Appropriations Outlook

STEP 1: White House OMB coordinates with federal agencies to formulate the President’s budget proposal.

STEP 2: Congressional appropriations committees consider President’s proposal & prepare legislation.

STEP 3: Congress reconciles & finalizes appropriations legislation & sends to the President.

STEP 4: President signs the appropriations bill into law making funds available for NIH & NCI.

FY 2018

FY 2019
### RPG Pool Trends

<table>
<thead>
<tr>
<th></th>
<th>FY2013</th>
<th>FY2014</th>
<th>FY2015</th>
<th>FY2016</th>
<th>FY2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of R01</td>
<td>4003</td>
<td>3847</td>
<td>4550</td>
<td>4758</td>
<td>5263</td>
</tr>
<tr>
<td>Applications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of R01 Awards</td>
<td>582</td>
<td>578</td>
<td>623</td>
<td>650</td>
<td>650</td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>15%</td>
<td>15%</td>
<td>14%</td>
<td>14%</td>
<td>12%</td>
</tr>
<tr>
<td>Non-competing</td>
<td>94%</td>
<td>97%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>support (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total RPG ($B)</td>
<td>1.854</td>
<td>1.858</td>
<td>1.927</td>
<td>1.967</td>
<td>2.070</td>
</tr>
</tbody>
</table>

**FY** stands for Federal Year.
Intergovernmental Affairs
Collaborating with FDA and CMS

Scott Gottlieb
Commissioner of FDA

- Oncology Center of Excellence
- Joint Training
- Data Sharing
- Compliance advice on cell manufacture

Seema Verma
Director, CMS

- Help with NGS coverage decision
- Data Sharing
- Discussions over enhanced coverage of clinical trials
Collaborating with DoD and VA
Interactions with HHS

Alex M. Azar II
Secretary, HHS

Eric D. Hargan
Deputy Secretary, HHS

Admiral Brett P. Giroir, M.D.
Assistant Secretary for Health
Congressional Outreach
Promoting Value, Affordability, and Innovation in Cancer Drug Treatment

A Report to the President of the United States from the President’s Cancer Panel
Updates
NCI recognizes that Early Stage Investigators (ESI) face challenges. In addition to increased ESI payline, NCI is announcing its new use of the MERIT Award in 2018. The award gives eligible investigators applying for first R01 the opportunity to obtain up to seven years of grant funding (5+2). This will provide critical time for ESIs to launch their careers and become more established before attempting renewal.
Sample questions

1. Balance of functions for CGH (representational vs. research)?
2. Portfolio analysis?
3. How to set priorities for NCI given the tremendous international burden of cancer?
Sample questions

1. Are award sizes for the different phases of funding for SBIR/STTR appropriate?
2. How to improve review?
3. What resources in addition to funding should SBIR provide?
4. How to speed delivery of funds to small companies?
Informatics Working Group

- Provide input into the role of the CBIIT director, focusing particularly on whether the duties of a chief information officer should be separate.
- Advise on expanding funding opportunities for data science and bioinformatics research across the NCI research portfolio and building a cancer-focused data science and bioinformatics workforce.
- Provide guidance for improving data sharing to maximize the impact of cancer research on patients.

Informatics

- Mia Levy, MD
  Vanderbilt University
- Charles Sawyers, MD
  Memorial Sloan Kettering Cancer Center
Cancer Moonshot

April 2017

Cancer Moonshot Implementation Teams Developed Scientific Proposals

May 2017

NCI Scientific Program Leaders reviewed and recommended

June 2017

NCI Board of Scientific Advisors reviewed and recommended

Oct 2017 ongoing

FY 2018 FOAs Released
Cancer Moonshot FOAs

- Close to **50** Funding Opportunity Announcements to date and more to come
- **6** intramural initiatives
- Requirements related to data sharing and health disparities/underserved populations
Partnership for Accelerating Cancer Therapies (PACT)

National Cancer Institute - Division of Cancer Treatment & Diagnosis

Cancer Immune Monitoring Analysis Centers (CIMACs)
- Dana-Farber
- Stanford
- Mount Sinai
- MD Anderson

Cancer Immunologic Data Commons (CIDC)
- Dana-Farber Cancer Institute

Partners:
- AbbVie
- Amgen
- Boehringer Ingelheim
- BMS
- Celgene
- Genentech
- Gilead
- GSK
- Janssen
- Novartis
- Pfizer
- Sanofi
Two New Immunotherapy Networks

ADULT CANCERS

Immuno-Oncology Translational Network
(IOTN, U01)

PEDIATRIC CANCERS

Pediatric Immunotherapy Discovery and Development Network
(PIDDN, U54)
Projects enter the pipeline on a competitive basis at any stage of the pipeline. Since inception in 2009, NExT has received over 650 applications.
**NExT Pipeline**

**Discovery**
- Target Validation
- Exploratory Screen Development
- Screening/Hit-to-Lead
- Lead Development

**Preclinical Development**
- MCL1 Inhibitor
- Mutant IDH1 inhibitor

**Development**
- Clinical Trials
  - Phase 0
  - Phase 1
  - Phase 2
  - Phase 3

**Candidate Selection**
- DNMT1 Inhibitors (TdCyd)
- 11-1F4 mAb Amyloidosis
- Endoxifen
  - Mer Kinase Inhibitors
  - NIR Fluorophore
  - EGFR Panitumumab
  - LUM015

**Ingredients**
- Artemis Endonuclease inhibitor
- AAA ATPase p97 inhibitor
- Taspase1 inhibitor
- WDR5-MLL1 inhibitor
- LDHA inhibitor
- SHP2 inhibitor
- PHGDH inhibitor
- Endoxifen
- MCL1 Inhibitor
- Mutant IDH1 inhibitor
- EGFR Panitumumab
- LUM015

21
Mcl-1 Inhibitor Discovery by Fragment-Based Methods & Structure-Based Design

### Hit to Lead

- **Fragment hits**
  - $K_i = 131 \mu M$
  - $K_i = 60 \mu M$

### Lead Optimization

- **Structure guided fragment merging**
- **Binding interface Expansion**
- **Structure guided Tethering**
- **Med. Chem. Optimization**

### In vivo Optimization

- > 200,000x improvement in affinity for target

### Leads feature

- $K_i < 0.3 \text{ nM}$ to Mcl-1
- IC$_{50} < 300 \text{ nM}$ in multiple cancer cell-lines
- Target-based on-mechanism activity (Caspase activation, JC-1/BH3 profiling, co-IP, multiplex PD apoptosis assays)
- Good PK properties

### Likely candidate profile

- $K_i < 0.3 \text{ nM}$ to Mcl-1
- Cellular IC$_{50} < 100 \text{ nM}$
- Oral bioavailability
- Robust pharmacodynamic response

### Current work

- Focused on identification of clinical candidate by profiling compounds for *in vivo* efficacy and therapeutic window.
Cigarette use in the United States

- Never: 25%
- Former: <10 cpd
- Daily: ¼
- Non-daily: 25%

Lifelong consistent low-intensity smokers had increased risk of mortality vs. never-smokers

Inoue Choi et al, *JAMA Internal Medicine*, 2017
Rural Cancer Control Update

BACKGROUND

• 14-19% of the US population lives in non-metropolitan (rural) counties

• Notable challenges, compared to urban areas:
  • Higher poverty
  • Lower educational attainment
  • Higher proportion of elderly individuals
  • Lower access to health services
  • Higher rates of behavioral risk factors (tobacco use, obesity)
Rural Cancer Control Update Planning & Engagement Efforts

- Rural Cancer Control Workshop, Memphis, May 4-5, 2017
- HRSA/NCI/CDC Webinar, Aug 30, 2017
- Understanding Definitions of Rural/Rurality, Oct 27, 2017
- National Academy Workshop on Small Populations, Jan 18-19, 2018
- Rural Health Policy Institute, Feb 6-8, 2018
- National Rural Health Assoc. Annual Meeting, May 8-11, 2018
Accelerating Research in Rural Cancer Control
Conference

May 30-31, 2018

Natcher Conference Center
National Institutes of Health | Bethesda, Maryland

Program Committee Chair: Robin Vanderpool, University of Kentucky
NCI-MATCH

Molecular Analysis for Therapy Choice
NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

- Precision medicine trial to explore treating patients based on the molecular profiles of their tumors
- 1,089 sites in U.S. across NCTN and NCORP
NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

Rare Variant Initiative:

• Patients with low frequency mutations (< 2%) where well qualified drugs/targets available

• Foundation Medicine, Caris Life Sciences, MDACC, MSKCC will notify treating physician at any of the MATCH sites when results of their NGS panel would make patient eligible for a MATCH treatment arm

• Results verified centrally by NCI-MATCH Oncomine® assay

• RFP from other NGS providers posted August 2017 and received January 2018 to broaden the base of patients available to enroll in precision oncology studies
### NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

<table>
<thead>
<tr>
<th>Time period</th>
<th># enrolled</th>
<th># first samples submitted</th>
<th># first sample fail</th>
<th># assay complete</th>
<th># assigned to Rx</th>
<th># enrolled on Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Pre Pause</td>
<td>794</td>
<td>739</td>
<td>116</td>
<td>645</td>
<td>54</td>
<td>27</td>
</tr>
<tr>
<td>Total Post Pause</td>
<td>5,602</td>
<td>5,222</td>
<td>428</td>
<td>4,913</td>
<td>938</td>
<td>662</td>
</tr>
<tr>
<td>Overall Total Screening Cohort</td>
<td>6,396</td>
<td>5,961</td>
<td>544</td>
<td>5,558</td>
<td>992</td>
<td>689</td>
</tr>
<tr>
<td>Total Outside Assay</td>
<td>104</td>
<td>59</td>
<td>3</td>
<td>102</td>
<td>88</td>
<td>71</td>
</tr>
</tbody>
</table>
First NCI-MATCH Efficacy Data: Nivolumab in MSI high cancers

• Median cycles 3.5 (range 1-13+ cycles)
• Median time to first response was 2.1 months (includes unconfirmed PRs)
• 6-Month PFS was 49% (95% CI: 32-67%)
• Median duration of response has not been reached (4-8+ months; 7/8 still under treatment at time of data cutoff)
• 11 patients remain on therapy at time of data cutoff
NCI-COG Pediatric MATCH
## Pediatric MATCH

### Active Therapeutic Arms

<table>
<thead>
<tr>
<th>Arm</th>
<th>Agent Class</th>
<th>aMOI Frequency</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>APEC1621 A</td>
<td>Pan-TRK inhibitor</td>
<td>2-3%</td>
<td>Larotrectinib (LOXO-101)</td>
</tr>
<tr>
<td>APEC1621 B</td>
<td>FGFR inhibitor</td>
<td>2-3%</td>
<td>Erdafitinb</td>
</tr>
<tr>
<td>APEC1621 C</td>
<td>EZH2 inhibitor</td>
<td>2-3%</td>
<td>Tazemetostat</td>
</tr>
<tr>
<td>APEC1621 D</td>
<td>PI3K/mTOR inhibitor</td>
<td>5-10%</td>
<td>LY 3023414</td>
</tr>
<tr>
<td>APEC 1621 E</td>
<td>MEK inhibitor</td>
<td>10-20%</td>
<td>Selumetinib</td>
</tr>
<tr>
<td>APEC 1621 F</td>
<td>ALK inhibitor</td>
<td>2-3%</td>
<td>Ensartinib</td>
</tr>
<tr>
<td>APEC 1621 G</td>
<td>BRAF inhibitor</td>
<td>5%</td>
<td>Vemurafenib</td>
</tr>
<tr>
<td>APEC 1621 H</td>
<td>PARP inhibitor</td>
<td>2-3%</td>
<td>Olaparib</td>
</tr>
</tbody>
</table>
Pediatric MATCH Enrollment

- First 131 patients:
  - 74 males, 57 females
  - Age 1-21, median age 12 yrs
- 35% patients AYA
- Tumor sequencing completed on 94 patients
- At least one patient has matched to each of the treatment arms

### Monthly Activity

<table>
<thead>
<tr>
<th>Month</th>
<th>Registration</th>
<th>Specimen Received</th>
<th>Assay Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017-07</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2017-08</td>
<td>7</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>2017-09</td>
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<td>2017-11</td>
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<tr>
<td>2017-12</td>
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<tr>
<td>2018-01</td>
<td>35</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>2018-02</td>
<td>25</td>
<td>20</td>
<td>23</td>
</tr>
</tbody>
</table>
National Cryo-EM Facility (NCEF)
FNLCR

• **Mission:** to address gap between need for cryo-EM and access to expensive instrumentation

• Opened in May 2017 with one Titan Krios microscope. Second will be operational in Fall 2018.

• Addition of third microscope in 2019 if demand continues to grow.

• Advisory committee provides oversight on a biannual basis.

• Over 70 cancer-related projects from 20 institutions across US have been completed; feedback has been very positive.

• First user publication has just appeared in *Nature Communications*. 
NCEF Usage Statistics

Cumulative Projects

- User projects
- Test/Maintenance projects

May, June, July, August, September, October, November, December, January, February, March

Frederick National Laboratory for Cancer Research
Envisioning Key Focus Areas – *In progress*

**We Must Always**
- ensure the health of the cancer research enterprise, and build our foundational knowledge.

**We Must Continue**
- to leverage investments, further advancing our understanding and translation of our knowledge.

**We Will**
- lead the nation’s efforts to develop new approaches, technologies, and applications to change the meaning of a cancer diagnosis.