

BioCentury

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FUNDING CONUNDRUM

BY STEVE USDIN, WASHINGTON EDITOR

Rivers of pharmaceutical industry cash are keeping U.S. patient groups afloat, but in the absence of widely adopted transparency and governance principles, the funding flows could erode the perceived integrity, independence and reputations of the recipients.

Confidence in the integrity of patient groups is important because regulators, research funders, politicians and many drug companies have coalesced around the idea that the patients who are represented by advocacy groups should play a central role in shaping the criteria for assessing drugs, priorities for publicly funded translational research and financial incentives for meeting public health objectives.

Non-profit groups that represent the voices of patients, like [Friends of Cancer Research](#) (Friends) and the [National Organization for Rare Disorders](#) (NORD), have changed the way medicines are developed in ways that benefit everyone touched by disease. Friends is responsible for FDA's breakthrough therapy pathway and other innovative regulatory policies, and NORD catalyzed the creation of the Orphan Drug Act. The Orphan Drug Act and breakthrough pathway, as well as other innovations conceived and nurtured by U.S. patient groups, have been emulated around the world.

In addition to reshaping policy, patients have banded together to lead the translational research that is essential to turn scientific discovery into medicine, and have helped regulators rethink the way they define benefit/risk thresholds (see "Patient-Led Science," page 4).

The ability of patient power to transform drug development would be undermined if the public and policymakers are led to believe that non-profit advocacy groups are acting to advance the financial interests of the companies that fund their operations rather than the patients they represent.

The potential for pharma money to influence patient groups — or appear to influence them in favor of



industry-friendly legislation and policies — is especially acute in the biomedical policy arena, where small organizations that receive half or more of their funding from industry have become very influential. Some groups are completely funded with pharma money, and those that refuse to disclose their sources of funds and their governance open all to accusations they are controlled by industry.

The conundrum is this: Patient groups need both financial viability and independence. From those that consist of a grieving mother with a Facebook page to national organizations that measure their budgets in hundreds of millions of dollars, all patient groups need money to be effective. There is another currency that is even more critical for success. All groups that seek to represent patients succeed or fail based in large part on their reputations.

Patient groups shouldn't be precluded from weighing in on topics that are aligned with the interests of their donors, but to be credible they must have the independence and resources needed to act independently of, and when necessary in opposition to, the interests of biopharma companies.

Financial conflict of interest can be managed, if not mitigated, through transparency and governance policies. While the industry in Europe has promulgated a code of behavior for its pharma contributors, transparency policies in the U.S. are voluntary and inconsistent. There is a wide spectrum of disclosure practices among biopharma companies and patient groups, from full transparency regarding corporate donations to complete opacity.

Likewise, patient group governance policies run the gamut from excluding board membership by employees of life sciences companies to allowing executives of drug companies to join, lead and dominate their boards.

There are no legal requirements and few guidelines regarding policies for biopharma companies to donate in ways that preserve the independence of patient group recipients, or about the role of pharma executives in the governance of patient groups.

In the absence of alternative sources of funding it is unlikely that U.S. patient groups will wean themselves from the financial lifelines provided

by industry or completely eliminate perceptions that drug company money influences their advocacy.

It is possible, however, that best practices for transparency and governance could be defined that would minimize the reality and appearance of financial conflict of interest.

Establishing norms for both industry and non-profit groups would make it possible to judge their behavior and discriminate between those that are clearly advancing the interests of patients and those that have other agendas.

CORPORATE TRANSPARENCY

Transparency would be the starting point for any attempt to define best practices for corporate contributions to non-profit groups.

The European Federation of Pharmaceutical Industries and Associations (EFPIA) has adopted a code that commits its members to disclose all contributions to healthcare organizations in Europe, including patient advocacy groups.

EFPIA's code does not apply to contributions to U.S. patient groups. Some EFPIA members list contributions to patient groups around the world, while others list only contributions to European patient groups.

PhRMA does not have a similar disclosure code for its members and is not contemplating creating disclosure requirements, spokesperson Robert Zirkelbach told BioCentury.

Nevertheless, all but one of the 10 largest pharma companies by market cap list at least some contributions to U.S. patient groups on their websites.

Novo Nordisk A/S discloses its contributions to European patient groups on its website. Spokesperson Marisa Sharkey said the company does not publicly report the information for U.S. contributions because the value of its contributions can't always be quantified.

"Sometimes it's by funding educational grants, community, and patient health education or charitable giving — and other times it's our employees donating their time and skills to causes they care about — so determining the actual value of these offerings is not always clear-cut," she said in an email.

The pharma companies that list contributions to U.S. patient groups do so inconsistently. Some include contributions to medical societies and to patient assistance programs that help cover out-of-pocket costs for drugs. Some corporate disclosure lists exclude “sponsorships” that can exceed payments of \$1 million or more to individual organizations.

Forms filed with the IRS indicate that PhRMA contributed about \$5.6 million to patient groups in 2014, and BIO contributed about \$1.6 million.

Zirkelbach declined to discuss the criteria PhRMA uses for determining which patient groups to fund. BIO declined to provide an interview to discuss its financial and non-financial contributions to patient groups.

According to BIO’s non-binding principles for interaction with patient advocacy organizations, the trade group “recognizes the importance of transparency and its role in developing trust-based relationships with stakeholders, the public, and the patient advocacy community.”

BIO’s principles do not include any specific recommendations for disclosure of contributions, and some member companies that offer financial support to patient groups do not publicly disclose them.

Both PhRMA and BIO urge their members to respect the independence of patient organizations and state that companies should not require that they be sole funder of an organization or program. But neither trade

of its peers, receives at least one-third of its funding from biopharma companies that sell and develop drugs to treat the condition that afflicts its members.

In 2015, NPF reported that donations from [Amgen Inc.](#) landed in the \$1 million+ range. [AbbVie Inc.](#), the Janssen Research & Development LLC unit of [Johnson & Johnson](#) and [Novartis AG](#) fell into the \$500,000-\$999,999 range, and [Celgene Corp.](#), [Eli Lilly and Co.](#) and [Pfizer Inc.](#) were in the \$250,000-\$499,999 grouping.

All told, 10 companies developing and manufacturing prescription drugs for psoriasis contributed at least \$3.4 million of the NPF’s \$9.2 million in revenue. At the high end of the ranges, their combined contribution could have exceeded \$5.9 million.

In addition to providing services to patients and funding research, NPF lobbied Congress in 2015 to pass legislation reducing out-of-pocket costs for specialty drugs — a priority for both patient groups and pharma companies. The NPF’s website credits its “direct advocacy and coalition work” for the enactment of 15 “pieces of access to care legislation.”

The lack of diversity of funding of groups representing pain patients came under particular scrutiny during investigations of the role of drug manufacturers in the opioid abuse epidemic.

In May 2012 the American Pain Foundation (APF) abruptly ceased



“THERE IS A REAL RISK OF NEGATIVE PERCEPTIONS, THERE IS NO QUESTION ABOUT THAT.”

MARC BOUTIN, NATIONAL HEALTH COUNCIL

association rules out contributions from a single company that would constitute the majority or all of the funding for a patient group.

It is impossible to determine how much most patient groups rely on funding from life sciences companies. Many groups do not disclose contributions, and those that do usually report what dollar range a donor’s contribution falls into rather than a precise amount.

Within the subset of groups that do provide enough information to calculate corporate contributions, it is not hard to find examples where biopharma companies contribute 25% or more of total funding.

The National Psoriasis Foundation (NPF) is just one of many. The group reports corporate contributions in ranges of dollars and, like many

operations and formally dissolved itself, citing “irreparable economic circumstances.”

The action came within days after the foundation received a letter from Senate Finance Committee Chair Chuck Grassley (R-Iowa) and Ranking Member Max Baucus (D-Mont.), who noted APF received “nearly 90 percent of its \$5 million funding from the drug and medical device industry” in 2010.

APF had disseminated reports and guidelines that minimized the need for legislative and regulatory restrictions on prescribing addictive pain medications.

[Endo International plc](#), which markets pain drugs, contributed 53% of APF's 2010 income according to the foundation's annual report. "Other industry" contributed 35%.

After the APF shut down, Endo adopted standards for its contributions to patient and medical groups, including a commitment to support only activities that are "organized and conducted completely independent of influence from Endo and its representatives and/or agents."

In addition to financial contributions, both PhRMA and BIO have staff dedicated to supporting patient groups. BIO's weekly newsletter for patient groups lists job openings at patient organizations, notes public comment deadlines and solicits support for public policy initiatives.

BIO has created and hosted websites for patient groups to sign on to letters to Congress and federal agencies on legislative and regulatory issues, and both trade associations have enlisted patient advocates to support issues that have tenuous links to the concerns of patients. These include lobbying the Obama administration to support IP rights for pharmaceuticals in international trade agreements and at the UN, and efforts to persuade Congress to exempt biopharmaceutical companies from administrative procedures for challenging patent validity.

Some patient groups sign letters advocating policies that are outside their core missions because they want to please corporate donors, according to Sharon Terry, president and CEO of the Genetic Alliance, a non-profit group that represents disease-specific advocacy organizations working to find treatments for genetic disorders.

"Sometimes the advocacy groups think this is a throwaway, it is not so important, so we can give something to the companies. It is often difficult for the little groups to understand the implications of what they are signing on to," she told BioCentury.

PATIENT GROUP TRANSPARENCY

While many patient groups list funding sources and corporate partners on their websites, some that attempt to shape public policy and public opinion do not disclose any information about funding.

A 2015 briefing between FDA and invited stakeholders to discuss PDUFA negotiations illustrates the point. Eleven of the 12 patient groups at the Dec. 17 meeting disclosed drug industry contributions in 2015.

FasterCures did not. It is one of the most prominent and active advocacy organizations on Capitol Hill, and a frequent participant in public and closed-door meetings at FDA, NIH and the White House. It does not provide any data about its funding or budget other than listing biopharma companies and trade associations that sponsor its meetings.

FasterCures did not respond to BioCentury's requests for information about its finances, other than to state that it is part of the Milken Institute. A form the Milken Institute filed with the IRS reports that it received \$77 million in contributions and grants in 2014, but it does not break out the FasterCures budget and does not name corporate donors to the institute.

Biopharma companies and PhRMA accounted for 15 of the 18 sponsors for FasterCures' 2016 Partnering for Cures meeting.

On the other end of the spectrum, there are numerous organizations that identify themselves as patient groups, provide little or no information

PATIENT-LED SCIENCE

While industry funding of patient group policy advocacy raises questions about conflict of interest, industry funding for and participation in patient-led precompetitive research collaborations is much less controversial.

Patients combine a passion for better treatments with intimate knowledge of the realities of the disease experience, and they have a unique ability to bring the stakeholders together to pursue common goals. The interests of industry and patients in learning from translational research are closely aligned, and research conducted and reported openly benefits everyone.

For many diseases, especially rare conditions, patient organizations are driving the search for treatments by funding translational science and serving as intermediaries linking researchers, companies and regulators.

For example, the Amyloidosis Research Consortium (ARC) received about 40% of its funding from private company grants in 2015. ARC hosted an amyloidosis patient forum with FDA in November 2015. Its annual report features an endorsement from Janet Woodcock, director of FDA's Center for Drug Evaluation and Research, stating that its "strategy is the only real way to get things done effectively in a rare disease."

The [Multiple Myeloma Research Foundation \(MMRF\)](#) pioneered the model. It has helped bring 10 new MM drugs to patients and led a large-scale collaborative research study that identified previously unknown molecular drivers of the disease.

MMRF has partnered with multiple drug companies and received 29% of its funding from biopharma and other healthcare companies in 2014.

— STEVE USDIN

about their funding sources, and have a presence primarily on the internet. Many of these groups submit comments to federal agencies and Congress that are closely aligned with the views of drug companies.

For example, Patients Rising, a non-profit organization that says it was "formed to stand up for patients," has a website devoted to criticizing the Institute for Clinical and Economic Review (ICER), a health technology assessment organization. The positions, and some of the wording on the Patients Rising website and in written comments to CMS, echo those of drug companies and their trade associations.

Patients Rising does not publish information about its funding, other than to list as "sponsors" Amgen, [Bristol-Myers Squibb Co.](#) and Celgene, as well as a multimedia production company and a magazine. Patients Rising did not respond to a request from BioCentury for information about its funding.



“AS MUCH AS I’D LIKE TO SAY MONEY DOESN’T MATTER, WE FEEL IT DOES MATTER AND IT INFLUENCES HOW ONE BEHAVES.”

SHARON TERRY, GENETIC ALLIANCE

Other organizations pop up when controversial legislation is being debated in Congress, claiming to represent patients while also espousing positions identical to those of drug manufacturers or insurance companies. These groups don’t disclose their funding and often disappear after a few months, but some have been in existence for years.

The Partnership to Improve Patient Care (PIPC), formed in 2008, maintains a website similar to those of non-profit patient groups, but it isn’t registered with the IRS as a non-profit and doesn’t disclose its funding.

PIPC says its mission is “to advance the principles of patient-centeredness in an evolving healthcare system.” Chaired by former member of Congress Tony Coelho, a Democrat from California, PIPC’s positions closely mirror those of drug industry trade associations. It has been pressing Congress and CMS to adopt positions on Medicare reimbursement policies, submitted comments to ICER and sought to influence public policy debates.

PIPC Executive Director Sara van Geertruyden and Deputy Director Andrew Rosenberg are partners at the lobbying firm Thorn Run Partners. PIPC and Thorn Run have the same address, and Thorn Run manages PIPC, van Geertruyden told BioCentury.

Thorn Run’s clients include six biopharmaceutical companies, and its congressional lobbying has focused on Medicare and Medicaid.

PIPC’s steering committee includes BIO and PhRMA, along with five physician organizations and four patient organizations — Alliance for Aging Research, Easter Seals, Epilepsy Foundation and National Alliance for Hispanic Health.

Van Geertruyden declined to provide information about overall funding, the proportion of the group’s funding provided by each member or whether patient organizations make any financial contributions.

In addition, many of the organizations that advise FDA on behalf of patients receive but do not routinely disclose substantial funding from FDA-regulated companies.

For example, individuals representing 13 patient or physician organizations testified at a July 12-13 meeting of FDA’s Arthritis Advisory Committee to review Amgen’s proposed biosimilar to AbbVie’s Humira

adalimumab and a proposed biosimilar from Sandoz to Amgen’s Enbrel etanercept. Sandoz is a unit of Novartis.

Presenters were asked to disclose financial relationships with “the sponsor, its product and, if known, its direct competitors.”

Everyone who presented on behalf of a patient or physician group said they had no conflicts. However, websites for 11 of the groups show each of them received funding from AbbVie, Amgen, or Novartis in 2015. Several of the groups also received funding from other companies that market arthritis drugs.

GOVERNANCE

Governance policies, especially regarding participation on a board of directors, can be an important indicator of a non-profit organization’s independence from corporate donors.

Strong, independent boards are important for the credibility of patient groups, according to Arthur Caplan, a professor of bioethics at [New York University’s Langone Medical Center](#). “You need to have boards that might be able to stand up to pressure, that are transparent and accountable,” he told BioCentury.

NORD doesn’t allow individuals who work for biopharma companies or companies that invest in the sector to serve on its board.

The board of the National Health Council (NHC), an umbrella organization that represents over 50 patient groups focused on chronic disease and disability, includes executives from biopharma companies, PhRMA and BIO, as well as insurance companies, but a majority of seats are reserved for the CEOs of patient groups to ensure that patients control its agenda.

NHC members include healthcare trade and professional organizations and companies, and it receives 60% of its funding from the biopharmaceutical industry.

Many patient organizations are created by individuals who have been touched by disease. Their boards often include family members, and some include executives at companies focused on finding cures.

Advocacy group Global Genes was formed by the parents of children affected by rare disorders. It is led by a board that is dominated by individuals who are both the parents of children with rare diseases and



“COMPANIES DON’T DO ANYTHING WITH PATIENTS UNLESS THERE IS SOMETHING IN IT FOR THEM.”

PETER SALTONSTALL, NORD

have founded or are senior executives in companies that are developing rare disease treatments.

STANDARDS OF EXCELLENCE

Some patient group leaders are concerned the entire patient community will be tainted by allegations that they have been corrupted by industry money.

“There is a real risk of negative perceptions, there is no question about that,” said NHC CEO Marc Boutin. “It becomes a very simplistic message, if you receive any funding from an external source you are doing their bidding.”

While this narrative is often wrong, said Boutin, there is a kernel of truth that makes it easy to question the integrity of all patient groups that receive industry funding.

“The challenge is there are historical examples where coalitions and groups have been formed by the biopharmaceutical sector to do their bidding and that creates a very negative perception,” he said.

NHC has tried to bolster the credibility of patient groups by promulgating transparency policies and running a Standards of Excellence Certification Program that audits and assesses compliance with those policies.

NHC members must disclose corporate funding above \$5,000 or 2% of the contributions the group reports to the IRS, whichever is greater. The disclosure must be “posted on the organization’s website in an easily accessible location within six months of the close of the organization’s fiscal year.” It must include the name of the corporation and the aggregate amount of support. Support can be reported in dollar ranges.

Corporate contributions to NHC members must be spelled out in contracts and those contracts must specify that there is no quid pro quo attached to the contributions. NHC members are prohibited from accepting sponsorships that are inconsistent with their mission and practices.

FUNDING CONUNDRUM

Patient groups can function with little or no pharma funding, but doing so requires them to struggle for resources and reduces their impact.

Terry of Genetic Alliance told BioCentury she “has intentionally kept industry contributions small.”

“As much as I’d like to say money doesn’t matter, we feel it does matter and it influences how one behaves,” she said.

The alliance has a \$5 million budget and will receive about \$80,000 from industry this year.

Genetic Alliance uses the industry money to convene meetings among industry and patient groups, “not for a specific Genetic Alliance agenda,” she said. “That keeps us safe from any undue influence from any group.”

“We don’t take industry contributions attached to any ‘ask’ for Congress or project,” Terry added.

“The vast majority of Genetic Alliance’s money comes from grants from government and foundations that are clear of undue influence from industry,” said Terry, who acknowledged it is difficult to obtain a funding stream from grants.

Limiting contributions from industry “is not business smart,” she added. “We could get buckets of money from pharma. With about two thousand advocacy groups under our umbrella we could give them a lot of access and we decided not to do that.”

Groups dedicated to high-profile diseases such as breast cancer, as well as those that focus on public policy, can raise funds from a wide range of corporations, but this isn’t easy for patient groups dedicated to rare diseases, according to Kenneth Hobby, president of Cure SMA.

The group, which supports research on potential treatments for spinal muscular atrophy (SMA) and provides support for families, receives most of its \$7 million annual budget in \$25 donations raised in bake sales and similar events, he told BioCentury.

The organization receives about \$250,000 a year from companies that are developing drugs for the condition and is trying to expand its corporate contributor base beyond companies working in the SMA space, Hobby said.

Drug companies that once relied on umbrella groups to identify and interact with the rare disease patient community now increasingly work directly with patient groups, Peter Saltonstall, president and CEO of the National Organization for Rare Disorders, told BioCentury.

A few rare disease groups are funded by a major donor, typically an individual or family that has been affected by a disease, Saltonstall said. “The average rare disease group doesn’t have that, so they rely on bake sales and so on. When industry walks up because they are interested in doing something in the space,” the contributions are welcomed, he said.

Saltonstall said patient groups need to have their eyes open. “Companies don’t do anything with patients unless there is something in it for them.”

NORD, which advocates on Capitol Hill and at FDA, NIH and CMS, is looking for ways to diversify its funding.

Currently it has two sets of financial interactions with companies. It administers patient assistance funds to help defray out-of-pocket costs, and it receives unrestricted grants and contributions from biopharma companies. The latter amount to about half of the organization’s \$3.8 million in funding, according to Saltonstall.

Friends of Cancer Research told BioCentury it receives about half of its \$3 million annual budget from pharmaceutical and biotech companies and trade associations. It does not disclose the names of its donors or the amount they contribute.

“ORGANIZATIONS SHOULD DISCLOSE DOWN TO THE \$10,000 LEVEL WHO IS FUNDING THEM AND HAVE PUBLIC CONVERSATIONS ABOUT WHY MAYBE THAT’S FINE.”

SHARON TERRY, GENETIC ALLIANCE

Friends has brought the patient community, physicians, researchers and companies together to reshape the landscape for cancer drug development. In addition to instigating FDA’s breakthrough designation, the organization has created a master protocol for adaptive lung cancer trials, persuaded Vice President Biden to include the consolidation of FDA’s cancer review portfolio under a single leader as part of the Cancer Moonshot Initiative, and many other policy innovations.

Friends has published criteria for corporate partnerships that include rejecting “targeted funding of any kind for policy-related projects,” and requires that relationships with companies “provide a meaningful mission-related benefit to cancer research, treatment or education.”

Friends also commits to conducting an annual evaluation of the “total amount of corporate support received as a percentage of total revenue.” Friends doesn’t “have specific numerical targets — just a principle to seek the greatest possible diversification,” VP of Public Affairs Ryan Hohman told BioCentury.

SOLUTIONS

The NHC’s transparency standards were issued six years ago and the organization is updating them, according to Boutin.

NHC has established a Public Accountability and Transparency Task Force to recommend revisions of its standards “with an emphasis on corporate relations and income diversity,” he said.

In addition to NHC members and staff, the task force includes representatives from the BBB Wise Giving Alliance; Independent Sector, a coalition of non-profits, foundations and corporate giving programs; and Community Health Charities, an organization representing charities providing research, community outreach and education.

NHC expects to make final decisions about any changes to its standards by December 2017.

Boutin said he anticipates NHC will strengthen its standards “by requiring the disclosure of specific total aggregate amount of corporate support and either requiring or at the very least recommending the reporting of health industry support as a percentage of total support.”

Terry of Genetic Alliance suggested that patient groups be challenged to report and explain all contributions. “I think these organizations should disclose down to the \$10,000 level who is funding them and have public conversations about why maybe that’s fine,” she said.

Creating standards for income diversity could help patient groups reduce the reality and appearance of conflict of interest, according to Caplan.

“To some extent the way you can minimize the conflict is to not have sole source from any single pharma or biotech company, to mix your funding on particular projects among companies and, ideally, to mix your funding among donors, companies and foundations so you don’t appear to be beholden to a particular company,” Caplan said. “You want to be able to say you are strong enough to be able to walk away from any single funder.”

Caplan noted that while corporate donors and patient groups are in the private sector, the public has a financial stake in their activities. “The companies that support the organizations get tax deductions, so we are supporting them to exercise some influence over patient groups,” he said.

Caplan’s solution to corporate funding and conflict-of-interest issues is to sever the financial relationships between individual companies and patient groups. “If companies cared about [avoiding conflicts of interest] they would create a pooled foundation so one company wouldn’t be supporting patient groups that would use their drug,” he said. [bc](#)

COMPANIES AND INSTITUTIONS MENTIONED

AbbVie Inc. (NYSE:ABBV), Chicago, Ill.
Alliance for Aging Research, Washington, D.C.
Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
Amyloidosis Research Consortium (ARC), Newton, Mass.
Biotechnology Innovation Organization (BIO), Washington, D.C.
Bristol-Myers Squibb Co. (NYSE:BMJ), New York, N.Y.
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Centers for Medicare & Medicaid Services (CMS), Baltimore, Md.
Cure SMA, Elk Grove Village, Ill.



COVER STORY

CANCER'S PHOENIX

Courier Therapeutics may have solved the longstanding problem of how to avoid the lethal side effects of IL-2 cancer immunotherapy without compromising efficacy.

TARGETS & MECHANISMS

T CELL GAS, TUMOR BRAKE

A trio of studies converge on a common pathway, headed by the PPAR co-activator PGC-1 α , to improve T cell immunotherapies and suppress cancer metastasis.

EMERGING COMPANY PROFILE

MICROBIOME GETS SKINNY

Xycrobe uses commensal skin bacteria as miniature drug factories for continuous, local delivery of dermal therapies.

TRANSLATION IN BRIEF

RANDOM MATH

Using a small set of probes and math optimized for detecting sparse signals, a Rice University team has created a diagnostic that can detect virtually any infection.

PARKINSON'S CHECKPOINT

A new study suggests blocking LAG3 could stop propagation of neurotoxic aggregates throughout the nervous system to treat Parkinson's disease.

BLUEPRINT FOR FUSION

Blueprint Medicines is developing inhibitors of a fusion protein that drives the rare type of liver cancer, fibrolamellar carcinoma.

DISTILLERY

This week in therapeutics

This week in therapeutics includes important research findings on targets and compounds, grouped first by disease class and then alphabetically by indication.

This week in techniques

This week in techniques includes findings about research tools, disease models and manufacturing processes that have the potential to enable or improve all stages of drug discovery and development.

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Easter Seals, Chicago, Ill.

Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.

Endo International plc (NASDAQ:ENDP; TSX:ENL), Dublin, Ireland

Epilepsy Foundation, Landover, Md.

European Federation of Pharmaceutical Industries and Associations (EFPIA), Brussels, Belgium

FasterCures, Washington, D.C.

Friends of Cancer Research, Washington, D.C.

Genetic Alliance, Washington, D.C.

Global Genes, Aliso Viejo, Calif.

Institute for Clinical and Economic Review (ICER), Boston, Mass.

Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.

Milken Institute, Santa Monica, Calif.

Multiple Myeloma Research Foundation (MMRF), Norwalk, Conn.

National Alliance for Hispanic Health, Washington, D.C.

National Health Council (NHC), Washington, D.C.

National Institutes of Health, Bethesda, Md.

National Organization for Rare Disorders (NORD), Danbury, Conn.

National Psoriasis Foundation (NPF), Portland, Ore.

New York University (NYU), New York, N.Y.

Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland

Novo Nordisk A/S (CSE:NVO; NYSE:NVO), Bagsvaerd, Denmark

Partnership to Improve Patient Care (PIPC), Washington, D.C.

Patients Rising, Washington, D.C.

Pfizer Inc. (NYSE:PFE), New York, N.Y.

Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.

U.S. Food and Drug Administration (FDA), Silver Spring, Md

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POLITICS, POLICY & LAW

CONFLUENCE OF INTERESTS

BY STEVE USDIN, WASHINGTON EDITOR

Pharmaceutical industry funding does not create an inherent conflict of interest for patient groups, according to Emil Kakkis, president of the EveryLife Foundation for Rare Diseases.

Kakkis, also president and CEO of rare and ultra-rare disease company [Ultragenyx Pharmaceutical Inc.](#), founded EveryLife in 2009 and continues to lead the foundation.

Kakkis told BioCentury he and his family have been the “major” source of funds for EveryLife. In addition to the Kakkis family, more than half of the donors listed on the foundation’s website are biopharma companies that develop drugs for rare diseases. Twenty-four companies that develop or market Orphan drugs, along with PhRMA and BIO, contributed to the foundation last year, according to the foundation’s 2015 annual report.

Even small amounts of money by biopharma standards can make it possible for advocates to have a great deal of influence on public policy. With 2015 expenses of \$1.6 million, EveryLife briefed congressional staff, lobbied members of Congress, convened scientific workshops that attract senior staff from FDA and NIH and provided consulting services for rare disease advocacy groups.

Kakkis rejects the idea that his contributions or contributions from pharmaceutical companies compromise EveryLife or other patient organizations, as well as the implication that EveryLife’s agenda is driven by the interests of its funders.

He also sees few alternatives to industry funding.

“If people are complaining about the conflict, I say, fine, you put your money together to fund patient groups,” Kakkis said. “I’d like to see people who complain about the conflict go into their 401(k)s and pay for patient groups.”

Drug company money is essential for patient groups, he said. “These groups can’t survive and help patients with bake sales.”

The foundation works primarily on issues where its view of the interests of patients overlaps with the interests of companies developing drugs for rare diseases. It has focused on working with FDA to change regulatory policies to facilitate the development of rare disease treatments, and on lobbying Congress to create new incentives for rare disease product development.

EveryLife’s regulatory activities are intended to advance the “development of new study designs and analyses, the specialization of the FDA drug review process and the qualification of biomarkers for rare diseases,” Kakkis said. “The failure to approve more appropriate biomarkers for use is the number one issue slowing up the development of treatments for rare diseases.”



SOURCE: EVERYLIFE FOUNDATION

“I’D LIKE TO SEE PEOPLE WHO COMPLAIN ABOUT THE CONFLICT GO INTO THEIR 401(K)S AND PAY FOR PATIENT GROUPS.”

EMIL KAKKIS, EVERYLIFE FOUNDATION

Kakkis said EveryLife benefits rare disease patients, not Ultragenyx or any other company, and the company’s activities are completely separate from the foundation’s. “Ultragenyx doesn’t support EveryLife in any way,” Kakkis said. “EveryLife’s plans and agenda are not based on Ultragenyx’s needs.”

The foundation is lobbying for enactment of the 21st Century Cures Act, which includes provisions intended to facilitate and incentivize the development of Orphan drugs. EveryLife’s signature achievements to date have been legislative and regulatory policies intended to facilitate the development and qualification biomarkers for rare diseases.

“Our general policy and rule is that we do not advocate for any specific products with any authorities or with Congress,” Kakkis said. “We are asked to do it and we will not.”

He added that EveryLife has resisted requests to lobby on pricing and reimbursement issues, which the foundation believes are “far too down the road” toward industry support.

Kakkis points out that a major focus for EveryLife, the Orphan Product Extensions Now (OPEN) Act, which was incorporated in the House 21st Century Cures Act (H.R. 6), would not benefit Ultragenyx.

The OPEN Act provides additional exclusivity for drugs that are repurposed for rare indications, a strategy Ultragenyx doesn't plan to pursue. EveryLife has worked to line up support for the OPEN Act from hundreds of patient organizations.

The bill has been a major focus of lobbying by the biopharmaceutical industry. It is opposed by the Obama administration and some Democrats in Congress who do not want to create additional market exclusivity incentives.

EveryLife also created and is the sole funder of Rare Disease Legislative Advocates. RDLA accounted for 31% of EveryLife's 2015 expenses, or \$522,019. Separately, EveryLife spent \$141,000 to lobby Congress and state governments on healthcare issues in 2015.

RDLA is led by two EveryLife staff members and a lobbyist whose firm's clients include PhRMA and biopharmaceutical companies. Kakkis said RDLA supports the advocacy of all rare disease patients and organizations, and EveryLife and Ultragenyx do not control its agenda. [b6](#)

COMPANIES AND INSTITUTIONS MENTIONED

Biotechnology Innovation Organization (BIO), Washington, D.C.

EveryLife Foundation for Rare Diseases, Novato, Calif.

National Institutes of Health, Bethesda, Md.

Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.

Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE), Novato, Calif.

U.S. Food and Drug Administration (FDA), Silver Spring, Md.

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TOOLS & TECHNIQUES

SLAYING SENESCENT CELLS

BY VIRGINIA LI, STAFF WRITER

With a whopper of a B round and a new publication demonstrating both a causal role of senescent cells in atherosclerosis, and a therapeutic effect of eliminating them, [Unity Biotechnology Inc.](#) is readying to push three senolytic programs into the clinic.

The lead program will be in osteoarthritis (OA) of the knee, followed by programs in ophthalmic diseases including glaucoma and age-related macular degeneration (AMD), because those diseases have more straightforward development and regulatory paths than atherosclerosis does.

An untranching \$116 million series B round announced last week provides enough runway to get clinical proof of concept for two programs and to enter the clinic with a third by 2019.

The company launched in stealth mode in 2011 and used an \$11 million series A round to dissect the role of senescent cell accumulation in several age-related diseases, and to build a platform to discover targets specific to senescent cells, along with corresponding therapeutic small molecules that can kill the cells.

Senescent cells are characterized by stress-induced growth arrest, secretion of proinflammatory cytokines and chemokines and expression of cyclin dependent kinase inhibitor 2A (CDKN2A; INK4a; ARF; p16INK4a).

President Nathaniel David said CDKN2A is expressed only on senescent cells, serving as a biomarker for these cells.

The company believes inflammation caused by senescent cells is the causative agent in numerous diseases of aging and that selectively eliminating the cells with small molecule therapeutics could halt or reverse disease progression, or prevent the onset of disease.

Initial mouse studies at the [Mayo Clinic](#) showed that removing cells expressing CDKN2A delayed the onset of several age-related disorders compared with untreated mice. The data were published in *Nature* in 2011. Unity co-founder Jan van Deursen, a professor of biochemistry and molecular biology at the Mayo Clinic, was a co-author.

On Oct. 27, a publication in *Science* described the first study to directly implicate senescent cells as a driver of a specific human disease and to show that eliminating senescent cells can have a therapeutic benefit on that disease.

van Deursen and colleagues from the Mayo Clinic, along with Unity co-founder Judith Campisi, first demonstrated that senescent cells drive atherosclerosis and disease progression in LDL receptor-deficient mouse models of atherosclerosis. The mice were given a high-fat diet, leading to the formation of plaque-promoting lesions that contained senescent cells.

“WE’RE RESETTING TISSUES TO HOW THEY WERE WHEN YOU WERE YOUNG AND THERE’S A CERTAIN SIMPLICITY AND BEAUTY TO THAT IDEA.”

NATHANIEL DAVID, UNITY

Campisi is a professor at the [Buck Institute for Research on Aging](#).

The group subsequently showed that killing senescent cells at various time points in disease progression led to therapeutic benefits including inhibition of lesion formation in early stage disease, reduction of plaque burden in mid-stage models of disease and plaque stabilization in advanced disease.

These therapeutic effects were replicated using four different senolytic mechanisms, including three transgenic systems and one therapeutic compound.

The three transgenic mouse models had senescent cells that were modified to include a kill switch activated by the synthetic FKBP ligand dimerizing compound AP20187, the antiviral drug ganciclovir or the antibiotic metronidazole.

The therapeutic compound, [AbbVie Inc.](#)’s navitoclax (ABT-263), is a B cell lymphoma 2 (BCL-2; BCL2) and Bcl-XL inhibitor that David said has shown senolytic activity in cell culture and in vivo.

In early stage models, mice treated daily with ganciclovir for nine days had smaller lesions compared to untreated mice. The results were replicated in mice treated with AP20187, metronidazole and navitoclax.

In mid-stage models, senescent cells secreted molecules that drove plaque growth, while removal of the cells via all four senolytic mechanisms reduced plaque number and size.

In models of advanced disease, senescent cells secreted enzymes that destabilized mature plaques, increasing the risk of plaque rupture and subsequent acute heart attacks or stroke. Removal of senescent cells from the advanced disease models using all four compounds led to more stable plaque formations.

Unity will not develop any of the compounds used in the *Science* study. AP20187, ganciclovir and metronidazole would require genetic



These transgenic littermates are both 24 months old. The mouse on the right received treatment to eliminate senescent cells. Source: Unity Biotechnology

modification that adds a kill switch to patients' senescent cells in order to exert their effect.

Navitoclax led to unacceptable toxicities. But the company said these were due to mechanisms unrelated to senolysis, including thrombocytopenia induced by inhibition of Bcl-XL, a protein required for platelet survival.

"We don't think clearing these cells is bad for you," David said. "Kids do not accumulate senescent cells. We're resetting tissues to how they were when you were young and there's a certain simplicity and beauty to that idea."

He did not respond in time for publication to BioCentury's questions about whether senescent cells might serve any beneficial purpose in older people.

"DIFFERENT PHARMACOLOGIES ARE REQUIRED BASED ON THE CELLS ONE NEEDS TO ELIMINATE."

NATHANIEL DAVID, UNITY

David said the company also has unpublished data in animal models of OA, glaucoma and AMD implicating senescent cell accumulation and subsequent inflammation in disease, and showing therapeutic benefits of senescent cell removal. He declined to disclose a publication timeline for the data.

According to David, across animal models tested so far, clearing about half of the senescent cells from disease sites led to amelioration of disease.

SEEKING SMALL MOLECULES

Unity is evaluating the role and effect of senescent cell removal in 21 preclinical models of age-related diseases.

The company has discovered and in-licensed from [Ascentage Pharma Group Corp. Ltd.](#) small molecules targeting senescent cells. The targets of all of the molecules, and the terms of the licensing deal, are undisclosed.

Neither would Unity discuss the discovery technologies it used to discover its initial set of compounds. But, going forward, Unity will use genetic screens to identify genes that enable the survival of senescent cells in various disease models and develop compounds against the corresponding genetic pathways.

David said senescent cell markers and targets vary depending on disease and tissue type. "This was not something we necessarily expected at the beginning. But different pharmacologies are required based on the cells one needs to eliminate," he noted.

The unnamed lead program is a locally injectable compound designed to treat OA of the knee that will enter the clinic in 12-18 months.

In parallel, Unity will identify a candidate this year for glaucoma and AMD that will also be locally administered.

The company is developing compounds for additional indications, including atherosclerosis, that could be administered systemically. CEO Keith Leonard did not disclose a development timeline for the atherosclerosis program.

SENESCENCE AND BEYOND

Given the potential for broad applicability of Unity's platform, its investors decided to ensure the company had enough runway to pursue multiple programs in parallel.

Founding investor [Arch Venture Partners](#) and new investor Baillie Gifford led the round, which closed on Oct. 27. New investors Fidelity Management and Research Co., Partner Fund Management, Bezos Expeditions and existing investors Venrock, [New WuXi Life Science](#)

Ltd.'s [WuXi PharmaTech Inc.](#) subsidiary and Mayo Clinic Ventures also participated.

Arch's Robert Nelsen said the preclinical work Unity performed between 2011 and now "proved to us this biology is real and targetable" and has potential applications across a large swath of diseases.

"This is not just a company betting on arthritis and the eye. We're arranging resources to go after many things at once," Nelsen told BioCentury.

"WE'RE ARRANGING RESOURCES TO GO AFTER MANY THINGS AT ONCE."

ROBERT NELSEN, ARCH

According to BioCentury's BCIQ database, the B round is the 12th largest since BioCentury began tracking biotech financings in 1994.

"For some investors this is a repeat investment into the management team," Leonard noted.

Arch, Partner Funds Management and Fidelity previously invested in dermatology company [Kythera Biopharmaceuticals Inc.](#), where David served as CSO and Leonard was president and CEO.

Prior to joining Venrock, partner Camille Samuels led Versant Venture's investment in Kythera, which [Allergan plc](#) acquired last year for \$2.1 billion.

Besides getting three programs into the clinic, Leonard said the B round will enable Unity to identify additional targets and compounds against senescent cells, as well as support research into other mechanisms of aging.

"We realize there are several primordial mechanisms beyond cellular senescence that collectively work together to create this thing we call aging, like stem cell exhaustion, metabolic control and loss of circulating youth factors," said David.

He declined to disclose specific mechanisms that Unity will pursue. [bc](#)

COMPANIES AND INSTITUTIONS MENTIONED

AbbVie Inc. (NYSE:ABBV), Chicago, Ill.

Allergan plc (NYSE:AGN), Dublin, Ireland

Ascentage Pharma Group Corp. Ltd., Hong Kong, China

Buck Institute for Research on Aging, Novato, Calif.

Mayo Clinic, Rochester, Minn.

New WuXi Life Science Ltd., Shanghai, China

Unity Biotechnology Inc., San Francisco, Calif.

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Baker, D., et al. "Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders." *Nature* (2011)

Childs, B., et al. "Senescent intimal foam cells are deleterious at all stages of atherosclerosis." *Science* (2016)



From left: Center for American Progress' Ezekiel Emanuel and Neera Tanden, the Manhattan Institute's Paul Howard and PhRMA's Lori Reilly. *Courtesy of Intelligence Squared U.S.*

POLITICS, POLICY & LAW

DEBATING DRUG PRICES

BY STEVE USDIN, WASHINGTON EDITOR

A recent debate pitting two of the Democratic Party's leading health policy experts against pharma advocates provides a glimpse of how a Hillary Clinton administration would follow through on her promise to rein in prescription drug prices.

On Oct. 13 at an Intelligence Squared debate in New York, Clinton advisors Neera Tanden and Ezekiel Emanuel squared off against PhRMA's Lori Reilly and the Manhattan Institute for Policy Research's Paul Howard to debate the motion that drug prices are fueling runaway healthcare costs.

Tanden and Emanuel — who are certain to be influential in a Clinton administration — spent little time debating the impact of drug prices on overall healthcare costs. Instead, they highlighted the struggles of individual patients to pay for life-saving medicines and argued that lower prices in other countries, as well as high drug company profit margins, are proof that companies overprice their products.

Tanden, president and CEO of progressive think tank the Center for American Progress (CAP), opened the debate by noting that drug costs are higher in the U.S. than in any developed country. She said industry's claims that the need for innovation drives up costs are false.

"When you really look at it, the truth is that the vast majority of pharmaceutical companies are spending more on marketing than they are on research," she said.

According to Tanden, spending on NIH is a "massive subsidy" for the drug industry, "which then turns around and charges all of us, who are subsidizing them through our taxpayer dollars, the highest price they can charge."

Echoing statements Clinton has made on the campaign trail, Tanden said, "The American consumer is really bearing this price on both ends. We are paying high prices, higher than anyone else in the world, and we are paying for the research."

Emanuel, senior fellow at CAP and chair of the Department of Medical Ethics and Health Policy at the [University of Pennsylvania](#), argued that drug prices, especially for medicines that aren't curative, do not reflect value.

"There are multiple drugs out there on the market that are about \$150,000 per year [that] don't cure anyone [or] ameliorate the disease, but are hugely expensive," he said.

He cited the example of Lemtrada alemtuzumab from [Sanofi](#). "It reduces multiple sclerosis flares from two and a half in every two-year period to 1.75 in every two-year period, does not cure one patient," he said.

"We believe that you should tie the pricing of drugs to how much benefit they produce for patients, including whether they forestall a surgical procedure, forestall a hospitalization," he said. Drug companies don't price drugs based on the health benefits they deliver, he said, because "you would not get \$150,000 cancer drugs or multiple sclerosis drugs that don't cure anyone and prolong life two or three months."

Throughout the debate Emanuel emphasized the drug industry's profitability to support the point that prices could be dropped without retarding innovation.

"The pharmaceutical industry is the most profitable industry in the United States," Emanuel said.

He added, “The average profit in the drug industry is 15%, but Gilead, which had that new hepatitis drug, [has a] profit margin [of] 55%, Biogen 33%, even behemoths like Pfizer are at 15%.”

He contrasted drug industry profits with those of other industries, pegging profits of automobile manufacturers at 6% and “big dangerous oil” at 8%.

The motion didn’t require the debaters to provide solutions, but Emanuel nonetheless recommended price controls.

“Every other country in the world regulates the prices,” he said. “So we have to actually control drug prices. Either the drug companies do it, or we do need the government to step in and actually control drug prices.”

Tanden presented two strategies to lower drug costs: negotiating Medicare drug prices and requiring transparency from manufacturers about their costs.

“A great way for us to instill some competition into the pharmaceutical market is for us to all as consumers have an assessment of these prices, what’s going into them, how much research dollars are driving the cost, how much marketing dollars are driving the cost. But they won’t share that information with us because they think that’s information only they should have,” Tanden said.

AGAINST THE MOTION

Reilly and Howard argued that drugs are not fueling runaway costs because government actuaries predict that the percentage of health spending on drugs will remain constant.

Reilly is EVP for policy & research at PhRMA, and Howard is a senior fellow and director of health policy at the Manhattan Institute, a conservative think tank.

“Over the next decade, spending for medicines will be in line with all other forms of healthcare spending costs,” Reilly said.

She said pharmaceutical companies favor moving to value-based pricing, but government regulations are getting in the way.

“Government regulation is stuck in a fee-for-service world, and we’re moving towards a value-based system,” Reilly said. “So, I would hope — and ask you if you would agree with us — that changing some of the current government regulations about how we communicate about our products, what we can do to support patients and ensure their adherence, are addressed so that we can move more rapidly to that system.”

The Democrats did not comment on her statement.

Howard argued that the drug industry needs to have higher profit margins than other industries because long development timelines delay returns on investments, and high failure rates make investments very risky.

“Look, 88% of drugs that go into clinical trials fail,” Howard said. “The entire biotech industry until just a few years ago was in the red. So we can look around and see, oh my gosh, there’s some remarkably profitable products here, but actually a lot of what they do is fail.”

Arguing against government-imposed price controls, Howard said prices in the U.S. are propping up global biomedical innovation. “The important thing is to continue innovation and expand access, because if we go down the road that other nations have gone down and use price controls to control investment in innovation in the industry, make no mistake, we will have fewer medicines, people will suffer and die unnecessarily.”

The live audience of members of the public and online participants found the pharma advocates’ arguments persuasive.

In a poll taken at the start of the evening 33% of the live and online audience agreed that big pharma is fueling runaway healthcare costs, 28% were against, and 39% were undecided.

After hearing both sides, the votes shifted, with 42% supporting the motion and 48% opposing it.

The pharmaceutical industry will face a much tougher audience in the White House if Clinton is elected in November. Clinton has already promised to make reducing the price and cost of prescription drugs a high priority.

Tanden is likely to have a senior role in a Clinton administration. Tanden was policy director for Clinton’s 2008 presidential campaign and is an advisor to the current campaign. She helped design and win congressional approval for the Affordable Care Act as a senior advisor to HHS Secretary Kathleen Sebelius, and kept then-Secretary of State Clinton informed of the bill’s progress.

Clinton helped her become president of CAP.

Emanuel also worked in the Obama White House on the ACA.

While the debate fleshed out the justifications Tanden and Emanuel will use to argue for a Clinton administration to reduce drug prices, CAP went farther last week when it proposed holding legislation boosting the NIH budget hostage to price controls.

The think tank sent a letter to the Democratic leadership of the House of Representatives and Senate urging them to withhold support for 21st Century Cures legislation in the lame duck session of Congress to provide an opportunity for the addition of drug price control provisions.

“While the Cures Act’s funding for the [National Institutes of Health](#) is a priority for many, it is critical that any legislation making changes to drug policies take steps to rein in the cost of prescription drugs,” the letter stated.

The letter concluded: “We respectfully urge you to delay action on this legislation until it can be included as part of a package that also addresses the high cost of prescription drugs.” ^{bc}

COMPANIES AND INSTITUTIONS MENTIONED

Biogen Inc. (NASDAQ:BIIB), Cambridge, Mass.

Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.

Center for American Progress, Washington, D.C.

Manhattan Institute for Policy Research, New York, N.Y.

National Institutes of Health (NIH), Bethesda, Md.

Pfizer Inc. (NYSE:PFE), New York, N.Y.

Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.

Sanofi (Euronext:SAN; NYSE:SNY), Paris, France

University of Pennsylvania, Philadelphia, Pa.

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Usdin, S. “Executive power.” *BioCentury* (2016)

Usdin, S. “Progressive ideas.” *BioCentury* (2016)

EBB & FLOW

QUARK'S GLOBAL AMBITIONS

After getting its toes wet with a couple of biotech seed investments and hiring a drug development veteran as partner and CEO, Canadian VC Quark Venture Inc. teamed up with GF Securities Co. Ltd. (SZSE:000776; HKSE:1776) to raise and manage a \$500 million fund.

The partners closed the first \$100 million of the Global Health Sciences Venture Fund on Oct. 17 and plan to announce six investments by year end.

Quark's team is new to life sciences investing, but not to biopharma. Karimah Es Sabar joined in July as partner and CEO after serving as president and CEO at Canadian not-for-profit accelerator [Centre for Drug Research and Development \(CDRD\)](#).

"I wanted to hire a team that came from industry and that understood the science, the ecosystem and the continuum. A team that had done drug development, taken drugs to market, spun out companies and knows what's involved in the health science space," Es Sabar told BioCentury.

New hires include CSO Zafrira Avnur, previously global head of academic innovation at [Roche Partnering](#), and Director of Business Development Kaley Wilson, who was CDRD's associate director of partnering.

Quark quietly began investing last year with a small seed fund. The seed fund's size is not disclosed. Its investments included nanoparticle play [Sitka Biopharma Inc.](#) and antiviral company [Aurora Lifesciences Corp.](#)

About 50-60% of the new fund will be deployed to therapeutics and the remainder to devices and health IT. Within therapeutics, the focus is oncology, infectious disease, inflammation and neurology.

About 60-70% will go to mid- to late-stage companies. The fund will invest in Canada, the U.S., Europe and Asia.

Its only disclosed investment so far is [MSI Methylation Sciences Inc.](#), which is testing Strada S-adenosyl-L-methionine (MS-195) in Phase II as adjunctive therapy for major depressive disorder (MDD).

LPs include China Merchants Capital, Sichuan Development Capital, [DaAn Gene Co. Ltd. of Sun Yat-sen University](#) and undisclosed international institutional investors.

Es Sabar noted the LPs and GF Securities can help portfolio companies access the China market. "The China market is massive and many people don't know how to enter the market, and often don't enter with the right partners. That's something we want to facilitate," she said.

Quark plans to launch a separate fund this year to invest in Chinese life sciences companies.

—Virginia Li

VENTURING INTO DEBT

After two decades of primarily focusing on equity investments, Perceptive Advisors LLC launched its first debt fund last week to expand its reach to healthcare companies that are seeking minimally dilutive financing.

The firm closed the Perceptive Credit Opportunities Fund at \$323 million, above its \$300 million target. LPs include undisclosed endowments, family offices and institutional investors.

The fund will provide debt financing for therapeutics, device, diagnostics and healthcare IT companies looking to reach key inflection points or make acquisitions. It plans to allocate \$10-\$50 million per company.

Perceptive's Sam Chawla said the firm plans to invest the fund in 20 private and public companies in the U.S. and Canada. The fund is agnostic to development stage and therapeutic area.

"I WANTED TO HIRE A TEAM THAT CAME FROM INDUSTRY AND THAT UNDERSTOOD THE SCIENCE, THE ECOSYSTEM AND THE CONTINUUM."

KARIMAH ES SABAR, QUARK

"WE FOCUS ON COMPANIES WHERE WE LIKE THE UNDERLYING EQUITY STORY AND LONG-TERM FUNDAMENTALS."

**SAM CHAWLA,
PERCEPTIVE ADVISORS**

Just under half of the fund has been committed. So far the fund has financed 10 companies, including antibody company [Zymeworks Inc.](#), drug delivery play [MonoSol Rx LLC](#) and [VBI Vaccines Inc.](#) (NASDAQ:VBIV; TSX:VBV). The rest are undisclosed.

Perceptive manages about \$2 billion, including over \$1.5 billion in equity funds. Since its inception in 1999, the firm has posted average returns of 30%.

With the debt fund, Perceptive expects to cater to companies that need cash to get to a milestone that would enable their next equity round, or to help finance a large acquisition.

“We’ve seen this shift over a 10-15 year period where incremental capital, in addition to equity, has come in the form of structured debt,” Chawla told BioCentury.

Debt “lengthens the runway on the balance sheet and compared to equity financing there’s typically a lot less dilution,” he said.

A portion of the fund will invest in Perceptive’s existing portfolio companies, but the majority will go to new companies.

“Good companies find a way to get funded through challenging and frothy market cycles,” said Chawla. “We focus on companies where we like the underlying equity story and long-term fundamentals.”

The average holding period for the fund will be three to five years. Chawla declined to disclose its target returns.

—Virginia Li

COMPLEMENT CASH

[True North Therapeutics Inc.](#)’s first clinical data for lead molecule TNT009 convinced new investor HBM Healthcare Investments to co-lead this month’s \$45 million series D round.

The other co-leads were new investor Redmile Group and existing investor Perceptive Advisors. They were joined by new investor Franklin Templeton Investments and undisclosed existing investors.

True North reported interim Phase Ib data in June at the [European Hematology Association](#) meeting in Copenhagen showing that four of five cold agglutinin disease (CAD) patients treated with TNT009 responded within 24 hours of the first dose.

CAD is an autoimmune hemolytic anemia for which there are no approved therapies. In CAD, autoantibodies bind to red blood cells (RBCs) at temperatures below 37°C, resulting in complement-mediated destruction of RBCs and causing anemia, fatigue and potentially fatal thromboses.

The five patients had median hemoglobin levels of 7.5 g/dL at baseline. After four weeks, three achieved a complete response, reaching normal hemoglobin levels of 12 g/dL or greater. Three patients who were transfusion-dependent at baseline became transfusion-independent.

HBM’s Andreas Wicki said the response rate, speed of response and magnitude of hemoglobin increase convinced HBM to back True North.

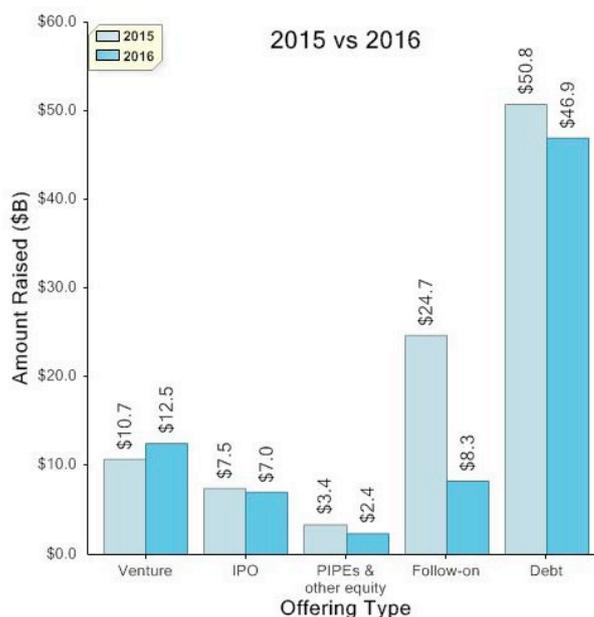
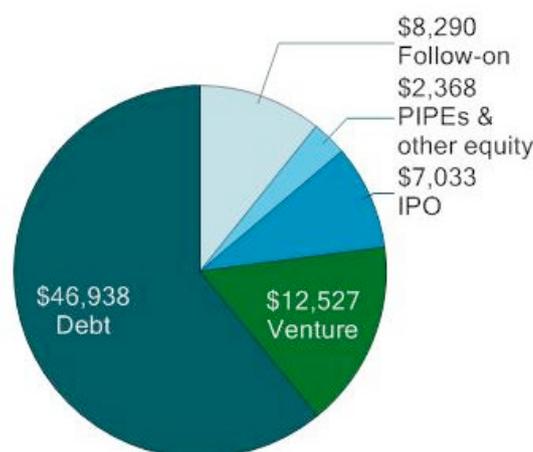
He added that the firm expects TNT009 to work in multiple indications.

“We hope and expect that there will either be more indications with the lead molecule or new molecules coming forward,” Wicki told BioCentury.

MONEY RAISED IN 2016

Last week, the biotech industry raised \$4,638 million, bringing to \$77.2 billion the total raised year-to-date. In 2015, a total of \$108.9 billion was raised, including \$54.8 billion in debt, \$29.6 billion in follow-ons, \$3.8 billion in PIPEs and other equity, \$8.1 billion in IPOs, and \$12.7 billion in venture capital. Totals include overallocments and warrants, and are rounded to the nearest millions.

Total YTD: \$77,157 (\$M)



TNT009 is a humanized mAb against complement component 1 s subcomponent (C1S), an upstream target in the classical complement pathway (see [BioCentury, April 21, 2014](#)).

In addition to CAD, the Phase Ib trial is enrolling patients with other complement-mediated disorders including bullous pemphigoid, warm autoimmune hemolytic anemia and end-stage renal disease (ESRD). The mAb has U.S. and EU Orphan Drug designation for autoimmune hemolytic anemia.

Wicki said the D round should enable True North to begin Phase II testing of TNT009 in CAD and obtain clinical data in other indications. CEO Nancy Stagliano said CAD is the lead indication, though she declined to disclose a development timeline.

True North also has next-generation mAbs against C1S for undisclosed indications driven by classical complement pathway dysregulation. [bc](#)

—Virginia Li

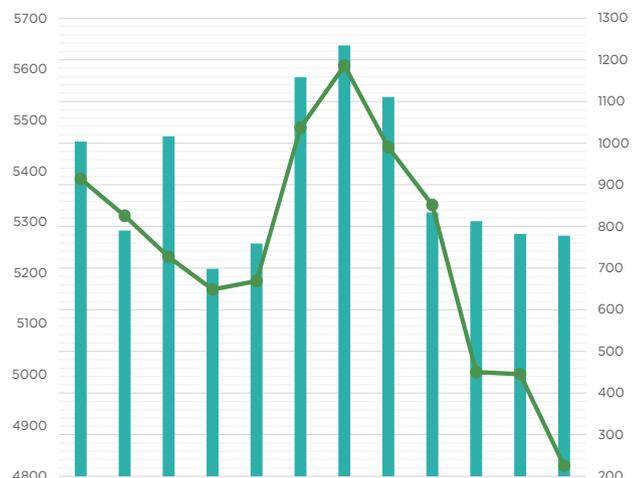
EARNINGS ON DECK

At least 23 biotechs and pharmas are expected to report earnings this week. (A) Fiscal 1Q; (B) Fiscal 2Q; (C) First half EPS; (D) Estimate from one analyst; (E) Fiscal 4Q

Company	Date	Pre/post mkt	3Q16 EPS est	3Q15 EPS	Expected chg
Bio-Techne Corp. (NASDAQ:TECH) (A)	10/31	Pre	\$0.79	\$0.79	0%
Luminex Corp. (NASDAQ:LMNX)	10/31	Post	\$0.10	\$0.15	-33%
Daiichi Sankyo Co. Ltd. (Tokyo:4568) (B)	10/31	NA	NA	¥101.47 (C)	NA
Eisai Co. Ltd. (Tokyo:4523)	10/31	NA	NA	¥38.50 (C)	NA
Incyte Corp. (NASDAQ:INCY)	11/1	Pre	-\$0.01	-\$0.22	NA
Shire plc (LSE:SHP; NASDAQ:SHPG)	11/1	Pre	\$3.20	\$3.24	-1%
Bio-Rad Laboratories Inc. (NYSE:BIO)	11/1	Post	\$0.51 (D)	\$0.59	-14%
Genomic Health Inc. (NASDAQ:GHDX)	11/1	Post	-\$0.09	-\$0.36	NA
Gilead Sciences Inc. (NASDAQ:GILD)	11/1	Post	\$2.85	\$3.22	-11%
Illumina Inc. (NASDAQ:ILMN)	11/1	Post	\$0.87	\$0.80	9%
Myriad Genetics Inc. (NASDAQ:MYGN) (A)	11/1	Post	\$0.25	\$0.41	-39%
Pfizer Inc. (NYSE:PFE)	11/1	Post	\$0.62	\$0.60	3%
Mitsubishi Tanabe Pharma Corp. (Tokyo:4508) (B)	11/1	NA	NA	¥51.96 (C)	NA
Alkermes plc (NASDAQ:ALKS)	11/2	Pre	-\$0.06	-\$0.19	NA
Allergan plc (NYSE:AGN)	11/2	Pre	\$3.58	\$3.48	3%
Genmab A/S (CSE:GEN)	11/2	Post	DKK1.11	DKK2.30	-52%
Vanda Pharmaceuticals Inc. (NASDAQ:VNDA)	11/2	Post	-\$0.11	-\$0.22	NA
H. Lundbeck A/S (CSE:LUN)	11/2	NA	DKK1.22	-DKK6.40	NA
Qiagen N.V. (Xetra:QIA; NASDAQ:QGEN)	11/2	NA	\$0.28	\$0.27	4%
Becton Dickinson and Co. (NYSE:BDX) (E)	11/3	Pre	\$2.09	\$1.94	8%
Ligand Pharmaceuticals Inc. (NASDAQ:LGND)	11/3	Post	\$0.59	\$0.56	5%
Spectrum Pharmaceuticals Inc. (NASDAQ:SPPI)	11/3	Post	-\$0.32	-\$0.28	NA
Regeneron Pharmaceuticals Inc. (NASDAQ:REGN)	11/4	Pre	\$2.71	\$3.47	-22%

BIOCENTURY 100 PRICE & VOLUME TREND

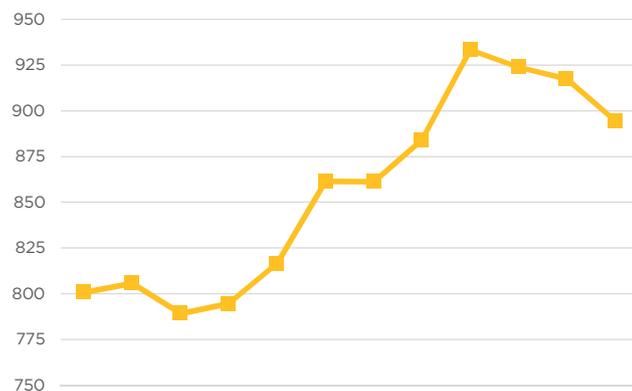
Cumulative weekly performance of 100 bioscience stocks. 12-week period. Line shows Price Level change (Left scale. Index base=1000 on May 10, 1996). Bars show cumulative volume in millions (right scale).



BioCentury tracks 833 issues that report prices and volume daily. The BioCentury 100 is a subset used to monitor price and volume trends

BIOCENTURY LONDON INDEX

Weekly change in the combined market capitalization for 14 bioscience stocks listed on the LSE or AIM, 12-week period. Index base =1000 on May 10, 1996.



BIOCENTURY 100 INDICATORS

Week ended 10/28/16



PRICES
4820.35
dn 4%

VOLUME
777.6M shrs
dn 1%

PRICE GAINS

Stocks with greatest % price increase in the week ended 10/28. (Priced above \$2; 5,000 minimum share volume)

Company	Ticker	\$Close	\$Chg	% Chg	Vol(00)
Unilife ¹	UNIS	2.800	1.050	60%	176891
Oasmia ²	OASM	3.610	0.910	34%	53647
Check-Cap	CHEK	2.240	0.470	27%	51894
CRISPR Therapeutics	CRSP	16.740	2.920	21%	6514
Alexion	ALXN	135.590	15.330	13%	137557
Curetis	CURE	€7.050	€0.750	12%	1015
Abivax	ABVX	€7.880	€0.710	10%	2501
Agile Therapeutics	AGRX	7.660	0.660	9%	4388
Gene Techno Science	4584	¥1590.000	¥130.000	9%	4974
BioGaia	BIOG B	SEK282.00	SEK22.000	8%	1960
Human Metabolome Tech	6090	¥1116.000	¥87.000	8%	20989
Probi	PROB	SEK383.00	SEK27.500	8%	797

PRICE DECLINES

Stocks with greatest % price decline (criteria as above).

Company	Ticker	\$Close	\$Chg	% Chg	Vol(00)
Proteostasis	PTI	7.230	-6.390	-47%	19775
Corbus	CRBP	5.250	-3.700	-41%	124035
Agenus	AGEN	4.090	-1.660	-29%	108946
Windtree	WINT	2.050	-0.800	-28%	17955
Dimension Therapeutics	DMTX	5.230	-1.970	-27%	3827
Catabasis Pharmaceuticals	CATB	3.570	-1.310	-27%	5523
Flex Pharma	FLKS	4.680	-1.500	-24%	6617
Theravance Biopharma	TBPH	25.420	-8.120	-24%	74058
Inovio	INO	6.430	-1.930	-23%	88514
Aldeyra Therapeutics	ALDX	5.250	-1.560	-23%	3778
Aeterna Zentaris ³	AEZS	3.820	-1.120	-23%	27112

VOLUME GAINS

Greatest changes in volume above 5,000 shares.

Company	Ticker	Vol(00)	%Chg	\$Close	\$Chg
Median Technologies	ALMDT	565	13548%	€8.430	-€0.060
Haohai	6826	18149	11609%	HK\$36.850	-HK\$0.150
Unilife ¹	UNIS	176891	3836%	2.800	1.050
ProQR Therapeutics	PRQR	37026	3451%	5.450	-0.950
Human Metabolome Tech	6090	20989	3416%	¥1116.000	¥87.000
Tiziana Life Sciences	TILS	101	2735%	188.5p	-1.5p
Check-Cap	CHEK	51894	2604%	2.240	0.470
Xenetic	XBIO	151	1481%	4.750	0.350
Gene Techno Science	4584	4974	1076%	¥1590.000	¥130.000
BioGaia	BIOG B	1960	870%	SEK282.00	SEK22.000

1 Includes volume from Australian Stock Exchange

2 Includes volume from Stockholm Stock Exchange and converted ADSs (1 ADS = 3 shares)

3 Includes volume from Toronto Stock Exchange

BIOCENTURY 100 ADVANCE-DECLINE TRENDS

Week ended	BC100 Price Level	BC100 Stocks gaining	Gaining vol. (00)	BC100 Stocks declining	Declining vol. (00)
Sep 30	5447.20	32	3358700	66	7701167
Oct 07	5333.41	36	2425703	64	5908449
Oct 14	5004.89	5	469493	95	7654115
Oct 21	5000.80	61	3643174	39	4176843
Oct 28	4820.35	13	1010081	87	6765701

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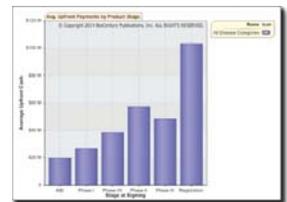
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