

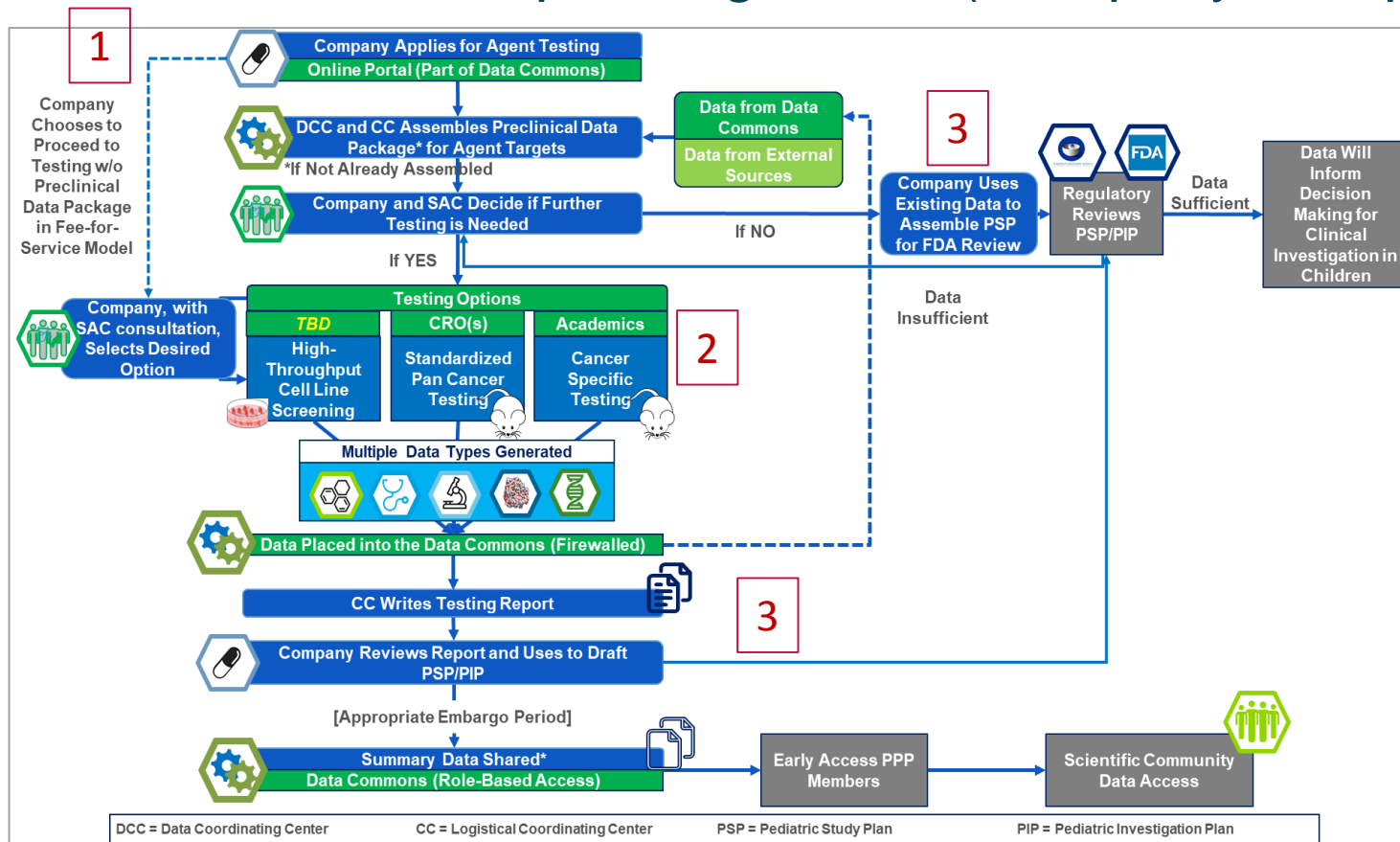
NCI and FNIH Pediatric Preclinical Testing Public-Private Partnership (PPTP3)

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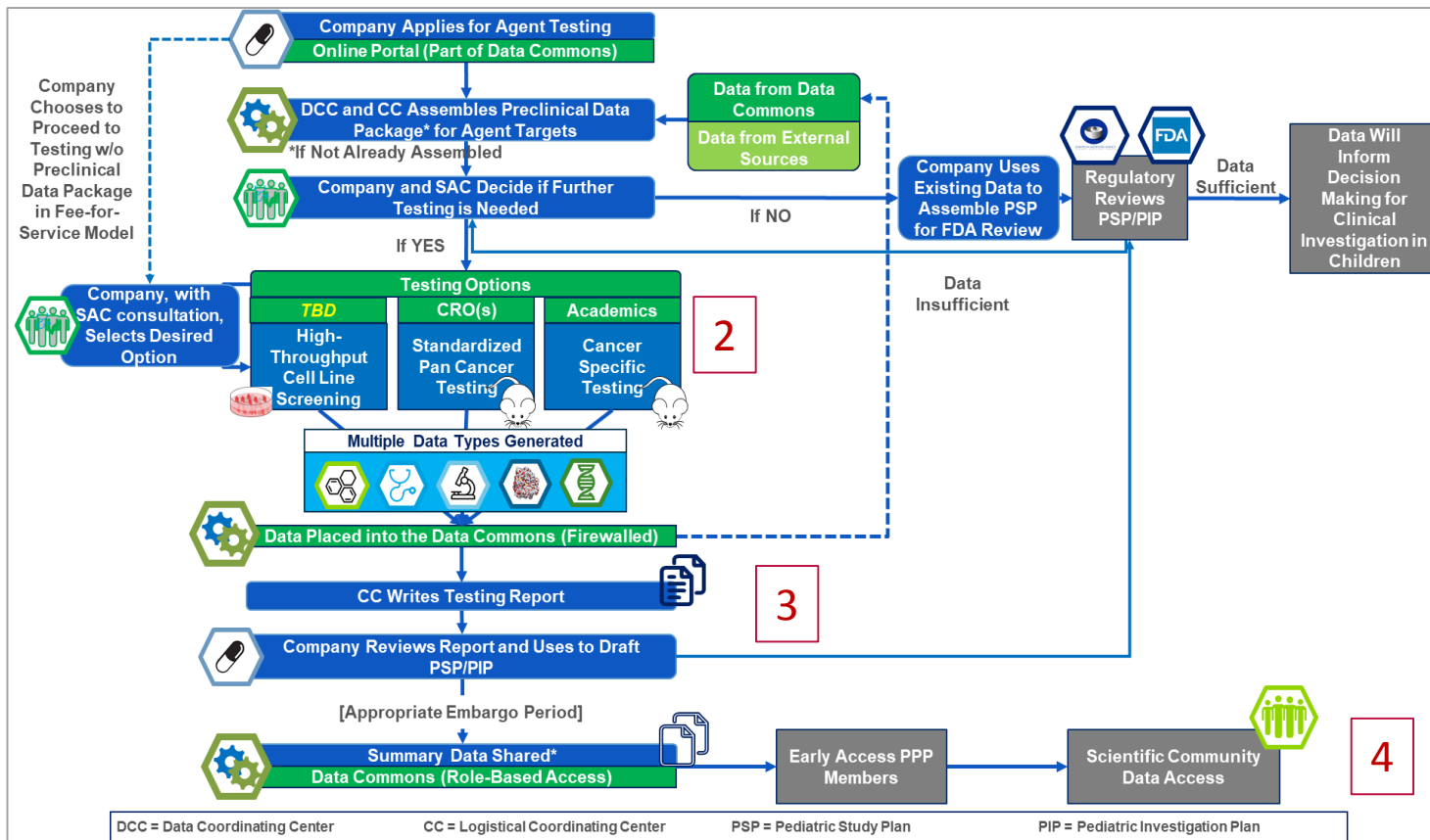
FNIH Preclinical Pediatric Oncology PPP

- Compliance with the Research to Accelerate Cures for Children (RACE) Act is the compelling ‘impending event’
 - RACE Act adds a new molecularly targeted pediatric investigation requirement for certain oncology medicine applications
 - Expansion of bandwidth for preclinical testing needed to inform evidence-driven prioritization decisions
- FNIH has established a partnership framework research agenda with all interested parties with White Paper released March, 2020
- Partnership includes Pharma, NCI, FDA, and Academia
- Partnership will involve both NIH funding as well as private sector funding

FNIH and NCI PPTP3 Operating Model (Company Perspective)

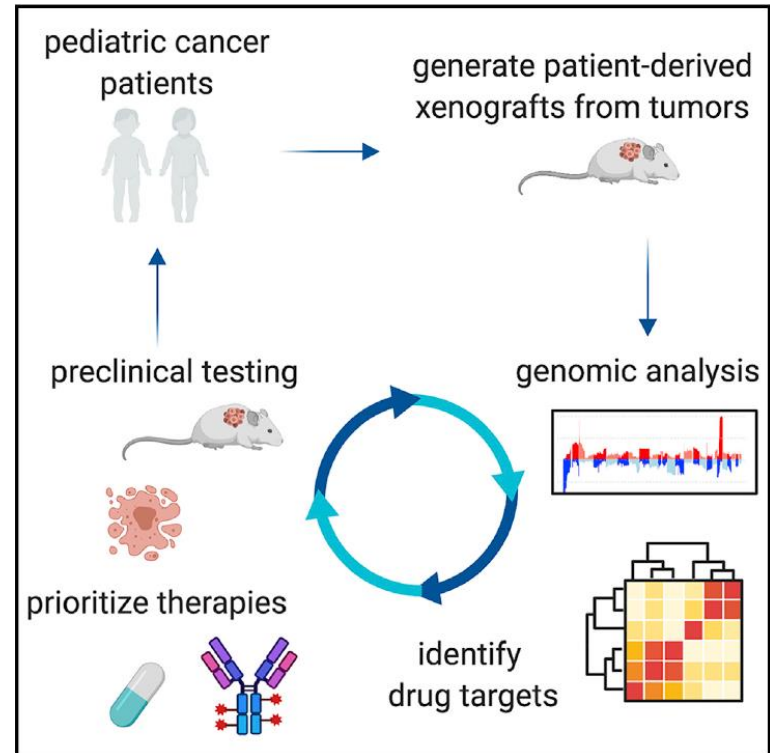


FNIH and NCI PPTP3 Operating Model (Academia Perspective)



PPTC Accomplishments – Genomic Characterization

- PPTC created an annotated genomic dataset of somatic oncogenic regulation across 37 distinct pediatric malignancies encompassing 261 patient-derived xenograft models
- Data available through PedcBioPortal <https://pedcbioportal.org/study?id=pptc#summary>
- Plans for additional genomic characterization of PDX and cell line models in FY2020



PPTC Accomplishments (examples)

- Validation of **DLL3** and **DLK1** as therapeutic targets for neuroblastoma
- Validation of **CD276** (B7-H3) as therapeutic target for multiple pediatric solid tumors
- Identification of **OBI-3424 (AKR1C3-activated alkylating agent)** as highly active for T-ALL → S1905 (NCT04315324)
- Identification of limited activity for **HDAC inhibitor** with SOC agents for RMS
- Identification of activity of **Aza-TdCyd** for pediatric ALL, but limited activity for TdCyd
- Identification of a **menin inhibitor** as highly active for ALL with MLL-rearrangement → NCT04065399 (SNDX-5613) (AACR 2020, Jerry McGeehan)
- Validation of **STEAP1** as an IO target for Ewing sarcoma using the extended half-life bispecific antibody AMG 509 (AACR 2020, Olivier Nolan-Stevaux)

Concept for NCI components of PPTP3

- PPTP3 In Vivo Testing Program
- PPTP3 Coordinating Center for the in Vivo Testing Program
- Future components:
 - High Throughput in Vitro Testing Program
 - Data Commons

NCI PPTP3 in Vivo Testing Program (inVivoTP)

- Plan for 8 awards for research programs for in vivo testing
- Open competition for in vivo testing sites with plan to encourage applications from new research teams
- Agnostic in terms of models (e.g., PDX in immunodeficient mice, murine genetic models engineered to reflect the characteristics of specific pediatric cancers, and murine syngeneic models)
- Potential disease areas of focus include: ALL, AML, neuroblastoma, osteosarcoma, rhabdomyosarcoma, Ewing sarcoma, renal and hepatic tumors, & CNS tumors

NCI PPTP3 in Vivo Testing Program (inVivoTP) - Continued

- Each team anticipated to test 8-10 agents per year
- Plan for broader utilization for single-mouse trial (SMT) design for agents for which tumor-regressing activity is sought
- Selection criteria to include:
 - Number and breadth of models proposed and the extent to which the proposed tumor panels faithfully recapitulate key biological characteristics of molecularly defined subtypes of specific pediatric cancers
 - Scientific leadership that the research team is anticipated to bring to the PPTP3 and its Scientific Advisory Committee
 - Ability to conduct testing with required throughput

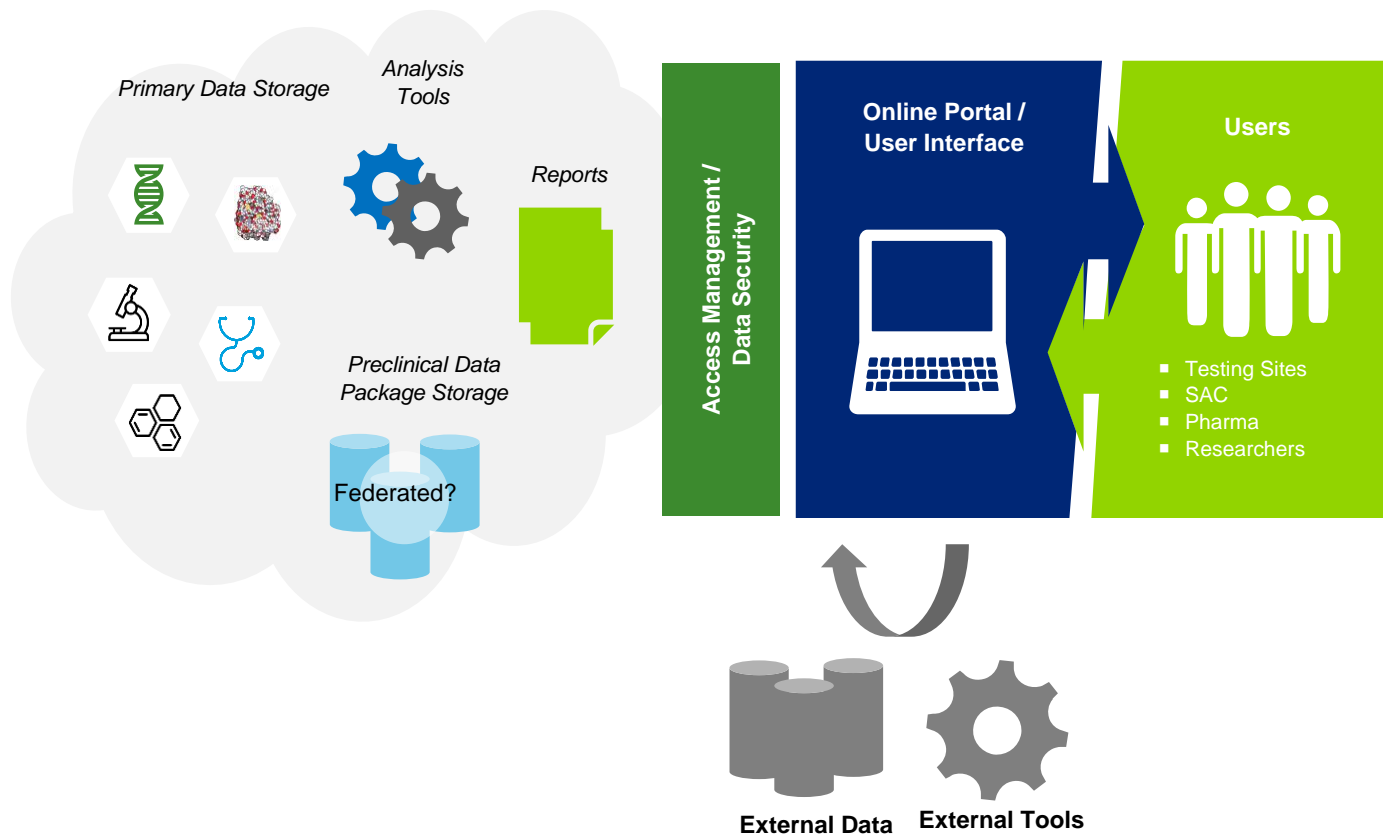
PPTP3 Coordinating Center

- Administrative management, logistics, & coordination of in vivo testing sites
- Establishment of a confidential and private project information site
- Development of quality assurance/quality control procedures
- Management of laboratory specimens and a biospecimen tracking system
- Coordination of shipments of compounds supplied by companies to testing sites
- Collection, analysis and storage of testing data from the testing sites
- Preparation of technical study reports for agents tested through the PPTP3
- Collaboration with research programs in developing, presenting, and publishing manuscripts

PPTP3 Data Commons (competed through future RFA)

- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for cell lines and PDX models from both PPTP3 research teams and from external research teams
- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for clinical specimens to establish as comprehensive a dataset as possible to facilitate robust comparisons to preclinical data
- To aggregate, store, and compare existing and new testing data both from PPTP3 research teams and from external research teams
- Provide analyses of genomic, proteomic and epigenomic data to support decision-making for preclinical evaluations and for clinical development plans
- Make data available in ways that are easily accessible by the research community

PPTP3 Data Commons



Timeline for Moving NCI Component of PPTP3 Forward

- June 2020 – Publication of RFA in NIH Guide
- Aug 2020 – Application receipt data
- Nov 2020 – Peer review
- April 2021 – Award

Budget

Component	Direct Costs Year 1	Total Costs Year 1
PPTP3 in vivo testing program (inVivoTP) (n=8)	\$3.2 million	\$5.1 million
PPTP3 Coordination Center	\$0.5 million	\$0.80 million
PPTP3 in vitro testing program (inVitroTP)	TBD	TBD
PPTP3 Data Commons	TBD	TBD
Total Combined	\$3.7 million	\$5.9 million



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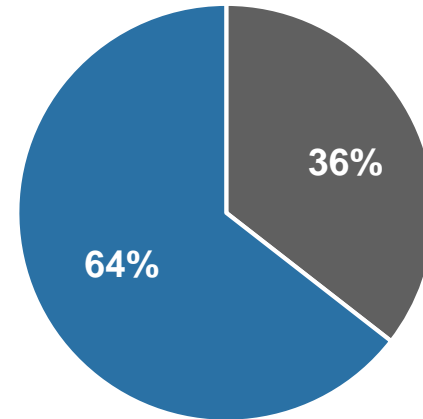
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Supplemental Slide

NCI Pediatric “Discovery Research”

- BSA Subcommittee asked for information on the funding committed by NCI to childhood cancer “Discovery Research”
- This research may make the discoveries required to address currently intractable diseases and therapeutic targets
- Estimate of extramural grants categorized as “Discovery Research” for FY19 is \$155,494,698, which corresponds to approximately 36% of total funding identified by RCDC as “childhood cancer” research
- Note: “Discovery Research” itself is not an RCDC category and that these figures are an estimate based upon an NCI portfolio analysis

Percentage of NCI Childhood Cancer Funding Represented by Extramural “Discovery Research”



■ Extramural "Discovery Research" ■ All Other