Fall 2016 HRA Members' Meeting – Executive Summary

September 27–28, 2016

HEALTH RESEARCH ALLIANCE MEMBERS' MEETING
Sponsored by: Foundation Fighting Blindness and Brightfocus Foundation

Members' Meeting Page: https://www.healthra.org/members-only/bethesda/
(for meeting agenda, participant list, speaker bios, and other meeting materials)

Session Summaries:

SESSION 1: FDA Priorities and Interactions with Non-profits

Speaker: Luciana Borio, MD
Acting Chief Scientist | U.S. Food and Drug Administration

Dr. Borio reviewed how the FDA is enabling innovation in three ways: (1) building scientific expertise, (2) enhancing its infrastructure, and (3) promoting collaborations within FDA and with other organizations. She discussed opportunities for the FDA and nonprofit medical research funders to partner.

(1) The FDA has launched several initiatives aimed at building scientific expertise. Through the Commissioner's Fellowship Program, health care professionals, scientists, and engineers spend two years at the FDA where they receive training in regulatory and scientific issues under the mentorship of an FDA scientist. The fellows then return to their institutions, as "FDA ambassadors" and share what they have learned. Another initiative, the New Frontiers in Science Distinguished Lectureship Program, is a collaboration with the HRA and focuses on professional development for FDA staff.

(2) FDA infrastructure has been enhanced with high-performance computing capabilities to incorporate big data into FDA programs and better handle the data now being submitted with grant applications. These computing capabilities are also needed to enable scientists to use big data to understand how products perform in different populations.

(3) She noted that no single institution has all the knowledge, and so the FDA must create collaborations with FDA centers and external organizations. To this end, the FDA has created Centers of Excellence in Regulatory Science and Innovation (CERSIs) at four academic health

centers in the U.S. The goal is to advance regulatory science and find new ways to evaluate the safety and effectiveness of products regulated by the FDA. Another mechanism for collaboration is FDA's program of Critical Path meetings to address issues in drug development, such as the use of biomarkers in early stage drug development.

The top challenges for the FDA:

- Lack of adequate resources. Therefore, leveraging the expertise provided by external organizations is critical.
- Protecting privacy and restrictions to share commercial confidential data make it a challenge to have transparent exchange of information among collaborators.
- FDA's silo organizational structure. Each center has its own budgets and need not "do something if it doesn't want to." However, the FDA is moving away from the center-based model to a more collaborative, multidisciplinary approach similar to that used in an academic health center. For example the new Oncology Center for Excellence leverages expertise of FDA regulatory scientists and reviewers with oncology clinical expertise in drugs, biologics, and devices.

She noted that for HRA members that deal with a specific disease focus but lack the resources of a large organization like the ACS, there are many points of entry, including her office, to FDA expertise and resources such as those in the Office of Orphan Products.

HRA Action Item:
Look into sponsoring an FDA fellow instead of or in addition to continuing the lecture series.

SESSION 2: Understanding Preprints, an Emerging Model for Publication in Biology

Speaker: John Inglis, PhD
Publisher and Executive Director | Cold Spring Harbor Laboratory Press
Cofounder | bioRxiv
Talk title: Science Preprints

Definition of preprint: A complete but unpublished manuscript yet to be certified by peer review. Because the process of peer review and journal publication can be lengthy, authors distribute manuscripts as "preprints" before peer review, allowing other scientists to see, discuss, and comment on the findings immediately.

Two preprint distribution models:

1) Publisher-specific, for-profit
    - Author submits manuscript to a journal
    - Journal makes manuscript publicly available as a preprint and manages peer review
    - Journal publishes the preprints that pass peer review
    - Article publication charges paid by authors support preprint distribution as well as publication
2) Publisher-neutral, not-for-profit (e.g., bioRxiv or OSF|*Preprints*)
    - Author posts preprint to a dedicated service
    - Posting and reading preprints are free of charge

- No peer review
- Author can revise the preprint
- Author can submit the manuscript to any journal willing to consider it
- The service is supported by institutions and foundations

Several preprint servers have been established, including CSHL's bioRxiv, the Center for Open Science's OSF|*Preprints,* and Cornell's arXiv.org. Preprints are an attractive model because the long time to publication through the traditional journal submission route can be a problem, especially for young investigators who need to prove productivity to grant-making organizations and their tenure committees.

Dr. Inglis noted that bioRxiv, established in 2013, spans all life sciences, including clinical trials and epidemiology. He outlined the submission process, noting that manuscripts undergo a two-stage screening: (1) in-house screening for format, completeness, and plagiarism and (2) high-level review by scientists in the relevant field. Approved manuscripts can be posted to the web in as little as 24 hours. Posted manuscripts have a date stamp, a citable DOI, and are indexed in Google Scholar. The manuscripts display usage metrics and comments (moderated). Readers can comment on the preprint and authors can revise the manuscript multiple times (revisions are date-stamped) before submitting it to a journal for publication. The preprint will display links to published versions.

To date more than 6,000 manuscripts have been posted on the server. Within two years after posting (median is 157 days), 60% of submitted preprint manuscripts have been published in journals (320 journals have published papers first posted to bioRxiv). These journals include some of the most selective and also include open access and subscription-based journals. With respect to the remaining 40% of manuscripts submitted to bioRxiv, Dr. Inglis noted that some of their authors think that posting to bioRxiv is sufficient. The website is being integrated with journals (e.g., eLife and PNAS) so that authors can submit to the journal directly from the bioRxiv server.

Progress:
- Behavior change: ever more biologists posting/reading preprints
- Policy change: majority of journals allow preprint posting
- Rule change: NIH biosketch now allows preprint citations
- Change in community awareness: ASAPbio is engaging stakeholders and the scientific community in implementing preprints as a way to rapidly communicate results in the life sciences.
- Institutional change: preprints are being considered in hiring/promotion decisions
- Reduction in preprint anxiety

What can funders do?
- Adopt clear policies on preprints
- Encourage grantees to post preprints of their papers and respond to community feedback
- Encourage grant review committees to consider preprints as evidence of productivity, especially by early-career scientists
- Facilitate coordination among not-for-profit preprint services across academic disciplines
- Financially support not-for-profit preprint services to maximize their benefits to science

Remaining issues:
- Priority claims and scooping
- Clinical scope

- Clinical criteria
- Citation linking/summing
- Discoverability
- Retractions
- License conflicts

Speaker: Jessica Polka, PhD
Postdoctoral Research Fellow | Harvard Medical School
President of the Board of Directors, Future of Research
Director | ASAPbio
Talk title: Preprints from the perspective of (junior, basic) biologists

Dr. Polka reported on a 2016 meeting held at the Howard Hughes Medical Institute to examine the role that preprints could play in communicating results in the life sciences and accelerating scientific discovery. Participants included junior and senior scientists, academic chairs/administrators, scientific societies, publishes, and public/private funders. There was consensus that preprints could move science forward, however there are many challenges and concerns associated with preprints. Dr. Polka shared those concerns and the arguments refuting them with the audience.

Concerns about preprints (and refuting arguments):

Concern: Scientists can't be trusted to share our work before peer review.
Scientists already share it in meetings.

Concern: Journals won't accept manuscripts if preprints have been published.
Journals are increasingly accepting preprint manuscripts for publication.

Concern: The researcher will be scooped.
On arXiv postings are accepted as date-stamped priority claims. In addition arXiv is developing a statement/pledge (currently in draft form) regarding disclosing and crediting scientific work. This standard is the goal of bioRxiv and should be of preprints in general. However, scientists need to be mindful that posting a preprint is considered disclosure, as it would be for a meeting presentation.

Concern: We need to ensure ethical disclosure of data.
Preprint servers should screen for reproducibility in several ways:
- Screen for human subjects research
- Ensure that all authors agree to posting
- State the requirement that methods are described thoroughly and completely

Concern: There could be inaccurate or misleading media coverage of results in preprints.
Authors should be transparent and include a statement that the paper has not been peer-reviewed. Granted, there are human health concerns if media jump on inaccurate clinically relevant research data released in a preprint, as there are with other methods of publication.

Concern: Junior researchers have "preprint anxiety" because they believe their career advancement is dependent on getting a peer-reviewed journal publication.
In fact, preprints are a good way for early career scientists to demonstrate productivity. Preprints enable trainees to have publicly disclosed work that can be evaluated for a PhD thesis, postdoc positions, fellowships, or jobs well in advance of a peer-reviewed publication. They can also raise the visibility of a junior researcher.

Other advantages to using preprints:

- Preprints are extremely valuable in providing access to publicly and privately funded scientific work, since preprints are immediately available to everyone around the world.
- Preprints can also address the unfortunate fact that information is being held within laboratories for longer periods of time. With preprints, new knowledge is immediately accessible, allowing research overall to advance. The immediate visibility of preprints also facilitates invitations to meetings, new collaborations, etc.
- Preprints have the potential to increase rigor and reproducibility by providing more (and timely) feedback on manuscripts than the traditional 2-3 anonymous peer reviewers.
- Preprints have a time stamp and DOI number. They provide evidence of what a scientist has accomplished while the work is being improved through peer review. Thus eliminating the lack of transparency and decreasing the length of review helps alleviate the difficulties in establishing priority of discovery.

ASAPbio survey results:

Dr. Polka reported on results of the ASAPbio survey (392 responses). The conclusion from the survey was that certain policy and attitude changes would increase the likelihood of researchers to submit preprints. For instance, a majority of respondents were likely to submit preprints if preprints were accepted as priority of discovery, if grant agencies and promotion committees accept preprints as evidence of productivity, and if all biology journals accept preprints.

She noted that the Simons Foundation is taking steps to encourage and normalize preprint use via an explicit statement in the grant award letter and updating its biosketch form to include space for applicants to list manuscripts deposited in preprint servers.

ASAPbio aggregator

Dr. Polka said that ASAPbio is proposing development of an aggregator (similar to PubMed or PubMed Central for preprints) to make preprints discoverable. It would be community governed, transparent and open in operations, be easy to access, and hold potential for further innovation. Ease of access (by both humans and machines) would be a top priority. Funders at the HHMI meeting asked ASAPbio to develop a proposal describing the governance, infrastructure and standards desired for a preprint aggregator service that represents the views of the broadest number of stakeholders. The presentation to funders is scheduled for January 2017.

During the discussion, HRA members raised the following questions and concerns regarding preprint aggregators: What is the sustainability of a preprint server? Is there a need for additional support to expand inventory of preprints?

The panel commented that because the current infrastructure is not able to scale up and cannot support a large increase of preprint submissions, there is a need for additional money to support the preprint infrastructure and governance structure. Private money is being sought as well as discussions about other revenue streams, such as journals paying small fee for connecting to preprint aggregator.

Speaker: Neil Thakur, PhD
Special Assistant to the Deputy Director | Office of Extramural Research | National Institutes of Health

Talk title: Interim Research Products

Dr. Thakur offered a broad working definition that is being used by NIH to describe interim research products: ***"Complete, public research products that are not final."*** Interim research products do not include research products specifically addressed in other policies, such as data, clinical trials, physical collections, etc."

Intended examples and current focus of the NIH Policy:
Preprints: complete and public drafts of scientific documents. Speeds dissemination, establishes priority, generates feedback, and may reduce publication bias.
Preregistering protocols: publicly declaring key elements of a research project in advance, such as hypotheses, measures, confirmatory research protocols and analysis plans. May reduce biases like p-hacking.

NIH is considering this now because there is growing recognition that interim research products could speed the dissemination of science and enhance its rigor. Many disciplines have been using preprints for years (e.g. economics, physics). Groups like ASAPbio suggest that expanding the use of preprints could increase the impact of NIH research. In addition to preprints, groups like the Center for Open Science (www.cos.io) suggest preregistration of research could enhance rigor of NIH supported research.

NIH advocates for adoption of stable rules that advance science. Listed below are suggested guidelines and standards for citing interim research products.

- Recognize common practices and encourage beneficial innovation
    - Allow disciplines to adopt interim research products at their own pace (and recognize that many already do)
    - Do not prevent innovation that increases rigor and dissemination
- Prevent bad practices from taking root
    - Clearly state standards NIH *cannot* accept as community norms are being established (Interim products that are not preserved OR risk NIH reviewer identity, etc, are not usable. Example: a file on a lab webpage is not an acceptable preprint.)

NIH is has developed an RFI on interim research products asking the community for:

- Feedback on what is considered to be interim research products and how they are used
- Insight on how particular types of interim research products might impact the advancement of science
- Feedback on potential citation standards
- Insight on the need and potential impact of citing interim products on peer review for NIH applications
- Advice on how NIH reviewers might evaluate citations of interim research products in applications

Implementation details under consideration include standards for citing interim research products. Possibilities Include:

- Registered or indexed (findable)
- Persistent identifier, that links to a repository that will maintain the privacy of the end user
- Use of the CC-BY license or not
- Readable by both human and machine
- Incudes a record of modifications, and a link to the final version

- Declares any competing interests
- Policy statement clarifying scope: "does not apply to research products specifically addressed in other policies, such as data (URL), clinical trials (URL), physical collections (URL), etc."

Standards specifically for preprints could include a clear statement in the document (understandable to non-experts) that the information is preliminary and concordance with standard practices for scholarly publication.

During the subsequent discussion, it was noted that senior scientists are less open to preprints, which means there is still much advocacy to be done. Their concerns include the acknowledgment of peer review's role as an important filter for quality. Peer review is a way to validate research results for rigor and reproducibility.

Another concern is that the "living document" concept of preprint server could be at odds with a system that rewards scientists who publish a lot. This system could allow the same paper to be republished multiple times with revisions. However, the ability to assign a DOI has "blessed" preprints, and that is a big step in establishing legitimacy.

HRA Action Items:
Continue to discuss the impact of encouraging awardees to use preprints in the OSTF.
Evaluate Simons' experience with changes encouraging the use of preprints.
Explore the possibility of having a separate field for citing preprints in applications and progress reports (not in the "other" field).
Work with NIH to learn how they will be training their reviewers to evaluate preprints.
Explore the various preprint server options that are currently available and discuss pros and cons of encouraging awardees to use them.

SESSION 3: Introduction to Our Meeting Sponsors

Speaker: Stephen Rose, PhD
Chief Research Officer | Foundation Fighting Blindness

FFB is the world's largest non-governmental source of research funding for orphan inherited retinal degenerative diseases. It does not have an endowment; annual fundraising defines its budget. FFB has raised almost $700 million over the past 45 years to support its research. FFB's strategy to fight inherited blindness due to retinal degenerations is to identify innovative therapies, fund cutting-edge research, and aggressively seek development and commercialization.

FFB's research portfolio includes career development award programs that provide support starting with beginning scientists (e.g., HHMI-FFB Medical Fellow), through all stages of clinician scientists' careers, awards to individual investigators, and awards to groups at clinical research centers whose projects are synergized around a common theme. In addition, FFB works to accelerate translational research through the Gund-Harrington Initiative, a collaboration with the nonprofit Harrington Discovery Institute, which seeks to identify therapies that can benefit from acceleration and create a commercially attractive therapeutic package by providing funding, experienced commercial project management, and access to pharma expertise. FFB's Clinical Research Institute is currently supporting many clinical trials and clinical studies and expects to support many more as the pipeline

has expanded greatly with many potential treatments coming forward. Most clinical studies have been launched within the past 5 years and leveraged by commercial investment.

Dr. Rose reviewed FFB's science pipeline, from pathway analysis and target identification through pre-clinical and clinical studies. In the pipeline are 31 projects of interest with potential to reach the clinic within 4 years. These include academic and biotech projects in need of funding (13 small molecule, 15 gene therapy, 3 cell therapy). Scientific areas of interest include novel medical therapies, regenerative medicine, as well as cellular and molecular mechanisms of disease.

Dr. Rose described FFB's Translational Research Acceleration Portfolio (TRAP). The goal of TRAP is to accelerate high-priority research through the pipeline to the clinic. The program has been successful, for example, a grant led to the start-up of Mitochem Therapeutics, which is developing a small molecule for mitochondrial stress.

Lessons from TRAP:

- Translation to IND-enabling studies are slow
- There is a lack of clarity on how to get to the clinic. Issues include lack of understanding of regulatory issues and quality issues and overlooking key aspects in early development (e.g., formulation)
- Disconnect between theoretical therapy and clinical practice
- Projects where FFB provided independent consulting did better
- Needs:
    - Active project management
    - TPP-oriented development pathway
    - Pharma expertise and input early

Dr. Rose described My Retina Tracker, a patient-driven registry for people affected by an inherited retinal degenerative disease. Patients build a health profile that includes family history, genetic testing results, and interest in participating in research studies. The goal is to capture the disease both from the patient's and the physician's perspectives.

Speaker: Diane Bovenkamp, PhD
Vice President of Scientific Affairs | BrightFocus Foundation
Talk Title: Helping Scientists, Clinicians, Families and Communities Stay Strong Through Research, Partnerships, and Information

Dr. Bovenkamp began by telling the audience that BrightFocus seeks to save mind and sight by funding highly innovative research worldwide on Alzheimer's disease, glaucoma, and macular degeneration. Since 1973, they have awarded more than $163 million to scientists in more than 1,300 innovative projects with the goal of seeking new approaches to prevention, diagnosis, and treatment of their target diseases. She went on to describe their initiatives which include: investigator-initiated research (basic, clinical, and translational) worldwide (no U.S. citizenship required); training grants for junior investigators; convening and sponsoring targeted scientific symposia and workshops; and the official journal of BrightFocus, the open-access *Molecular Degeneration* (in partnership with BioMed Central). BrightFocus also helps to shape the next generation of science and scientists at the "BrightFocus Alzheimer's Fast Track" (and the inaugural 2017 "BrightFocus Glaucoma Fast Track") workshops that offer graduate students and postdocs an immersive opportunity to learn from

experts in the fields of Alzheimer's disease and glaucoma. Dr. Bovemkamp told the audience about online educational materials including "tool kits" for Alzheimer's disease, glaucoma, and macular degeneration, a listing of all grants funded since inception, and complimentary electronic and printed materials for healthcare professionals to provide to affected individuals and families. Other scientific initiatives include the funding and support of: the Health-eBrain mobile platform study to assess the cognitive toll of caregiving and testing of various support networks provided to caregivers; the creation and launching of the EyesOnALZ "Stall Catchers" which uses citizen science gaming to speed up Alzheimer's research; and the convening of an expert panel drawn from various disciplines and institutes to accelerate the development, testing and dissemination of home-based dementia care interventions (now designated pre-summit activity to inform the planned 2017 Research Summit on Care and Services for Persons with Dementia and Caregivers, as recognized by members of the National Advisory Council on Alzheimer's Research, Care, And Services).

SESSION 4: Interaction with Industry

Speaker: Christopher Penland, PhD
Vice-President of BioPharma Programs | Cystic Fibrosis Foundation
Talk title: Cystic Fibrosis Drug Discovery and Development: More Than Venture Philanthropy

Dr. Penland discussed CFF's venture philanthropy model and what CFF brings to a successful relationship with industry. CCF's Therapeutics Development Network comprises 82 research sites, and 150 investigators. He noted that CFF Therapeutics has contractual agreements with several companies to receive royalties related to drugs that are developed as a result of CFFT funding. Any royalties CFF receives are used in support of its mission.

Dr. Penland briefly described the partnerships with the pharma companies Orkambi and Kalydeco that led to the development of CFTR modulators Lumacaftor (with Orkambi) and Ivacaftor (with Kalydeco) that led to promising results of Phase 3 clinical trial of Lumacaftor + Ivacaftor (VX-809 + VX-770).

Philanthropies can engage pharma companies to be involved in an orphan disease they deem "too risky" to invest in by following the tenets of venture philanthropy listed below.

- Tailored financing
- Multiyear support
- Performance measurement
- Engagement
- Organizational capacity building

Additional measures CFF has taken:

- Non-monetary assistance (CFTR Toolbox)
- CFTR functional and mechanistic assays
- Access to non-commercial resources
    - CFTR modulator panel
    - CFTR antibodies
    - CF human airway epithelia

- Independent testing
    - CFFTI Lab
    - Clinical Trial Finder (online resource in which patients enter their information to find clinical relevant clinical trials)
    - Chantest (a division of Charles River)

Member Presentations

Speaker: Mari Candelore, MA
Associate Director, Research Business Development | JDRF
Talk title: JDRF Industry Partnering Strategy

As many as 1.5 million Americans have Type 1 diabetes (T1D) and incidence is increasing worldwide. Current treatments and technologies are not meeting the challenges of TID management. Existing sources of early stage funding for novel therapy development are inadequate. Most venture capital funders shun the early stage and large pharma companies are risk-adverse and seek mostly Phase 2 assets.

JDRF-industry partnerships are critical:

- Leverage JDRF financial contribution
- Expertise in in delivering results to patients
- Deep subject matter expertise,
- Various funding vehicles, access to pharma and VCs
- Contacts with regulatory agencies

JDRF's strategy for accelerating translation to the clinic is to use diverse funding vehicles to match the specific scientific and commercial opportunity. To date there have been 88 grant awards/collaborative partnerships with 56 companies.

Strategic, nonfinancial research partnerships

External: Industry discovery and development partnership (IDDP)

- Specific POC project, go/no-go
- JDRF provides partial, milestone-based, non-dilutive funding
- Royalty payback linked to development milestones

Internal: Joint funding partner-ready projects

- JDRF and pharma partner co-fund academic translational research project
- Recruits early industry engagement
- Facilitated transfer to industry

Either external or internal program: Equity-based transactions

- Pre or at Series A funding; JDRF may participate as part of a syndicate (Pharma/VC)
- Payback through equity ownership

Speaker: Maneesh Kumar, MD, PhD
Scientific Program Manager | Breast Cancer Research Foundation
Talk title: BCRF Investigator-Initiated Drug Research Program

BCRF is partnering with Pfizer on a drug research program. The goal is to fund independent, innovative and high-quality, investigator-initiated research. BCRF presents drug lists to BCRF investigators and investigators tell BCRF what they can do with the drugs. The scientists have access, at no cost, to 16 study drugs that can be sued in human studies. Additional Pfizer agents may be added over time.

The RFP announced in March 2016 and proposals will be reviewed and identified for funding by December 5. Clinical trials managed by the TBCRC (Translational Breast Cancer Research Consortium). Pre-clinical, mechanism of action and similar studies are managed by BCRF. Additional companies are under discussion to join this program.

Challenges in partnering with industry include:

- Reputational Risk – risk of associating with pharma industry that may not always have the best image
- Risk of influence and review—BCRF creates a firewall between pharma and the investigator (e.g., pharma can't participate in grant reviews).
- Intellectual property—what happens if the investigator finds a different application for the drug? Is it covered under the original IP agreement?

Speaker: Mary DeRome
Translational Research manager | Multiple Myeloma Research Foundation
Talk title: MMRF Interactions with Industry

Multiple myeloma is the second most prevalent blood cancer, and has no cure. There are significant benefits that both MMRF and pharma can derive from a partnership. Ms. DeRome discussed the ways MMRF partners with industry; which are detailed below.

Benefits for MMRF (with support from industry):

- Grant funding to support young investigator grant programs
- Grant funding to support patient/caregiver and clinical (CME) education
- Grant funding to support several research roundtables yearly
- Clinical trial support (12 year, $40 million longitudinal CoMMpass study)
- Support and collaboration for translational research projects
- Support and collaboration for Phase 1 and 2 clinical trials in MMRF's clinical consortium

Benefits for industry:

- Significant ROI

MMRF-Industry Partnerships also result in significant ROI for industry as detailed in the examples below.

MMRF's CoMMpass Trial is a $40 million study—in partnership with Amgen, Bristol-Myers Squibb, Takeda, and Janssen—of 1000+ patients over 8 years. The pharma partners finance half of the cost and data are freely available to researchers at nonprofit institutions. The ROI for pharma partners is:

- First and best access to CoMMpass data (6 month embargo on data; during this time the newest data is available only to our pharma partners; release of data to non-profit researchers occurs when the embargo ends)
- Yearly meetings representatives from nonprofit, academic and pharma organizations (CoMMpass Data Jamboree) to brainstorm on new analyses of data and discuss collaboration on new studies.

Another partnership is the MMRC (Multiple Myeloma Research Consortium). The consortium, founded in 2004, consists of 22 leading academic clinical sites. Phase 1 and Phase 2 clinical trials (both ISTs and CSTs) of promising drug candidates are run through the MMRC. To date there are 71 trials, jointly funded by MMRF and pharma, of 36 compounds. The MMRF/pharma partnership offers fast trial start-up, fast patient recruitment, and access to key opinion leaders for trial proposals.

Through MMRF Translational Initiatives, MMRF initiates and guides collaborations between pharma partners and academic labs to test new compounds using banked patient samples and in novel multiple myeloma cell and animal models.

Additional points raised in the ensuing discussion:

- Nonprofit medical research funders know the disease of interest and often can provide pharma with an accurate snapshot of patient population (where they are, exclusive criteria, etc).
- Nonprofits have access to patients that industry needs for clinical trials.
- Nonprofits can facilitate connections with pharma and help establish personal relationship with pharma representatives. For example, scientific meetings are a great place to meet – and provide opportunities for funders to approach the chief scientific officer at a pharma's orphan disease unit, for example.
- For early career scientists, if a foundation knows industry is interested in an early research focus, it can bring them together.
- To facilitate recruitment for clinical trials, funders can open up multiple avenues to engage patients and alert them to clinical trial opportunities. In addition a research coordinator could be more fully engaged in the process (more "present") than a physician. Monetary incentive to centers is also a strategy.

HRA Action Items:
Continue to explore synergisms between foundations and industry in webinars or additional meeting sessions. There might be a need to publicize the benefits of these relationships to patient groups (and the general public?).
There was a recent Medscape article which called out several HRA Members and posited that that these relationships "were not in the patient's best interests." HRA members listed might want to contact the author to begin a dialogue.
http://www.medscape.com/viewarticle/871964

SESSION 5: Mainstream Media Distorting Science – and What as Funders Can We Do About It?

Speaker: Paula Waters
Executive Vice President | Health Chicago
Talk title: Mainstream Media Are Distorting Science. What Can Funders Do About It?

Same data, opposite conclusions to TauRx Study presented at the Alzheimer's Association International Conference (AAIC) 2016:

- Wall Street Journal: "Experimental Alzheimer's Drug Fails in Clinical Trial"
- The Telegraph: "Breakthrough as scientists create first drug to halt Alzheimer's disease"

The decline in number of reporters in mainstream media has resulted in fewer special interest reporters. The internet has become a prominent news source and has created a new definition of "journalist."

- Bloggers
- Biased websites
- Tweeters who re-tweet incorrect information, spreading it further
- Sponsored content taken as news (e.g., "5 early signs of a heart attack," "always eat these foods")
- Headlines are written to produce clicks
- Google tops media sources in trust
- Entertainment is masked as credible advice (e.g., Dr. Oz); reality TV has become "reality science."

What does this mean for us?

- Do not assume what is clear to scientists will be clear to reporters
- Provide content for media that is pre-digested and ready for online use
- Put in the time to pre-brief media and others who will be likely to comment
- Recognize that *newswire* stories are likely to be printed and read on the news and invest time in these reporters (e.g. AP, Reuters, Bloomberg, Dow Jones, HealthDay)

Successful Strategies:
Prepare assets (communications strategy) in advance

- Messages and key supporting points
  - Summary of the research
  - Core take-away points
  - Questions the research does not answer
  - Resist the impulse to be too detailed
- Identify key audiences you want to get the information directly and the media that reach them
  - Donors and potential funders
  - Policy makers and analysts
  - Other researchers
  - Patients, advocates and the general public
- People (Decide who will speak for the data)

    - Investigator(s)
    - Representative from the funding organization
    - Validators and endorsers (academics and patient advocacy/disease-related associations)
    - Give them training or at least practice on messages and techniques.
- Media monitoring mechanisms
    - Google alerts are not good enough, - need good monitoring to enable quick pivoting to correct errors)
- Media assets
    - press release
    - tweets
    - infographic illustrating key finding or findings
    - YouTube interview with the investigator
    - Fact sheet on the disease and unmet need addressed by research
    - Fact sheet on you as a funder
    - Bios of the researchers

Important: In the press release, start with the conclusion and then summarize the proof points. Make the press release succinct so reporters can understand. The headline needs to be clickable.

<u>Foster accuracy by making it easier for reporters</u>

- Provide content that's clear, concise, easy for media to drop into their coverage or share on social media.
- Prepare multimedia news releases—press kits that offer a one-stop content shop for time-pressed journalists. Infographics, photos and videos can be shared as-is by reporters, who are often hungry for social media-friendly visual content.

<u>Before the announcement (be ready to pre-brief reporters):</u>

- Identify 5 key media outlets, including the newswires like AP
- Offer a spokesperson for embargoed briefings
- Schedule meetings
- Go through the key points and offer media materials and interviews

<u>Day of announcement</u>

- Release or hold press conference (these have become much less frequent)
- If data are being presented at a meeting, work with the organizers to coordinate announcement
- Schedule availability to take media calls or give in-person interviews
- Pitch story to media who may not have attended/called in
- Follow up with key reporters to ask if they need anything else
- Monitor coverage

<u>After the announcement</u>

- Correct errors
- Reach out to media outlets to correct their coverage (they want to get it right)
- Check to see whether they have made the correction and call back if not
- Send emails to document your requests and follow-up

Speaker: Jessica Firger
Senior Health Writer | Newsweek
Talk title: Helping Journalists Make and Break News

Types of coverage:

- Proactive and reactive
- Single study stories (mostly embargoed)
- Hard news (new CDC guidelines, FDA drug approvals, NIH grant announcement, more cases of Zika)
- Analyses and explainers (Robin Williams and Lewy body dementia, why no one agrees on mammography guidelines)
- Features (patient/physician profiles, trends, controversies)

Problem 1: We have short attention spans.

- Pitches and story ideas look similar
- Pitches may seem too narrow
- Pitches seem too specialized
- Deadlines, deadlines
- Fickle editor

Tips:

- Know the publication's lead time
- Don't pitch too far in advance unless it's a monthly (especially for online publications)
- Issue gentle reminders
- Ask when to follow up
- Try to find a news hook
- Anticipate when journalists need experts
- Try to establish relationships with journalists
- Offer exclusives
- Offer other assets (video, photos, graphics)

Problem 2: We move on quickly.

- Relentless news cycle
- Reporters and editors get story fatigue
- Once a study is covered it may be over
- Publications priorities change

Tips:

- Strike while the iron is hot
- Know about embargoes ahead of time
- Remind journalists you have a useful expert for ongoing news
- Offer to help build a narrative (e.g., put reporter in contact with a patient or researcher)
- Explain why it matters by providing more background information
- Don't make promises you can't keep
- Just check in

Problem 3: Reporters are "not great at math."

- Questionable statistical significance (or data that should be questioned)
- Inconsistent data
- Limited time for number-crunching
- A single study's data doesn't exist in a vacuum

Tips:

- Contextualize findings of new study (does it reinforce other research findings?)
- Explain why the numbers matter
- Provide data in an easily digestible way
- Offer up researcher to explain the data (perhaps by email?)

Problem 4: Clicks and page views matter.

- Publication's style and editorial voice may favor hyperbole
- Keywords often determine copy
- A need to stand apart from competition
- Need to win the Google News race
- Need to get the story out quickly
- Placement doesn't drive a story's success; SEO (search engine optimization) & social media do

Tips:

- Produce press materials that reflect the way journalists write headlines.
- Put keywords in ***your*** headline
- Know that every nuance won't make it into coverage
- Anticipate the possible errors journalists may make
- Offer to share story on social media
- Encourage your experts to be on social media
- Keep an eye on Google News
- Prioritize ahead of time what is worth being angry about – do not be adversarial with media

How do journalists decide what's newsworthy? They consider what is breaking news and want to back up their reporting with data. Therefore, funders should be familiar with trending stories. They can be a trusted source to journalists on a topic. In addition, they look for interesting stories that no one else is telling. Funders can make it translatable to journalists to they can see the interest. It's also helpful to know what the journalist likes to cover.

Foundations often don't get mentioned in article. It's up to the investigator to talk about foundation's funding support to try to make sure the funder is mentioned in the article. Sometime, due to space constraints it is tough for journalists to mention funders in article.

Member Speakers

Speaker: David McKeon
Chief of Staff | New York Stem Cell Foundation
Talk title: Preparing for controversy and controlling the message

Prepare for controversy

- Anticipate the issues
- Brief staff members and board members
- Prepare and practice
- Develop talking points, FAQs, statements
- Conduct proactive outreach to colleagues to align the messaging
- Hold press conference to brief journalists

Control the message

Mr. McKeon recommended using terminology that correctly describes the science. It is also helpful to standardize the (accurate) language to be used by collaborators, funders, foundations, and patients. As an example of how research can be misconstrued, he offered examples of how news outlets covering a story on preventing mitochondrial disease fashioned their reporting around the "Nuclear genome transfer in human oocytes eliminates mitochondrial DNA variants." The NY Times Magazine Headline read: "The Brave New World of Three-Parent I.V.F."

Speaker: Alycia Halladay, PhD
Chief Science Officer | Autism Science Foundation
Talk title: Autism and vaccines

Dr. Halladay noted that reporting research on autism and vaccines can be tricky. She talked about the 1998 *Lancet* article that was later retracted. Unfortunately with regard to vaccine-autism debate, responses are reactionary. On public health issues, it is important to have clear and concise messages with no equivocality at all. Autism Science Foundation has formed partnerships with the CDC, NIH, and AAP, and trained researchers to strategize how to deal with press inquiries. She also commented on the importance of teaching researchers how to talk to the press and relate the key message.

Speaker: Krishna Knabe, MS
Director of Communications | Alzheimer's Drug Discovery Foundation
Talk title: Brain Health, Dementia, and the News

People are yearning for good news about Alzheimer's. An example is the following heading from the Fox News website: "Maple syrup isn't just delicious; it could also cure Alzheimer's disease." Another example from the Chicago Tribune: "12 herbs to boost your brain power."

CognitiveVitality.org is a a program of the Alzheimer's Drug Discovery Foundation developed to help the public interpret scientific findings on brain health. The program reviews all the current research

including meta-analysis or systematic reviews, randomized controlled trials, epidemiological studies, and in vitro and in vivo testing. Among the site's resources is an "evidence guide" to safety and effectiveness that translates research into easy-to-understand ratings. The database can be searched and filtered. Ratings results provide indicate strength of evidence used to support the claim, safety, and effectiveness. Ratings are reviewed by an external advisory group.

SESSION 6: Communicating the Impact of Our Funding

Speaker: Diana Shineman, PhD
Senior Director, Scientific Affairs | Alzheimer's Drug Discovery Foundation
Talk title: Communicating the Impact of Our Funding

Dr. Shineman introduced the audience to the "HRA Toolkit: Communicating Impact of Our Funding." The organizers of this session asked HRA member organizations to share specific examples ways they have successfully (and not so successfully) communicated research funding impact on advancing science and accelerating new treatment developments. The Toolkit compiles information about members' experiences, metrics of impact and interest, success stories, and lessons learned from not-so-successful efforts. There were 51 responses representing 40 organizations. The toolkit can also be accessed via the HRA website. Dr. Shineman's presentation summarized the important findings captured in the Toolkit.

The survey asked respondents about the quantitative outcomes used to track their funded research. The top five were publications (96.1%), patents/intellectual property/commercialization and licensing (82.4%), additional follow-on funding received from other organizations (76.5%), presentations (70.6%), and career advancement (66.7%).
A majority of respondents (72%) used external resources to assess funding impact.
Resources included:

- PlumX, NIH RePORTer, Scopus, SciVal, ÜberResearch, Lexis/Nexis,
- iMIS Database to track in-house funding and follow-on funding
- Qliksense (metrics platform provided through proposalCENTRAL)
- Customized database through SmartSimple
- WizeHive
- Faculty who have a special (research) interest in the topic
- External evaluator (often first or senior author on a scientific publication related to the analysis)
- Ad hoc academic advisory group

But there were many other resources used to assess funding impact including:

- Grantee progress reports
- On-line survey tools, Alumni network
- Data mining
- Grants systems
- Grantee CVs (career development)
- Pubmed alerts, web of science, Altmetrics
- Twitter
- Google analytics, google patent, google scholar, google alerts for grantees ("internet stalking")
- Data analysis in Excel, Prism, Systat

- Graphic designer for infographics
- Could the new gHRAsp system help survey a given research field?

Different metrics are used to communicate impact to the 3 most important target audiences (Donors, General Public, and Boards.)

Metrics of Interest to Donors:

- Drugs/treatments developed
- Science leading to treatments
- Donors like to see they are acknowledged in both scientific and general publications
- Increasing visibility of foundation/disease
- Impact to patient care

Metrics of Interest to the General Public:

- Drugs/treatments developed
- For case studies:
  video interviews
  "breakthrough results"
- What will help the patient (it's not about the scientist)
- Blogs
- Making the connection that funding research=cure

Metrics of Interest to Boards:

- Drugs/treatments developed
- Returns on investment
- IP
- Awards (i.e. Nobel Prize)
- Breadth of programs and funding
- Innovation/uniqueness of programmatic efforts
- Infographics
- Opinion from outside experts
- Comparison to similar programs
- Media coverage

Specific member organization Toolkit examples can be found on the HRA members-only website: https://www.healthra.org/members-only/bethesda/#measuring

Strategies that have NOT worked:

- Videos, newsletters—impact is not clear and high cost/time. Press releases, pitching stories more valuable
- Non-concrete examples (e.g., "could" lead to a treatment), conveying "technical" lingo
- Using metrics to engage with major "gifts" part of an organization—hard to speak the same language
- Data-driven outcomes don't help connect to donors/public—need a story
- Complex analyses (e.g., tying value to disease mechanism) is hard to translate — simpler is better
- Plum

- Text-heavy documents— infographics work better
- Communicating the incremental progress of science— people want breakthroughs
- Blogs—not widely read

Challenges remain:
- How to assess whether communication strategies are working
- Balancing effort and internal resources vs. impact (i.e., is it worth it??)

Speaker: Cecilia Arradaza
Head of Marketing, U.S. | Brunswick Group
Talk title: Communicating Impact of Funding

Ms. Arradaza offered the perspective of a marketing professional who has assisted nonprofits in communicating the impact of their funding.

Data from the Association of Fundraising Professionals' Fundraising Effectiveness Project (2016 survey): Every 100 donors gained was offset by 96 donors lost through attrition; every $100 gained was offset by $91 lost.

How can organizations make their programs stand out and communicate their achievements? The organizing principles of a successful communications strategy are:

Who you are, (mission and vision)
What you do, (programs and priorities)
How you talk about it, (communications tactics)
Should be aligned, (integrated and connected)
If you are to engage and convince. (progress and impact)

Communications is a core business imperative, not an "add-on." In being intentional about communications other important points to note are:
- Words should match your actions and you should always endeavor to do what you say
- Bring communications team together early and often
- Don't get caught up in analytics—pay attention to the things that matter
- Everything you do—or don't do—communicates
- Leading is communicating; you can't separate communications from leadership

Bring to life what you do:
- Headline: Should be compelling, with a concise point of view
- Facts: Present data that instills emotion and ignite action
- Anecdotes: Bring facts to life. Make it relatable. Communicate through simple stories, photos, images (teasers to get people to access more detail)
- Bottom Line: Call-to-action

Create a style guide for how to communicate about your organization and its mission. Decide how you want to talk about your work (e.g., decide to not talk about cures for autism, but talk about treatment instead).

For meaningful metrics, measure tactics against key goals and objectives. Communications is an iterative process, each outcome informing future actions.

Tactics matter: social media (real-time engagement), traditional media (proactive outreach), push mechanisms (newsletter, annual report), and external platforms (speaking at conferences). Nevertheless, the quality of the communication is better than the quantity. Do one thing and do it well.

Seven trends to consider:

- Business pressure changing media (use of new media growing, radical new revenue models, journalists doing more with less)
- Perishable content (e.g., 1 in 3 visitors spend less than 15 seconds reading articles they land on)
- Dominance of visual content (50x easier to get a video on the first page of Google)
- Algorithms are the new editorial (news stories written and published by an automated system)
- Death of organic reach (it will become more and more rare for people to seek out information)
- The second screen in the board room (e.g., executives now bring "the office" with them)
- Digital comes of age (you have to be where people are—send your research/messages through mobile devices)

Measurement sophistication is starting to prove its value. Predictive communication (from message testing to online behaviors) allows hypertargeting of messages.

Measurement Matters: The key is to measure tactics against key goals and objectives.
State of the Science: Have your programs changed the state of the science around the disease?
Patient Engagement: How well do you know the needs and expectations of your patient population and what have you done to address them?
Scientific Community: How have you engaged the best and brightest? Have you brought in new collaborations and allowed different disciplines to converge?

Each output brings about changes in outcomes – articulate them.

Integrated Evaluation Framework, developed by AMEC (Association for the Measurement and Evaluation of Communication), is an online tool. http://amecorg.com/amecframework/

HRA Action Items:
Explore the potential usefulness of the Integrated Evaluation Framework.

SESSION 7: Interactions with National Center for Advancing Translational Sciences (NCATS)

Speaker: Christopher P. Austin, MD
Director | NCATS | NIH
Talk Title: Catalyzing Translational Innovation

Dr. Austin reviewed NCATS' approach to accelerating transitional science and how the center works with foundations and patient advocacy organizations to minimize risk.

The NCATS Mission: To catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

Treatment of disease has not kept up with scientific discovery. There are about 5,500 human conditions with a known molecular basis (a result of sequencing data becoming part of public databases) but only 500 of these conditions have treatments. The number of FDA-approved drugs has halved roughly every nine years since 1950, despite the technology-driven changes in scientific discovery (e.g., genomic productivity, computers). It takes about 15 years to test new drugs, then another 15 years to have new drugs adopted by the population. Dr. Austin noted, "We look at the current state of science as patients do. We are impatient… not satisfied with the progress."

Fundamental science has advanced unprecedentedly, but health outcomes have not kept up due to:

- Poor transition of basic or clinical observations into interventions that tangibly improve human health
- Drug/device/diagnostic development expensive and failure-prone
- Clinical trials system inefficient
- Poor adoption of demonstrably useful interventions

NCATS was created to catalyze the development of innovative methods and technologies for treatment that can be applied to all diseases and improve the translational process so these new treatments can be delivered more quickly. NCATS collaborates with scientists from NIH, academic research institutions, funders, industry, and with patient advocacy organizations. Patient advocacy groups are bringing an urgency and focus to collaborations with industry. Patient advocates have "the moral authority" and it is motivating for scientists to interact with them.

Definition of Translation: Translation is the process of turning observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public - from diagnostics and therapeutics to medical procedures and behavioral changes.

Definition of Translational Science: Translational Science is the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process.

NCATS studies translation as a scientific and organizational problem.

Scientific translational problems on NCATS' to do list:

- Predictive toxicology
- Predictive efficacy
- Derisking "undruggable" targets/untreatable diseases
- Data interoperability
- Biomarker qualification process
- Clinical trial networks
- Patient recruitment
- Electronic Health Records for research

- Harmonized IRBs
- Clinical diagnostic criteria
- Clinical outcome criteria (e.g., PROs)
- Adaptive clinical trial designs
- Shortening time of intervention adoption
- Methods to better measure impact on health (or lack of)

Organizational translational problems on NCATS' to do list;

- Data transparency/release
- IP management
- Integration of project management
- Incentives/credit for team science
- Incentives/credit for health improvements
- Education/Training (scientific and cultural)
- Collaborative structures (public-private partnership models)
  Dr. Austin noted translation science is a "team" science. However, researchers who have been trained as basic scientists have been trained to and are used to working by themselves and might need to be re-trained to work in teams.

NCATS uses the "3D's" to increase effectiveness:
Develop
Demonstrate
Disseminate

Dr. Austin reviewed some of NCATS' clinical translation initiatives.

- Clinical Translational Science
  - Clinical and Translational Science Awards (CTSA)
  - Rare Disease Clinical Research Network
  - New Therapeutic Uses program
- Preclinical Translational Science
  - NCATS Chemical Genomics Center
  - Therapeutics for Rare and Neglected Diseases program
  - Bridging Interventional Development Gaps program
- Re-engineering Translational Sciences
  - Toxicology in the 21st Century
  - Microphysiological Systems (Tissue Chip) program
  - Office of Rare Diseases Research

Under the Division of Clinical Innovation, NCATSs sponsors the Clinical and Translational Science Awards (CTSA) Program which:

- Is a national consortium of medical research institutions
- Improves the way clinical and translational research is conducted nationwide
- Accelerates the research translation process
- Provides innovative training for clinical and translational researchers

These Collaborative Consortia for Translational Research form virtual teams, share information and tools, connect data systems, collaborate on multisite clinical trials, and integrate care and research. This enables CTSA's to have a great impact together.

NCATS/CTSA Partnerships with foundations include the University of Wisconsin–Madison partnership with JDRF on a pilot project to deliver family-centered self-management resources.

Under the Office of Rare Diseases Research NCATS sponsors several programs:

- Rare Diseases Clinical Research Network (RDCRN) *(also partners with foundations)*
  - 22 consortia at 250 institutions worldwide
  - Studying >200 diseases with 83 active protocols, and
  - More than 85 patient advocacy groups participating
- Genetic and Rare Disease Information Center (GARD)
- Scientific Conferences Program
  - Identify scientific opportunities and establish research agendas
  - Patients + NCATS + NIH ICs + FDA + Biopharma
- Global Rare Disease Registry (GRDR)
  - 15 GRDR patient registries + 19 existing registries
  - Ability to conduct cross-disease analysis and recruitment

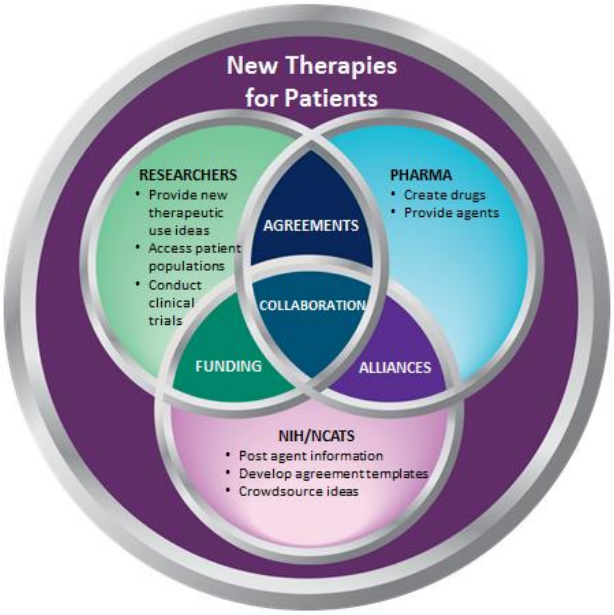
The Rare Disease (RD) Patient Toolkit Project:

- Provides a centralized web portal to online tools and resources that patient groups can readily access to accelerate their work
- Focus on tools/resources across the drug development process (Discovery & Pre-clinical, Trial readiness, Trials, Post-Approval Activities)
- "How-to" perspective, e.g. "How To Establish and Utilize a Patient Registry"

The RD Patient ToolKit is being developed through community engagement.

- Working groups that represent diverse rare disease stakeholder community
- Conducting landscape analysis of current tools and resources for all phases of drug development
- Gaps identified will be filled with new tool development
- Prototype demonstration/dissemination meeting Spring 2017

The New Therapeutic Uses Program:



NCATS also advances clinical translational science through its New Therapeutic Uses program, in which researchers at academic research institutions collaborate with pharma, and NCATS' Preclinical Translational Science program. This program aims to repurpose the ~4 late-stage investigational drugs available for new indications finding for every 1 drug approved.

There were 9 projects in 8 diseases funded in Round 1.
Translational Innovation Success Measures:

- Does use of template agreements speed negotiation time?
- Does crowdsourcing of indications generate new ideas?
- Do studies result in new indications/approvals?

Another example of NCATS' work with patient advocacy organizations is the Children Tumor Foundation Collaboration.
PIs: Annette Bakker (CTF), Jaishri Blakeley (JHU), Marc Ferrer (NCATS)
Disease focus: Neurofibromatosis 2 (NF2), characterized by multiple tumors on cranial and spinal nerves, and other lesions of the brain and spinal cord.
Goal: Discover new single drug and drug combination treatments for NF2.
Scope/Progress: CTF investigators (Synodos collaborative project funded by CTF) provided NCATS with NF2 Schwannomas and Meningiomas that have been screened with the NCATS MIPE 4.0 oncology collection (1,913 compounds). Selected compounds are being screened in dose response matrices to discover synergistic combinations.

NCATS Therapeutics Development Programs:
Therapeutics for Rare and Neglected Diseases (TRND)
Bridging Interventional Development Gaps (BrIDGs)
These programs enable collaborations between NCATS labs that have preclinical drug development expertise and organizations with disease area/target expertise.

NCATS Tissue Chip Program:
Seeks to develop an in vitro platform that uses human tissues to evaluate the efficacy, safety and toxicity of promising therapies.

NCATS Trial Innovation Network:
Will optimize clinical trials enterprise to accelerate translation:

- Data-driven "learning clinical studies system" so trials can recruit more quickly, retain participants, finish on-time and on-budget, and produce impactful, high-quality data
- Leverage the talent, expertise & resources of the CTSA Program to transform clinical trials

Key components of the network, awarded in July 2016:

- Recruitment Innovation Center (RIC): develop and implement strategies to engage patients and communities in clinical trials
- Trial Innovation Centers (TICs): IRB, contracting, GCP training to improve efficiency and effectiveness of clinical studies

NCATS CTSA I-Corps Training Program (developed at the National Science Foundation):
An entrepreneurial immersion course aimed at providing teams with skills and strategies to reduce commercialization risk.

- NCATS is training new I-Corps educators at CTSA institutions who in turn can provide entrepreneurship training for other translational scientists
- NCATS provided supplements to active CTSA grants to participate in the I-Corps Train-the Trainer Program
- 10 CTSAs were awarded supplements and are participating in the pilot program
- Plan is to expand program to other CTSAs utilizing feedback and learnings from pilot program

The NCATS portfolio is unique in that a significant number of inventions relate to new therapeutic molecules and novel processes, and inventions are much more advanced compared with other NIH centers. In addition, there is a high percentage of jointly owned inventions, which reflects the culture of NCATS aimed at using collaborations, alliances and partnerships to enhance positive outcomes and new cures.

HRA Action Items:
Identify a liaison in the NCATS and together explore partnerships and collaborations, and other ways HRA and NCATs can work together.

SESSION 8: Scientific Session

Speaker: James Richardson, PhD
Deputy Chief Preclinical Translational Research Program Officer | Foundation Fighting Blindness
Talk title: Translational Science: From Bench to Clinic (and beyond)

Early funding from non-profits is critical to the creation of new therapies. Attracting funding from government and non-government sources depends on lessons learned:

- Translation to clinical studies is slow and costly–need to educate investigators
- Lack of clarity on how to get to clinic
    - Lack of understanding of quality, regulatory issues
    - When/how to engage/manage CROs
    - Missing key aspects in early development (formulation, etc.)
    - Disconnect between theoretical therapy and clinical practice
- Projects where we provided independent consulting did better
- Oversight of integrated activities requires active project management
- Funding translational activities without supplying expertise leads to waste of scarce resources

Investigators need:

- CMC Support
- Pharm/Tox Support
- Regulatory Support
- Project Management Support
- Clinical Support

No one approach to managing translational activities works for all diseases, products. Strategies to reduce risk include:

- GAP analysis to identify and mitigate risks

- Product development planning (PDP) and Target Product Profile (TPP)
- Learn from others' mistakes and manage expectations of team members
    - Invest in expertise (regulatory and "Chemistry, Manufacturing, and Controls" or CMC) as early as possible
- Outsource carefully, with appropriate oversight (compliance audit, quality review by sponsor)

Target Product Profile: This is a useful tool for planning research and managing development activities. It identifies the characteristics of the marketed product and can help stakeholders focus on goals and understand the end results of development efforts. It is a living document that changes as new information is added.

FDA Guidance:
https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080593.pdf

Product Development Planning: A PDP is a tool for assessing and planning the development path (road map). It includes an assessment of the expertise found in the investigator's lab. It contains an intellectual property assessment and an assessment of feasibility. It can be used by investigators to obtain funding and establish pipeline priorities and future funding needs. It is a living document, with iterative review/milestones.

Speaker: Sue Washer, MBA
President and CEO | AGTC
Talk title: Visionary Science for Life-Changing Cures

AGTC is developing genetic therapies to treat patients with inherited diseases. Treatments are designed to meet the needs of each specific genetic disorder. AGTC's most advanced gene therapy programs are designed to restore visual function in patients with rare blinding diseases.

AGTC has more than 100 patents and patent applications protecting candidate genes, vector capsids, manufacturing and delivery. Ms. Washer reviewed the gene therapy development pipeline (some therapies are in partnership with Biogen, others are AGTC-owned) which includes multiple gene therapy programs.

AGTC focuses on rare blinding diseases because of the unmet need. In addition, preclinical data supports safety and efficacy and well-defined clinical endpoints. In addition, there is significant opportunity to expand: 290 genetic causes of blindness and more than 65 genetic causes of deafness mapped to a single locus.

A clinical study is under way on treatment for X-linked Retinoschisis (XLRS) – a disease causing poor vision caused by missing structural protein and for which there is currently no treatment. Enrollment in a natural history study is complete and a Phase 1/2 clinical study is active at 7 centers in the U.S. But to arrive at this point FFB played important a roll in funding early academic research, design and screening of a gene therapy vector, and pre-clinical safety studies. FFB was critical to generating the early data and the AGTC partnership with FFB to design/screen gene therapy vectors and conduct preclinical safety studies was critical to accelerating the path to the clinic.

For companies, partnering with patient organizations has numerous benefits. The first money in often gets the key first data and later stage partnerships often include a payback of investment if the product is commercialized. Patient foundations confer credibility, provide access to scientists and key opinion leaders, and provide access to patients to obtain their input. Combining funding and areas of expertise with patient organizations is a strategy for success.

Getting clean, solid data at the beginning will lead to treatment development costing less, and it gets easier to raise funding the further along the pipeline you go.

By "de-risking" the technology (e.g., gene therapy) for companies, it could be possible to make smaller target patient populations more attractive. In addition, efficiencies can occur with a suite of programs developed around the same cell type.