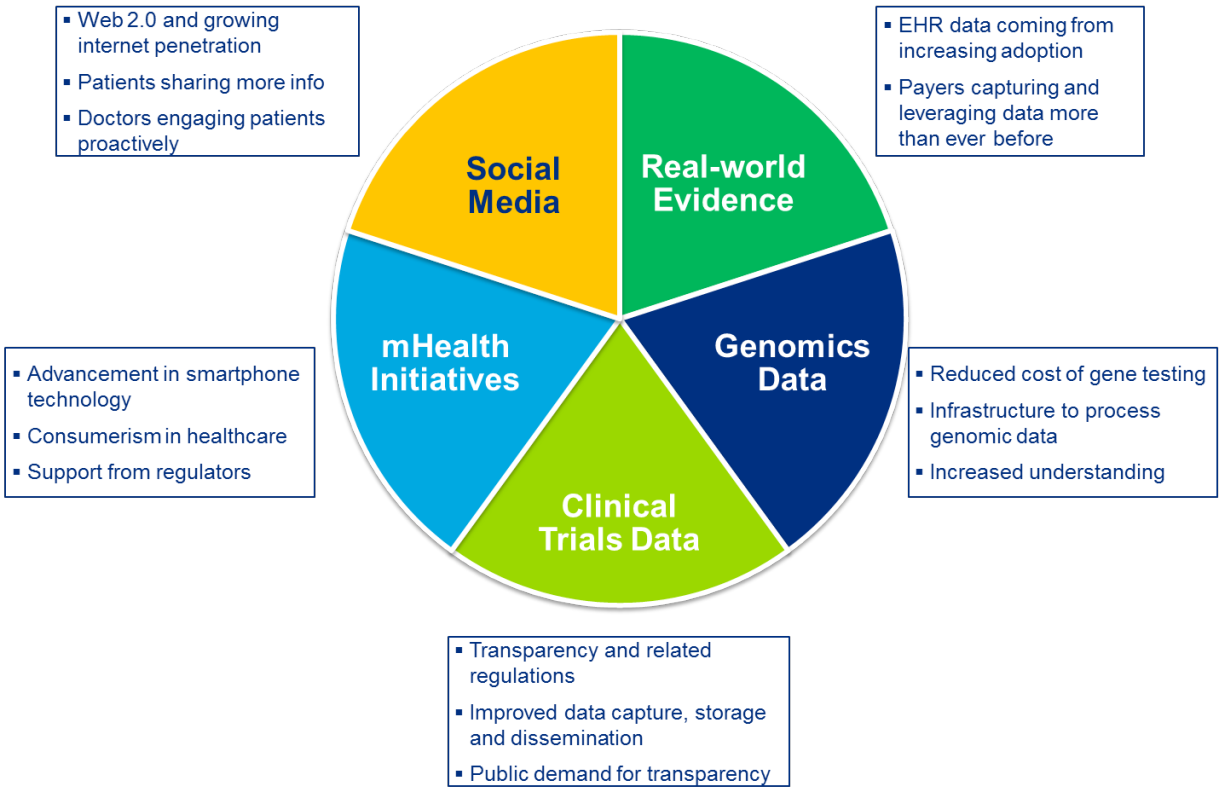
Define Parameters that will Capture Value: Once it has been identified what value a new innovation is going to bring, the next critical step is to define parameters that will demonstrate that value. A systematic approach to capture this value at every step of product development needs to be outlined and studies and projects need to be planned. Understanding this **Framework of Differential Value** is critical for innovator companies in order to demonstrate the value of their innovation and to then gain market acceptance.

Demonstrate and Capture Value: Last, and most important, is a strategy to capture value by designing and conducting real world studies that capture patients' perspectives and show economic benefits. In the current environment, it has become critically important to be successful in demonstrating value to all these stakeholders and to do so early in development. This new paradigm is what we call "**Value-Driven Drug Development**."

By doing so, companies can mitigate key risks in development, such as discontinuation in Phase 3 caused by lack of efficacy, regulatory failure due to lack of favorable benefit-risk profile and commercial disappointment either as a result of poor market access or poor patient/provider acceptance — due to a lack of differentiation or not taking into account the patient's perspective and unmet need.

Focus on Real World Data

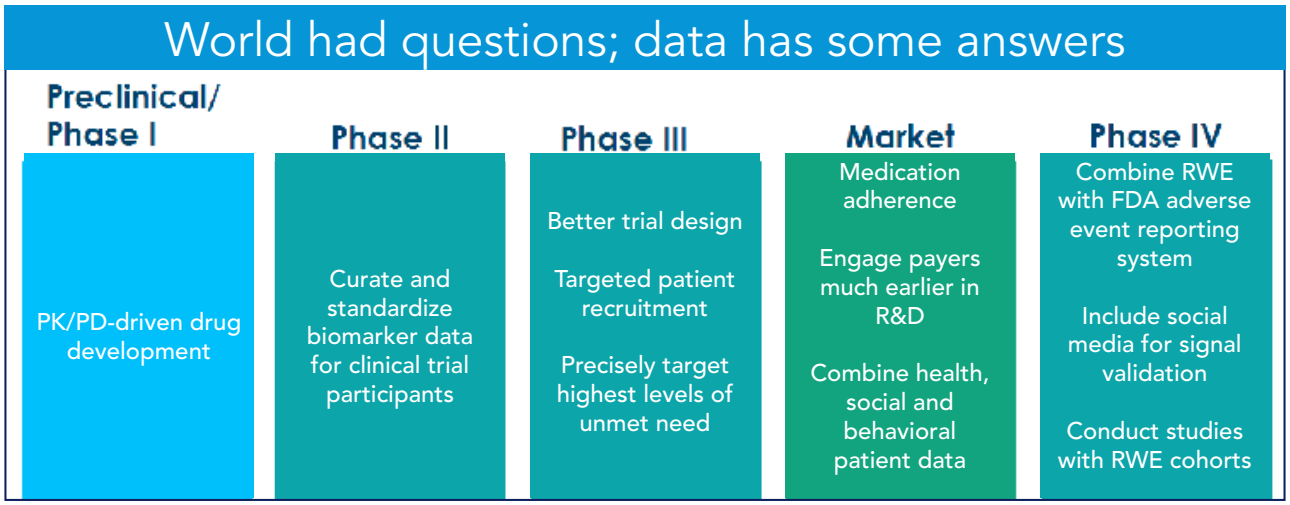
An unprecedented amount of data is generated in today's world and that volume is primarily driven by five key phenomena:



Total data are being generated with great velocity, volume and variety. It's no longer a question of whether data will be available but rather a question of volume. Per the International Data Corporation, 153 exabytes of healthcare data was produced in 2013 and an estimated 2,314 will be produced in 2020. (one exabyte = one billion gigabytes)

The key challenges that innovators have are how to access the data in a cost-effective manner and how to derive meaningful, actionable insights.

Real world data has a role to play in every step of product development as shown in the Table below:



The key question is how to get access to the right data and analytics tools at the right time in a cost-effective manner.

There are several data e-sources available today:

1. **Marketplace for healthcare data:** There are companies that have curated and linked different varieties of data that are easily available for use by biopharmaceutical companies. One such example is Healthverity.

2. **Build your own registry:** Biopharmaceutical companies can invest early on in building their own real world repository and registry. De-identified data can be bought from insurance company and EMR vendors, such as Express Scripts.

3. **Build a coalition:** A coalition of healthcare centers can be built to collect disease-specific data and this data can be analyzed to answer various critical questions.

4. **Mining data from social network sites:** Social network forums and patient groups share patient impressions and very rich data are being generated in these forums. They provide insights into unmet needs and patients' perspectives. There are companies today that leverage this data and provide insights to biopharmaceutical companies. One such example is PatientsLikeMe.

5. **Medical Expenditure Panel Survey (MEPS):** MEPS is a set of large-scale surveys of families and individuals and their medical providers and employers across the United States. MEPS is the most complete source of data on the cost and use of healthcare and health insurance coverage. It is publicly available real world longitudinal data.

The Need for a New Analytical Framework

Biotechnology and pharmaceutical companies, including those developing medicines for rare diseases, can no longer depend on insurers covering their products without conditions. Increasingly, patient access to new medicines will be limited through step therapy, prior authorization, quantity limits, non-therapeutic drug switching and cost sharing.

Improving access and adherence requires predictive models to support personalized medicine. Using patient level real world data requires more than traditional analytical approaches. That is because approaches used by innovator companies often employ manual, time-consuming, single hypothesis algorithms which are limited in their ability to integrate multiple data types. As a result, they can only produce predictions of population-averaged approaches to what is already known.

Companies should adopt the use of machine learning platforms that can quickly generate any number of "what if?" simulations of a variety of interventions, across patients in order to determine optimal therapies.

Putting Patients in the Center of Drug Discovery: Identifying Stakeholders and Engaging Them

Another important aspect is getting an understanding of key constituents, when to engage them and how to engage them.

Besides the usual constituents (e.g. regulatory agencies, payers or risk-bearing organizations and healthcare providers), patients are a key stakeholder who need to be kept front and center. Innovators often miss the patient perspective during drug development.

Much of the patient experience is not captured in medical records. Moreover, current methods of capturing such insights — surveys and questionnaires — fail to capture the social, behavioral and economic context that shapes an individual's response to their illness. Studies demonstrate that patients frequently do not share relevant information about drug adherence, well-being or life events.

There are multiple ways patient perspectives can be included early on in drug development. For example, collaboration with patient advocacy groups to understand their unmet needs and patient views is very important. There are many examples of when a drug has not been successful because patient perspective was not considered early on.

However, an example of what works and what to do to engage patients is the initiative launched by the Parent Project Muscular Dystrophy (PPMD), a non-profit organization leading the fight to end Duchenne Muscular Dystrophy (Duchenne). PPMD worked with innovator companies and the FDA to ensure that endpoints of value to families were included in the guidance document used to facilitate the development of medicines for Duchenne.

PPMD also established a partnership with THREAD, a company specializing in remote/virtual patient research via their platform, to enhance patient engagement and created care management tools for their existing Duchenne Registry.

As a result of efforts such as this, the cost of creating virtual registries that provide a holistic understanding of patient level experience and treatment response has been dropping.

CASE STUDY: Pancreatic Cancer Action Network and TYME Technologies

Pancreatic Cancer Action Network's (PanCAN) Precision Promise "is the first adaptive clinical trial platform for pancreatic cancer patients in the world" and is PanCAN's "initiative to dramatically improve patient outcomes and advance the organization's goal to double survival by 2020." Designed with a nationwide team of leading clinicians, researchers and diagnostic and drug developers, Precision Promise will continuously and rapidly bring new treatment options to patients and transform the future of clinical research.

TYME Technologies, Inc. has included its SM-88 (an oral medicine that interrupts the metabolic processes of cancer cells) as an experimental arm in the novel Precision Promise adaptive Phase II/III trial platform sponsored by PanCAN. This partnership has allowed TYME to benefit from in-depth biomarker and genomic profiling to be performed on all participants that in turn can be used to identify which patient subtypes benefit from which experimental therapies. The Precision Promise Platform also collects data on changes in health-related quality of life using patient-reported outcomes following treatment with SM-88. Finally, using PanCAN's clinical trials database, TYME is able to improve outreach for its study by determining how many patients search for clinical trials after having received two or more previous treatment regimens.

Beyond the Pill Approach: The Time is Now

There has been a lot of talk about the 'Beyond the Pill' approach for many years, as companies have tried to create services and solutions that are complimentary to their drugs. With more pressure on innovator companies to demonstrate impact on outcomes and to illustrate value, companies are looking at strategies to improve patient outcomes and diversify revenue sources that go far beyond the pill. Beyond the Pill should also be regarded as beyond the point of sale.

- Better patient engagement is a nearly universal goal for healthcare providers, however, real barriers exist.
- Nearly two-thirds (63%) of respondents to *New England Journal of Medicine* (NEJM) Catalyst Insights Council's latest survey on patient engagement said the time investment required by health teams was their biggest challenge in designing patient engagement into care delivery.
- The underlying issue is that reimbursements and incentives [for patient engagement] are not aligned. The time and effort to educate, motivate and troubleshoot issues regarding patient engagement are not paid for nor are they tied to reimbursement.

For example, Biogen has used Fitbits to monitor the walking activity of patients with multiple sclerosis, previously only measured during visits to the doctor's office.

Wearables, ingestables and implantables offer many new opportunities for innovator companies to become involved in the overall health of their customers, as well as to know how well their medicines are working. As technology becomes an integral part of our lives and innovator companies are more open to adopting technology, it is likely that medications will have an accompanying mobile app, with devices to track a drug's outcome.

To be successful in the Beyond the Pill approach, the innovator must also engage with providers and patients to ensure that their efforts are trusted and offerings are useful and of value.

Most patient engagement programs only look at refill or first-fill rates to measure adherence. Moreover, such adherence efforts are one-size-fits-all. They ignore the day-to-day and behavioral factors that influence treatment patterns and, therefore, fail to provide patients at the greatest risk of non-adherence-related disease progression the customized support they need, especially when they are alone or outside a treatment facility or the care of a physician.

Such patient engagement programs should identify factors — ranging from adverse events, costs and barriers to access and individual experiences or perceptions — that shape treatment activation.

That information can be used to identify and predict which patients are at greatest risk of poor health because of lack of medication adherence as well as to identify patients most likely to abandon or fail to consistently use their medications.

Next, innovators, along with patients, should identify which of the new and potential technologies, as well as communication mechanisms, are meaningful.

From there, it is important to:

Identify Value Delivered to all Stakeholders:
It is important to identify all stakeholders as well as the value delivered to each. As innovator companies design new solutions and services, it is necessary to consider the needs of the entire health ecosystem and to develop solutions that provide value to all stakeholders.

In particular, any Beyond the Pill platform must be trusted by patients and providers. Specifically, they should be able to customize supportive and motivational messages that can be sent to a patient at any hour of the day, either based on the patient's perceived needs, or based on actual requests from the patient.

Define a Business Model Upfront:
Many Beyond the Pill efforts fail because a clear business model with multiple revenue streams is not clearly defined. Moreover, the program should generate evidence needed to show health economic benefits and prove value beyond the clinical trial stage. Ideally, the evidence collected should help demonstrate how a proposed new treatment's costs compares to the patient's current costs in the healthcare system and how the patient's quality of life is improved. Such evidence can support market access and patient advocacy efforts as well as be used to transparently differentiate a product as it faces future competition.

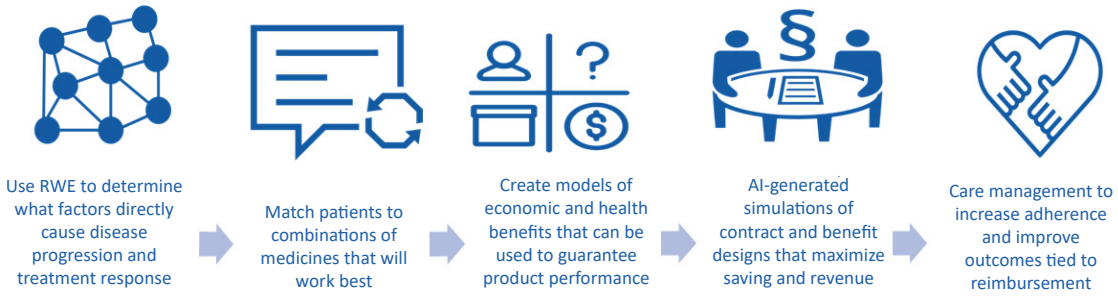
Gain Internal Alignment and Support from Leadership:
Since this is a new approach, it is important to gain alignment from leadership and to take a strategic approach to develop services and solutions to go with and Beyond the Pill.

Explore New Partnerships and New Disruptive Models:
Launching the Beyond the Pill approach requires careful consideration of these approaches and requires a new set of capabilities. To be successful, it will be important to partner with organizations that have experience developing and delivering these types of offerings. A good example is Sanofi partnering with Verily (formerly Google Life Sciences) to develop new technologies and services for diabetes patients. Another example is Otsuka America Pharmaceutical's partnership with Proteus Digital Health.

The opportunity to expand Beyond the Pill is pronounced, particularly as wearables and digital become an integral part of our lives. The data generated through these devices can be used to provide real-time collection and analysis of patient level data to customize therapies, monitor and optimize treatment response and optimize medication adherence.

It is important to stress that such strategies must be more than just efficient ways to collect data. An app alone may not be sufficient. We need platforms that leverage data collected from patients and provide actionable insights to help patients quickly and effectively navigate a path to better health based on their individual lifestyle, preferences and condition severity. Such platforms can be used to both improve and measure patient activation, resiliency and satisfaction while reducing costs of care. Finally, it's important that such platforms seamlessly integrate with caregivers and physicians alike.

Putting it All Together: A New Model for Demonstrating and Delivering Value



As discussed earlier in the paper, real world data and appropriate analytics should be leveraged across the lifecycle. The flow chart above demonstrates how data and analytics can be used to identify the right medicine for the right patient at the right time. Such an approach can be used for measuring, demonstrating and increasing the value of new medicines. In essence, to deliver value, companies must establish a distribution system for personalized, prospective medicine that supports outcomes vs. rebates-based care.

Innovators will have to forge new relationships with third parties that measurably add value or share the risk of value-based arrangements. Innovators should shift the money — currently distributed to companies that are part of the supply chain, such as PBMs — to reduce a patient's out-of-pocket costs and improving their well-being.

Instead of step therapy or prior authorization, innovator companies will be able to combine lower net pricing with performance guarantees to market precision or orphan products directly to physicians and patients. This approach can help innovator companies provide better access to their medicines at optimal pricing by re-investing money previously used to pay for rebates and patient assistance programs to support Beyond the Pill strategies.

EXAMPLE:
AveXis, a Novartis company, recently announced innovative access programs for Zolgensma® — a one-time treatment designed to replace lifetime of chronic therapy for all pediatric patients with SMA. AveXis is working closely with payers to offer pay-over-time options up to 5 years and outcomes-based agreements up to 5 years, as well as providing a patient program to support affordability and access.

Ideally, these relationships involve physicians, patients, insurers and companies to establish what outcomes are most important and rely upon the same data to measure outcomes, address non-compliance and adverse events and recommend changes in treatment or customer support at the patient level. Pairing net pricing with support of meaningful patient engagement platforms, enables innovator companies to become trusted partners in an effort to improve outcomes and generate value. The evidence of such value depends on demonstrating that matching patients to the treatments that work best is the best way "to enhance health, prevent disease, track its development, intervene early and manage disease most effectively if it occurs."[1]

[1] Ralph Snyderman, **Personalized health care: from theory to practice**. Biotechnol J. 2012 Aug;7(8):937-9. doi: 10.1002/biot.201100297. Epub 2011 Dec 16.

Author Biographies

Robert Goldberg, Ph.D., Vice President & Founder, Center for Medicine in the Public Interest

Prior to founding CMPI, Dr. Goldberg was Director of the Manhattan Institute's Center for Medical Progress and Chairman of its 21st Century FDA Task Force that recommended ways to reduce the time and cost of getting innovative medicines to patients. Many of these recommendations are included in the 21st Century Cures Act.

At CMPI, Dr. Goldberg has advised the U.S. Department of Health & Human Services (HHS), Veterans Administration (VA) and U.S. Food and Drug Administration (FDA) on the limits of traditional approaches to data analysis currently being used to assess public health benefits and risks. Dr. Goldberg's work focuses on generating reliable real-world consumer-level evidence.

Dr. Goldberg is an advisor to Nonpareil, a biotech commercialization accelerator, as well as CEO and Co-founder of Thrive HealthRx, a company that uses artificial intelligence to improve health by matching patients with the medicines that will work best for them. He also consults for several biopharmaceutical companies on reimbursement, market access and patient-centered value.

Dr. Goldberg is the author of "Tabloid Medicine: How the Internet is Being Used to Hijack Medical Science for Fear and Profit" (Kaplan, 2011). In addition to publishing in peer-reviewed journals, such as *Pharmacoeconomics*, *JAMA* and the *Journal of the NCCN*, he writes for *The Wall Street Journal*, *Scientific American*, *The New York Post*, *Morning Consult* and *Real Clear Health*. Along with CMPI Co-founder Peter Pitts, he writes for Drugwonks.com, one of the mostly widely read blogs on medical innovation and drug regulation.

Dr. Goldberg received his Ph.D. in Politics from Brandeis University.

Shailja Dixit, M.D., M.S., M.P.H., President & Founder, ApexBio

Dr. Dixit is an accomplished healthcare executive with more than 15 years of industry experience. She has served in a variety of leadership roles and has a 360-degree understanding of the healthcare industry. She has been instrumental in laying the foundation for new HEOR and value model, collaborative research with academia and stakeholder engagement strategies.

Dr. Dixit has headed numerous successful global product launches and has led teams whose responsibility is to develop "end-to-end evidence" to support market access and reimbursement. Dr. Dixit conceptualized and launched a unique platform for real world research for collaboration and knowledge exchange called SHARE-ID. Having also worked in the device industry for GE Healthcare, she led the incubation team; giving her experience in taking a new product from concept to product to market.

Dr. Dixit has presented at multiple conferences and has patents for her work. She was featured on the cover of *Pharma Executive Magazine Real-World Evidence: From Volume to Value* (Oct 13, 2016, Volume 36, Issue 10) and was recognized at the Phacilitate's Big Data Leaders Forum as a Top 50 big data leader influencing the pharmaceutical and health plan industries.

Dr. Dixit is a trained physician and has a Master's degree in Informatics from the University of Medicine and Dentistry of New Jersey and a Master's degree in Public Health/Health Management from Columbia University, NYC. She is a Senior Fellow and member of the Health Innovation & Technology Lab at Columbia University, NYC. Dr. Dixit sits on the boards of many small biotech companies.

About BioNJ

BioNJ is the life sciences trade association for New Jersey with nearly 400 Member companies representing research-based life sciences organizations and stakeholders across the ecosystem from the largest biopharmaceutical companies to early stage start-ups. BioNJ is dedicated to ensuring a vibrant ecosystem where Science is Supported, Companies are Created, Drugs are Developed and Patients are Paramount. Because Patients Can't Wait®, BioNJ supports its Members in the discovery, development and commercialization of therapies and cures that save and improve lives and lessen the burden of illness and disease to society by driving capital formation, fostering entrepreneurship, advocating for public policies that advance medical innovation, providing access to talent and education and offering a cost-saving array of critical commercial resources. For more information about BioNJ, please visit **www.BioNJ.org**.

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