



# Target Practice

The orphan-drug market was flying high before President Obama announced plans to devote \$215 million to the funding of a Precision Medicine Initiative. Imagine the excitement among interested audiences now that those plans have picked up momentum. **Frank Celia** reports

**AN ALREADY-ESCALATING ORPHAN-DRUG MARKET RECEIVED** an added lift when President Obama, in his State of the Union address in January, announced plans to finance a Precision Medicine Initiative with \$215 million in this year's proposed budget. If passed, the funds would go toward establishing a voluntary million-patient data bank to leverage advances in gene sequencing and big data analytics. They would also be used to bolster efforts to identify genomic drivers in cancer treatment and develop interoperability and privacy standards for sharing clinical data across large platforms.

Opportunities for precision medicine—the latest term for personalized medicine—have grown exponentially in the past several

years, Obama subsequently noted in a press conference. In 2000, sequencing a human genome cost \$100 million. Now it is less than \$2,000. “Wearable electronics make it easier than ever to record vital signs, from your blood sugar to your heart rate,” the president added. “Electronic medical records let doctors and researchers across the country collaborate more closely than ever before. And more powerful computers help us analyze data faster than ever before.”

The proposal was widely viewed as good news for the rare-disease market, which is deeply embedded in precision medicine, cancer and genomics. About a third of rare diseases have genetic origins, and genomic medicine has achieved most of its success thus far finding rare-disease mutations. Additionally, atypical cancers represent the biggest target for orphan drugs.

Once considered a remote backwater of R&D efforts, orphans have proved their blockbuster potential. Nearly one-third of rare-disease drugs marketed after 2001 generated sales of over \$1 billion during at least one year of their life cycles. In 2013, 41 of the top-selling 100 drugs serviced patient volumes of fewer than 100,000. Last year 41% of all new drugs approved by the FDA targeted rare diseases, the highest proportion ever. Moreover, spending on orphan drugs has increased sixfold since 2001.

If pricing complications can be avoided, the presidential initiative should only invigorate an already-buoyant market. Here are some areas set to benefit and some concerns that must be addressed:

**Cancer genomics:** The National Cancer Institute is to receive \$70 million to scale up efforts to identify genomic drivers in cancer and apply that knowledge to developing better treatments. Writing about the proposal in the *New England Journal of Medicine*, NIH director Francis Collins and NCI director Harold Varmus noted that although ambitious projects like this cannot be planned entirely in advance, oncology represents the clear first choice for initial efforts.

Inherited genetic variations can contribute profoundly to cancer risk, they note. “This new understanding of oncogenic mechanisms has begun to influence risk assessment, diagnostic categories, and therapeutic strategies, with increasing use of drugs and antibodies designed to counter the influence of specific molecular drivers,” the article states. The authors conclude that if these strategies can succeed in cancer, they will provide a template for adopting precision medicine in other fields, the most obvious being inherited genetic disorders and infectious diseases.

**Big data:** Perhaps the most ambitious goal will be encouraging the adoption of big data analytics and sharing electronic medical records over large platforms. The initiative pledges \$130 million to the NIH for developing a national research cohort composed of one million or more volunteers who will share genomic information and biological specimens along with electronic health records and lifestyle data tracked through mobile health devices. Another \$15 million will go to the FDA and the Office of the National Coordinator for Health Information Technology to set up regulatory databases and develop interoperability and patient privacy standards for securely exchanging data across large systems.

Increased access to clinical data in digital clearinghouses could help solve two big problems: diagnosis and identifying existing patients. “With rare disease, the whole process of finding the right treatment for the patient is backwards,” says Mike Luby, founder and CEO of BioPharma Alliance, a management consulting firm. “It’s a brutal process of having these terrible symptoms and getting pushed around to every specialist and not finding out what kind of disease you have, let alone your options. On average it takes seven years just to get the right diagnosis.”

**New networks:** Another major objective is to increase networking among clinicians, patients, caregivers and other stakeholders. According to the NIH website, the Precision Medicine Initiative will “support a national network of scientists who possess the talent and skills to develop new approaches for answering critical scientific questions.” An organizational focal point would benefit rare diseases, according to Wendy White, SVP, rare diseases at Dohmen Life Sciences Services.

“My daughter has a rare disorder called nail-patella syndrome,” she says. “Here are some of the doctors who treat this one genetic defect: a nephrologist, orthopedic surgeon, ophthalmologist and other specialists who do not talk to each other on a regular basis. Who

brings all the information together? The patient or the caregiver.”

To that end, another benefit would be good public relations, White adds. “It signals an awareness on the part of the medical community that these strategies are where medicine will achieve the most success in the future.” The president’s words also signal to industry that the federal government is growing more comfortable with personal genetic testing. For example, in February the FDA announced it would allow 23andMe to market a genetic test for carriers of Bloom syndrome and that other carrier screening tests would no longer require pre-market approval.

**Organs-on-a-chip:** The most recent NIH budget proposal includes a clue as to where extra resources might be diverted. In addition to highlighting the Precision Medicine Initiative, one of the few specific technologies the budget mentions is “organs-on-a-chip.” This nascent research tool is basically a highly enhanced, in-vitro cell culture. But unlike simple cultures, it contains functioning, interconnected tissue with a variety of different cells all performing as they would in a specific organ.

Such technologies could help alleviate researchers’ traditional reliance on animal and human test subjects—and offer particular value within the rare-diseases space, where large patient groups are hard to find and organize. Additionally, owing to the FDA’s flexibility on surrogate markers and nontraditional endpoints, rare diseases present optimal testing grounds for organs-on-a-chip technology.

“I don’t think there’s ever going to be an in-vitro test of any kind that will completely obviate demonstrating in human beings that you can make the sick well,” cautions Tim Coté, founder of the consulting firm Coté Orphan. “But this might help speed and facilitate the process.”

**Financial pushback:** If there is a worm in this apple, it is cost. The ascent of orphan drugs has strained budgets. Last year the average orphan-drug cost per patient was \$137,782, compared to \$20,875 for non-orphans. This large discrepancy is starting to cause pushback.

Last summer the Department of Health and Human Services announced that orphan drugs’ exclusion from the 340B drug-discount program would not apply when the drugs were used on non-orphan diseases, a move trade group PhRMA is challenging in federal court. Higher patient cost-sharing, tighter conditions of reimbursement and cases of outright formulary exclusion are becoming more common. For example, a Medicaid agency in Arkansas reportedly implemented step therapy to limit financial exposure to Vertex’s cystic fibrosis drug Kalydeco.

To highlight the importance of continued financial support, the Precision Medicine Initiative could make the case that success in rare disease often results in advances to broader areas of health-care, according to White. A classic example? Research on familial hypercholesterolemia led to the development of PCSK9 drugs that reduce high cholesterol in nearly everyone.

“Innovation happens at the periphery,” White explains. “The rare informs the common. Rare disease is where precision medicine was born.” ■

THINKSTOCK



## SkillSets

Looking for a good **Rare Diseases** partner? Check out our showcase of companies with the right credentials—pp. 50–51.