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Patient Group Collaboration In Rare Diseases Offers Model For Cell/Gene Therapy Firms

by Joseph Haas

Companies doing groundbreaking work in cell and gene therapies should look to how rare disease drug developers partnered with patient advocacy groups and disease foundations to advance their shared goals, suggested speakers at the Cell & Gene Exchange conference.

Companies trying to bring cell and gene therapy products to market might do well to model their R&D and commercial planning efforts on drug makers working in the rare disease space, where partnerships with disease-specific foundations and patient advocacy groups have provided access to some financing as well as expertise in clinical trial design and help with trial enrollment while laying the groundwork for pricing acceptance by patients and clinicians.

Rare disease drug development has provided a model for what patient and disease advocacy groups can bring to the table, *Fibrocell Science Inc.* CEO John Maslowski said during a May 22 panel at the Alliance for Regenerative Medicine/EBD Group's Cell & Gene Exchange partnering conference in Washington, D.C. Fibrocell develops autologous cell and gene therapy applications for skin and connective-tissue disorders, with a lead candidate, FCX-007, in Phase I/II for recessive dystrophic epidermolysis bullosa. (Also see "*Fibrocell acquires rights from UCLA; seeks a lead on adult mesenchymal stem cells from dermal skin cells*" - Scrip, 17 May, 2012.)

"A lot of these diseases, there aren't models, there aren't validated clinical endpoints as there are for large, higher-prevalence diseases," Maslowski said. "You need to learn a lot about that and there's ways to do that. One of the ways is through natural history studies and through other analyses, and how you do that is you really need to know the patients and where to access them." The typical patient identification strategies used for larger indications usually won't prove very useful, he added.

"It is really important to partner early on with these organizations and then when you go to FDA and they start asking questions like 'How are you going to prove efficacy and potency?' you need to have learned a lot about the disease to answer those questions," he continued. "If you go in without anything, they're going to send you back to start collecting this data. And the first place to go, I think, is advocacy groups that are designed to be sophisticated and have these data, have control over them, and also know the patients, know what their needs are, what endpoints are really important to them."

CAR-T Cancer Drugs Front And Center At ARM Investor Day

By Amanda Micklus

17 May 2017
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Read the full article here

Working with larger, umbrella organizations like the Alliance for Regenerative Medicine and Global Genes – a genetic-disease focused patient advocacy group with a mission to "eliminate the challenges of rare disease" – is one way to find models for successfully developing cell and gene therapies, *Abeona Therapeutics Inc.* CEO Tim Miller noted.

But disease-specific groups are the best source to learn about the biomarkers and biophysical changes that will matter most to that patient population, he added. "This is how these therapies are going to be measured for success and it's by engaging these rare disease communities that you are able to do that," Miller said. Abeona's two lead programs (ABO-101 and ABO-102) are adeno-associated virus (AAV)-based gene therapies for two types of Sanfilippo syndrome. (Also see " *Video Interview: Abeona Breaking Into Rare Diseases* " - Scrip, 12 Feb, 2016.)

"The individual disease foundations are the ones where you're going to get the endpoints and learn about the disease and what qualitative outcomes are going to be important, because again there's little [data] out there to be judged against."

A Network Of Alliance Partners

Both Abeona's and Fibrocell's websites include sections titled "Patients & Families" that list the advocacy groups each works with and provides links and further information on those organizations.

For its lead indication, recessive dystrophic

Providing The 'Low-Hanging Fruit' Big Pharma Seeks

Ron Bartek, president and co-founder of the Friedreich's Ataxia Research Alliance and a National Organization for Rare Disorders board member, explained that

as larger companies began facing patent cliffs and other headwinds during the past decade or so in more common disease areas, they would tell groups like NORD that they were looking to move into rare disease drug development. But these companies also stressed that their initial focus would be on "low-hanging fruit."

"So, a lot of our foundation leaders ran back to our boards of directors and staffs and said, 'What we've got to do now is grow low-hanging fruit,'" he said. "And we have defined low-hanging fruit ... as doing the things that our pharmaceutical partners – of which we had none at the beginning – need to develop rare disease therapies. Things like funding the basic discovery science ourselves – a lot of our foundations have done just that."

Doing that has helped characterize the diseases and identify the most viable targets for therapy, Bartek added. "We've established patient registries, natural history databases, and supported clinical networks consisting of clinicians and coordinators that know our patients, know our disease. We've done a lot of match-making between our discovery scientists and the biopharmaceutical industry. We've created translational tools, the assays, the cell and animal models, the biomarkers, the biorepositories that [industry] uses to advance its research. We've assembled and supported the field; we've grown the field."

epidermolysis bullosa (RDEB), Fibrocell lists *DebRA* (the Dystrophic Epidermolysis Bullosa Research Foundation of America) and is supporting that group's 19th annual benefit in October as well as its fundraising golf event in November, and the *EB Research Partnership*, as well as NORD and Global Genes. In 2014, Fibrocell announced that it would present on the potential of its genetically modified autologous fibroblast technology at DebRA's Patient Care Conference to demonstrate its "commitment to engage and support advocacy groups for patients with rare diseases."

Abeona's site lists and links to an exhaustive list of research advocacy and patient-support groups for Sanfilippo syndrome and related conditions such as Batten disease. It outlines 12 US organizations – including *The Children's Medical Research Foundation*, *Cure Sanfilippo Foundation*, *Team Sanfilippo Foundation* and *Batten Disease Support & Research Association*. In addition, it links to similar groups in Australia, Canada, Ireland, Mexico, Spain and Switzerland.

As cell and gene therapy technology matures, drug developers are able to take advantage of this more mature patient and disease organizational landscape. For a field that has exploded in recent years, and as the first few products near the market, alliances with advocacy organizations can go a long way toward understanding the disease, how to study it and preparing the market for advanced therapeutics.

Bartek noted that when his Friedreich's ataxia group held its first scientific conference in 1999, it

had 80 participating scientists and no biopharmaceutical industry partners. When the group's sixth scientific meeting convenes later this year in Italy, there will be roughly 400 participating scientists and representatives from about a dozen biopharma companies in attendance. The group works with roughly 35 companies, he said, with nine sponsoring clinical trials.

> *"You do a clinical trial very quickly; you can recruit it in hours, not months or years." – NORD board member Ron Bartek*

Patient advocacy groups are also working with the National Institutes of Health and the FDA, "another aspect that our pharma partners find very attractive," Bartek said. "The net result is that we go from clinical trials that are poorly organized, in which the endpoints don't match with what's important to the patients, to clinical trials that are well organized, very well matched to the patients' needs, procedures that are tolerable, and the endpoints are recognized by the FDA as validated. You do a clinical trial very quickly; you can recruit it in hours, not months or years, so you have a clinical trial that has a much better shot on goal and very few amendments, if any; very few dropouts, if any."

A key lesson learned in the past five to 10 years, said Wendy White, board chair of Global Genes, is that for companies trying to address a rare disease without consulting with advocacy groups "if they don't have the natural history, if they haven't done ethnographic research and really talked to patients, they can end up three or four years down the road and come up with something that's not going to be accepted at the FDA. Sometimes, what they find out are things they could have learned had they talked to patients at the very beginning."

Fibrocell's Maslowski noted that the rare disease community has provided a model for working with advocacy and patient groups on cell and gene therapy approaches to rare skin disorders. Abeona's Miller, however, warned that when such groups participate in a financing round, that can create potential conflicts of interest, such as a small family-run foundation wanting some guarantee that their kid will get enrolled in a clinical trial.

"Up front, when you're getting involved with a foundation, you have to have very clear lines of expectations," he said. "A very simple thing to think about is to make sure that they're involved with the enrollment criteria. For many of the gene therapies, especially AAV gene therapy, there are some exclusion criteria, particularly if you have neutralizing antibodies against that particular [therapeutic candidate]. It's very easy to come up with a line that says we're going to

consider all comers, but within this realm of criteria, we can't sign over any one child or any one family, but here's what we're going to be looking at."

Partnering On The Rationale For Pricing

In an era of widespread concern about drug pricing, communicating with advocacy groups early on also can build understanding and even buy-in about how a drug for rare, unmet medical need must be priced for its development to be economically viable, the speakers said. Just as ultra-orphan drugs can carry extremely high costs, personalized therapies or gene therapies that represent a cure are likely to have high prices.

Bartek recommended talking to advocacy groups early on about a formula for making the process workable for the entire health care system, with White adding that "the earlier, the better" for such discussions.

"I would begin with what I call an algebraic formula. It's pricing-plus-reimbursement equals access-plus-sustainability," Bartek explained. "For patient groups like ours, it's really all about access, but access can't be sustained if pricing goes way past reimbursement and our health care system can't be sustained unless pricing-plus-reimbursement is feasible for the whole health care system."

A related consideration, White said, is communicating about the possibility of compassionate use protocols for high-priced medicines. Again, she stressed talking to advocates as early as possible if a company is not planning to do compassionate use.

"If you're going to decide that you're not going to do compassionate use, then you better say that really early and give a really good reason," she said. "It can't be 'Oh, we don't have enough,' because nobody really believes you."