Table of Contents

About Project Impact & Defeat Pediatric Brain Tumor Research Collaborative ..........p.3

Speaker Bios ..............................................................................................................................................p.4

Pediatric Brain Tumor & High-Grade Glioma Stats, Facts & Figures .........................p.7

The “Defeat” Model & Pediatric Cancer Cure, LLC.................................................................p.9

The Defeat Pediatric Brain Tumor Research Collaborative Scientific Plan .................p.12

Media Contact Info & Spokepeople .................................................................................................p.16
“Project Impact: A Campaign to Defeat Pediatric Brain Tumors” is a new capital campaign that seeks to raise resources to fund the Defeat Pediatric Brain Tumors Research Collaborative. This Collaborative will establish an integrated consortium of leading pediatric neuro-oncologists in a ‘pre-clinical to clinical’ research program and is designed to accelerate the pace of discoveries and their translation into new treatments. The Defeat Pediatric Brain Tumor Research Collaborative is a unique approach that seeks to fundamentally change the way pediatric cancer research and drug discovery is funded and conducted, starting in the area of most urgent need: pediatric high-grade gliomas (including diffuse intrinsic pontine glioma, or DIPG), the deadliest pediatric cancers. Monies raised from the Project Impact capital campaign will go directly into the Collaborative, which has been in development with the leading minds in pediatric brain tumor and cancer research since 2014 and aims to develop the first-ever standard of care for pediatric high-grade gliomas.

The Defeat Pediatric Brain Tumor Research Collaborative scientific plan and Principal Investigators incorporate the best-of-the-best in the world of pediatric brain tumor research. The scientific plan divides the full scope of research work into multiple “Cores” that operate simultaneously and in concert with one-another to expedite progress, maximize synergies and expertise, and reduce duplication.

The structure of the Defeat Pediatric Brain Tumors Research Collaborative is built to facilitate collaboration between the Cores of investigators and enable easy sharing of data, information, and material. The Defeat Pediatric Brain Tumors Research Collaborative puts scientists to work in areas where they can leverage their expertise while coordinating across a multidisciplinary team. The scope of scientific endeavors in the Collaborative’s Cores cover the entire spectrum of preclinical research from basic science and target discovery to translational research and ultimately drug discovery. The preclinical research within the Defeat Pediatric Brain Tumor Research Collaborative will then collaborate with, and leverage, the clinical trial infrastructure developed by the Pacific Pediatric Neuro-Oncology Consortium for early phase clinical studies and reverse-translation.

The Defeat Pediatric Brain Tumor Research Collaborative is currently the only effort in the field of pediatric neuro-oncology tackling all of these areas at once in a multifaceted, coordinated, and integrated approach. This model for research was designed to convene the top minds in the field so they can work together, while utilizing their own areas of expertise to accelerate the translation of basic research into clinical candidates for human trials.

National Brain Tumor Society (NBTS) created a subsidiary, “Pediatric Cancer Cure, LLC,” to govern the Defeat Pediatric Brain Tumors Research Collaborative. Pediatric Cancer Cure, LLC is directed by a Managing Board and employs a Research Management Organization (RMO) to oversee the operational needs of the Collaborative. NBTS acts as the RMO for the Pediatric Cancer Cure LLC. As RMO, NBTS is responsible for administrative activities of the Collaborative, including negotiating agreements, managing the budget and finances, managing the IP portfolio, conducting marketing and communications, providing data and infrastructure support, coordinating meetings and research reviews, and driving fundraising efforts. These groups then work with a Strategic Scientific Advisory Council (SSAC), chaired by a Scientific Director, which provides oversight to the scientific projects evolving within each of the four Cores.

This initiative enables researchers to focus on the science and not administration nor other competing incentives that have traditionally slowed and impeded progress in pediatric cancer research.
Speaker Bios

David F. Arons, JD
Chief Executive Officer
National Brain Tumor Society

David Arons is the Chief Executive Officer of National Brain Tumor Society. He also serves as the National Brain Tumor Society’s Chief Public Policy and Advocacy Officer. He previously served as the Director of Government Relations for the American Cancer Society in Minnesota and was the Co-Founder and Co-Director of the Center for Lobbying in the Public Interest. He is the author of several books, including Power in Policy: A Funder’s Guide to Advocacy and Civic Participation, Strengthening Nonprofit Advocacy, and A Voice for Nonprofits. He serves as Chair of the National Cancer Institute’s (NCI) National Council of Research Advocates, as well as on the NCI’s Clinical Trials Advisory Committee. In 2016, Mr. Arons was named to the Blue Ribbon Panel of experts selected to help advise the National Cancer Moonshot, being led by Vice President Joe Biden.

Roger J. Packer, MD
Senior Vice President, Center for Neuroscience and Behavioral Medicine
Director, Gilbert Neurofibromatosis Institute
Director, Brain Tumor Institute
Children’s National Health System

Roger J. Packer, MD, is Senior Vice-President, Center for Neuroscience and Behavioral Medicine, Gilbert Distinguished Professor of Neurofibromatosis, and is Director of both the Gilbert Neurofibromatosis Institute and the Brain Tumor Institute of Children’s National Health System. Dr. Packer’s present academic titles include Professor of Neurology and Pediatrics at George Washington University and Clinical Professor of Neurosurgery at the University of Virginia in Charlottesville, Virginia.

Prior to coming to Children’s National, Dr. Packer was Director of the Brain Tumor Program and Professor of Neurology and Pediatrics at the Children’s Hospital of Philadelphia, University of Pennsylvania.

Throughout his career, Dr. Packer has been heavily involved in clinical and applied basic science research. His clinical research has touched on various aspects of adult and child neurology and neuro-oncology, including adult and pediatric brain tumors.

Presently, Dr. Packer is principal investigator at Children’s National for the Pediatric Brain Tumor Consortium (PBTC), formed under the auspices of the National Cancer Institute; Chairman of the PBTC Low-Grade Glioma Committee; Group Chair of the Neurofibromatosis Clinical Trials Consortium; is Chair of the Medulloblastoma Committee of the Children’s Oncology Group; P.I. for the Institution as part of the NINDS-sponsored Neuro-NEXT Clinical Trials Consortium; and P.I. of its NSADA award. He has worked closely with the NCI and NINDS, and has served on multiple committees setting the directions for neurologic clinical and basic science research for the future. He headed the efforts in pediatrics for the program review, held by the NCI and NINDS, for brain tumors.
Much of Dr. Packer’s clinical research has been translational in nature. He has been part of studies evaluating the molecular genetics of childhood and adult neurologic diseases and also has coordinated the first gene therapy study for children with malignant brain tumors in the U.S. The majority of the studies now being coordinated by Dr. Packer are studies evaluating innovative agents aimed at the molecular underpinnings of neurologic disease. He has published over 325 original articles and 300 reviews and chapters.

**Academic Appointment(s)**

- Professor of Pediatrics, George Washington University School of Medicine and Health Sciences
- Professor of Neurology, George Washington University School of Medicine and Health Sciences
- Professor of Neurosurgery, University of Virginia

**Suzanne Baker, PhD**

*Director, Brain Tumor Research Division*

*Co-Leader, Neurobiology & Brain Tumor Program*

*Endowed Chair in Brain Tumor Research*

*St. Jude Children’s Research Hospital*

Dr. Suzanne Baker is Director, Brain Tumor Research Division; Co-Leader, Neurobiology & Brain Tumor Program; and Endowed Chair in Brain Tumor Research at St. Jude Children’s Research Hospital. She is a leader in the field of pediatric neuro-oncology, and a lead investigator in the National Brain Tumor Society’s upcoming Defeat Pediatric High-Grade Glioma research program. At St Jude, she has directed her efforts towards understanding how disruption of key signaling pathways contributes to the development of high-grade gliomas, including diffuse intrinsic pontine glioma (DIPG) in children.

A generous grant from the National Brain Tumor Society helped to launch her research into DIPG, which suggested differences in the genetic changes driving DIPG compared to adult glioblastoma. This was confirmed when she co-discovered high frequency histone H3 mutations in DIPG and pediatric glioblastoma. These were the first histone mutations identified in human cancer, yielding new insights into disease pathogenesis of these devastating childhood brain tumors, and opening a new avenue to study how chromatin regulation contributes to cancer. Additional unexpected mutations in pediatric brain tumors co-discovered by Baker’s group further demonstrate unique connections between development and cancer that are also a focus of her ongoing research.

Throughout her career, Dr. Baker has focused on identifying genetic alterations driving human cancer and determining their functional consequences. As a graduate student, she was the first to identify TP53 as the tumor suppressor gene targeted by mutation in tumors with chromosome 17p deletions. This discovery sparked an explosion of research on TP53, which is now known as the most commonly mutated gene in human cancer. Additionally, in 2010, Suzanne Baker, PhD, and colleagues described a new paradigm they established as a systematic way to collect brain tumor tissue suitable for molecular analysis and applicable to children with diffuse intrinsic pontine glioma. When they evaluated the DNA and RNA integrity and found that most tumor samples collected were, indeed, suitable for genome-wide analysis. Previously, tumor samples had not been collected systematically for large cancer studies. Now, after analysis of these and other collected specimens, researchers have identified potential therapy targets, and opportunities exist to conduct studies using small molecule inhibitors.
Dr. Baker’s laboratory employs the latest technologies to identify the mutations that drive DIPG, and then incorporates the genomic discoveries into the design and analysis of relevant model systems for mechanistic studies and preclinical testing of new therapeutic agents.

**Cord Schlobohm, DMD**

Cord Schlobohm, DMD is the Vice Chair of the National Brain Tumor Society Board of Directors. He has been a practicing dentist in Bethesda, MD for over 25 years. Dr. Schlobohm became involved with the National Brain Tumor Society after losing his daughter to a brain tumor. He recently served as a patient advocate on the Peer-Reviewed Cancer Research Program of the Department of Defense’s Congressionally Directed Medical Research Programs, and has spoken on NPR on behalf of the National Brain Tumor Society.

**Danielle Leach, MPA**

*Sr. Director of Advocacy and Government Relations*

**St. Baldrick’s Foundation**

Mrs. Leach has more than 20 years of experience in the health nonprofit Industry, having held leadership positions at the American Cancer Society, Ovarian Cancer National Alliance, and Strang Cancer Prevention Center. Additionally, Mrs. Leach spent six years in Latin America, where she served as an international development consultant for American Cancer Society, CARE, Catholic Relief Services, United States Agency for International Development (USAID) and PLAN International, working on AIDS and cancer-related programming and resource development training.

In addition to her role at the St. Baldrick’s Foundation, Mrs. Leach currently serves as the Co-Chair of Alliance for Childhood Cancer, a national coalition tackling childhood cancer policy issues. She also served on Vice President Biden’s Cancer Moonshot, as part of the Pediatric Cancer Working Group.

Mrs. Leach is also a dedicated volunteer and advocate for cancer and children’s issues. She is the founder of the Mason Leach Superstar Fund at Children’s National Medical Center and American Childhood Cancer Organization, in memory of her son, Mason, who died of pediatric brain cancer in 2007. She runs a yearly event called Superstar Family Fun Day and the Mason Mile, which has raised over $130,000 and increased childhood cancer awareness in her community. She also trains residents and nurses in partnership with Children’s National Medical Center to highlight the needs of families, especially at the end of life. She holds a Master of Public Administration degree in Health Policy and Management from New York University.
Incidence/Prevalence/Diagnoses

• This year, more than 4,600 children and adolescents (0-19 years) will be diagnosed with a pediatric brain and central nervous system (CNS) tumor in the U.S.
• Overall, more than 28,000 children and adolescents (0-19 years) are estimated to be living with a pediatric brain and CNS tumor.
• Pediatric brain and CNS tumors (0-19 years) are the most prevalent form of pediatric cancer.
• Brain and CNS tumors are the most commonly occurring tumor across a majority of age groups 0–14 years.
• Overall, an estimated 5.57 of every 100,000 children and adolescents will be diagnosed with a brain tumor.

Pediatric High-Grade Glioma-Specific Stats & Facts

• Pediatric high-grade gliomas make up an estimated 11% of all pediatric brain tumors - roughly 500-600 new diagnoses each year.
• Pediatric high-grade gliomas are WHO Grade III and Grade IV gliomas, including: pediatric glioblastoma (GBM); glioma malignant, NOS; pediatric anaplastic astrocytoma; anaplastic oligodendroglioma; giant cell glioblastoma; gliosarcoma; and diffuse intrinsic pontine gliomas (DIPG).
• Diffuse intrinsic pontine gliomas represent around 80% of childhood brainstem tumors with 200-300 new cases diagnosed each year.

Prognoses, Survival Rates & Mortality

• Pediatric brain tumors are the deadliest form of cancer in all children under the age of 14 (0-14 years), recently surpassing leukemia.
• An estimated 47,632 years of potential life are lost each year due to pediatric brain and central nervous system tumors.
• It is estimated that more than 500 American children will die this year from a brain tumor.
• Five-year relative survival rates for children diagnosed with pediatric high-grade gliomas are only 15-30% on average.
• For DIPG, the diagnosis is “uniformly fatal” with most children only surviving 9 months - about the length of a typical school year - beyond diagnosis. The five-year survival rate for patients with DIPG is around only 1%.

Clinical Facts & Realities

• There has never been a drug developed specifically to treat pediatric brain tumors.
• Pediatric high-grade gliomas, specifically, do not even have a standard of care.
• The few treatments that are available to children with brain tumors were not developed with a child’s developing brain in mind, and can cause high toxicities in pediatric brain tumor patients.
• Patients that are able to survive their tumor, are often left with a life-time of physical, psychological, cog-
nitive, and other deficits as a results of their treatment
• In contrast to adult clinical trial participation, where it is estimated that less than 6% adults with cancer will enroll in a clinical trial, an estimated 60% of children with high-grade gliomas will enroll in a clinical trial. This number could potentially be even higher, but there is a significant lack of trials open for children with high-grade gliomas. For example, the largest clinical trial sponsor in pediatric neuro-oncology, the National Cancer Institute (NCI)-funded Children’s Oncology Group (COG) does not have a trial for newly diagnosed DIPG or other high-grade gliomas open at the moment (August 2016)
• For pediatric high-grade glioma, in addition to having no standard of care, there are very few treatment options for clinicians to even pull from. Despite extensive testing, chemotherapies have not been shown to provide significant clinical benefit to these children. No targeted therapy or immunotherapeutic has been approved - and very few have even been tested. Radiation is thus often the one and only treatment option for children, especially for those whose tumors cannot be surgically removed.
• A recent study showed that in children (0-14 years of age) most tumor types have seen relative survival rates improve over the last 30 years. However, survival rates of children with high-grade glioma trends toward worsening over the years, with 1-year survival rates of 59.3% from 1982–1986, 54.2% from 1997–2001, and 57.1% from 2007–2011; 5-year survival was 33.2% from 1982–1986 and 27.9% from 1997–2001, and 25.3% from 2007-2011; 10-year survival was 30.8% from 1982–1986 and 24.7% from 1997–2001 and an estimated 25.7% from 2007-2011.

R&D and Funding Facts & Realities

• The biopharmaceutical industry’s investment in pediatric brain tumor R&D is negligible, as industry largely has yet to see a favorable economic incentive to invest
• Small patient populations mean trials will need to include international sites, yet global regulatory bodies, chiefly the U.S. Food and Drug Administration and European Medicines Agency, have often conflicting regulations for pediatric clinical research
• Small patient populations have also created the current situation in which few, predictive preclinical models exist for drug screening. This means that industry is even hesitant to release their compounds for preclinical testing – or move them into early clinical studies – because preclinical data is not produced at adequate and requisite levels
• Government is thus by far the biggest investor in pediatric brain tumor R&D. Yet, NCI only devotes 4% of its extramural research budget to pediatrics. Leaders of COG say that their funding remains flat to decreased, if adjusted for inflation and does not even begin to cover the costs of the research that is performed.
The "Defeat" Model & Pediatric Cancer Cure, LLC – The Engine Behind the Defeat Pediatric Brain Tumor Research Collaborative

Facilitating New Approaches to a Deadly Disease

Decades of conventional nonprofit advocacy and grant-making has failed to move the needle for pediatric high-grade glioma patients. New approaches are critically needed so:

- Researchers desperate to exploit new breakthroughs don’t have to wait to get to work;
- Pharmaceutical companies don’t have barriers to evaluate new ways to treat our most vulnerable of patients;
- Children don’t continue to die or suffer life-long deficits due to lack of progress.

Pediatric Cancer Cure, LLC, a subsidiary of the National Brain Tumor Society (NBTS), seeks to fundamentally transform the way pediatric brain tumor and cancer research is funded and conducted. The “Defeat” model, on which the LLC is built, harnesses an infrastructure that facilitates global collaboration, data and information sharing, and puts scientists to work in areas where they can leverage their expertise while coordinating across a multidisciplinary team all pulling toward a singular goal. This allows scientists to stay focused on the laboratory instead of diverting their attention to chase funding.

Structure, Governance, and Accountability

NBTS’ “Defeat” program model is a unique business approach to science, which facilitates leadership and cooperation, as well as provides direction and coordination for the small but competitive world of neuro-oncology.

For our pediatric initiative, Pediatric Cancer Cure, LLC was established as subsidiary to govern the Defeat Pediatric Brain Tumor Research Collaborative. The LLC is directed by a Managing Board, and employs a Research Management Organization (RMO), led by a President, to serve as a central hub that oversees the operational needs of the Collaborative. NBTS’ Chief Executive Officer, David Arons, will serve as the President of Pediatric Cancer Cure, LLC, and the National Brain Tumor Society will serve as the RMO.

As RMO, NBTS is able to facilitate all administrative activities between the participating institutions and individuals in the Collaborative, such as negotiating agreements, managing the budget and finances, managing the joint IP portfolio, conducting marketing and communications, providing data and infrastructure support, coordinating meetings and research reviews, and driving fundraising efforts. The RMO and Managing Board then works with a Strategic Scientific Advisory Council (SSAC), chaired by Scientific Director Dr. Roger J. Packer of Children’s National Health System, which provides over-
sight to the scientific projects. The Scientific Director is responsible for managing the research portfolio, including developing a Strategic Research Plan, nominating individuals or entities to conduct or support research, and establishing and evaluating annual research milestones.

Luminaries in the world of pediatric neuro-oncology joining Dr. Packer on the Strategic Scientific Advisory Council include:

- **Susan Blaney, MD** – Deputy Director of the Texas Children’s Cancer and Hematology Centers; Executive Vice Chair, Department of Pediatrics, Baylor College of Medicine (BCM); Vice President, Clinical and Translational Research, BCM; and holds the Martha Ann and Harold M. Selzman, M.D. Endowed Chair in the Institute for Clinical and Translational Research at BCM; Vice Chair of the Children’s Oncology Group
- **Richard Gilbertson, MD, PhD** – Li Ka Shing Chair of Oncology and Director of the Cambridge Cancer Centre (England)
- **Scott Pomeroy, MD, PhD** – Neurologist-in-Chief and Chairman, Department of Neurology, Boston Children’s Hospital; Consultant, Pediatric Neuro-Oncology, Dana-Farber Cancer Institute; Bronson Crothers Professor of Neurology, Harvard Medical School
- **Raphaël Rousseau, MD, PhD** – Group Medical Director / Global Franchise Head, Pediatrics, Genentech, a member of the Roche Group
- **Robert Wechsler-Reya, PhD** – Director, Tumor Initiation and Maintenance Program, Sanford-Burnham Medical Research Institute

Philanthropic and patient advocacy organizations, foundations, and individuals may join Pediatric Cancer Cure, LLC as Partners, thereby providing additional financial investment and community engagement. Additionally, Founding Research Collaborators – representing investigators within the Collaborative – provide scientific expertise and institutional resources to support the research cores of the Collaborative. The St. Baldrick’s Foundation has already providing investment into the Collaborative to become its first strategic partner.

**The Power of the “Defeat” Model**

The “Defeat” model is defined by two major characteristics:

1) A collaborative scientific research structure that consists of multiple interrelated “Cores” that work on critical areas of research simultaneously and share data, information, and materials between them in real-time. The “Cores” design allows new findings in one area of the Collaborative to quickly move on to its next stage of research without barriers or typical delays. This significantly speeds the whole research process.

2) A business and research management model that facilitates all of the Collaborative’s operational and administrative needs so that researchers can spend more time in the lab and less time doing paperwork.

The “Defeat” approach is completely unique in its relationship to traditional research funding by nonprofits, which typically rely on a standard RFA grant-making process, where checks are distributed to individual labs that apply for grant funding.

The Defeat Pediatric Brain Tumors Research Collaborative’s adult counterpart, the Defeat GBM Research Collaborative, has shown proof-of-concept by accelerating the process from research discovery to advancing a clinical candidate for evaluation by at least one to two years.

**Benefits of the “Defeat” Model for Pediatric Brain Tumor Research**
• **Consensus Design:** The initiative was built based on input from all key stakeholders—researchers, industry, government, and nonprofits/advocates—to determine the real barriers to progress.

• **End-to-End Approach:** This is the only effort in this field ambitious enough to tackle the challenges from basic science to the clinic (pre-clinical to clinical), including powerful international collaborations and integration with leading clinical trial consortium, the Pacific Pediatric Neuro-Oncology Consortium (PNOC).

• **Best of the Best:** A team of top advisors helps identify and select the best, most qualified researchers from around the world to match with key projects within the Collaborative.

• **Power Creates Incentives:** With top labs from around the world working together, quality and well-powered data is produced at a level requisite for beginning first-in-human trials, which will help de-risk early entry of biopharmaceutical companies into pediatric brain tumor trials.

• **Contracts Not Grants:** Collaborative Agreements will be used with the institutions representing participating researchers within the Collaborative, as opposed to traditional grants. These agreements will enable researchers to more seamlessly share data and transfer materials among Cores. The agreements aim to allow NBTS to facilitate potential IP issues and biopharmaceutical industry engagement, so that researchers can spend more time in the lab.

• **Deep-funding:** By aiming to provide sustainable commitment to the Collaborative, researchers can focus on science, not grant applications nor other competing incentives.

• **No Overhead:** 100% of the funding goes to the researchers; NBTS does not pay for institution’s indirect costs.

• **Command-and-Control:** The world-leading experts making-up the SSAC, advising the management of Pediatric Cancer Cure LLC, help ensure that the Collaborative is on track and making optimal progress. Course corrections can be made quickly, and priorities can be shifted to capitalize on new findings.

In short, participating world-class researchers leverage their strengths and expertise, and NBTS, via Pediatric Cancer Cure LLC, provides the infrastructure to move the science forward.
The Defeat Pediatric Brain Tumors Research Collaborative: A Preclinical-to-Clinical Plan for Translating Science into Survival

The Defeat Pediatric Brain Tumors Research Collaborative is an audacious precision medicine-and consortium-based model for pediatric brain tumor research. The Collaborative connects world-class scientific and clinical investigators from across the globe through an infrastructure and research management platform that requires, as well as enables, easy sharing and transfer of data, information, and materials between “Cores” of research teams working synergistically on projects that encompass basic, translational, preclinical, and early clinical research. This model for research was designed to get the top minds in the field working together – yet in their own areas of expertise – and accelerate the translation of basic research into clinical candidates for human trials. The Collaborative will first tackle the area of most urgent, high-unmet medical need in pediatric brain tumors, and indeed across all pediatric cancers: pediatric high-grade gliomas (pHGG), including diffuse intrinsic pontine gliomas (DIPG).

Background and Scientific Rationale

Contrary to long-held assumptions, recent results from comprehensive molecular profiling and DNA sequencing studies have found that pHGGs are distinct from adult high-grade gliomas, despite looking the same under a microscope. In fact, this research has revealed alterations and mutations selective for pHGGs and never before seen in other human cancers.

Specifically, discoveries found that pHGGs are “epigenetic” disorders of the developing brain – “brain development gone wrong.” Epigenetic means alterations in the expression of genes that occur in cells that are not caused by changes in the DNA sequence. In the case of pHGGs, mutations have been found in a particular protein – called a histone – that helps wind and package the DNA in a cells’ nucleosome.

These discoveries have positioned the field of pediatric neuro-oncology to finally begin creating therapeutic strategies that are pHGG-specific, by targeting the epigenetic regulators and associated genetic alterations for precision medicine-based treatments.

But more work must be done to:

- Identify and further understand the impact that these epigenetic and other alterations have on the rest of cells’ functions;
- Identify and validate suitable diagnostic, prognostic, and predictive biomarkers;
- Generate and characterize a trustworthy platform of pHGG disease models (genetic mouse models and patient-derived xenografts) that confidently recapitulate the human disease;
- Use these models for preclinical drug screening; and
- Identify – both upfront and acquired – potential resistance mechanisms

These are the scientific areas that the Defeat Pediatric Brain Tumors Research Collaborative will address in concert with one another.

End-to-End Approach

The scope of scientific endeavor still needed covers the entire spectrum of preclinical research, from basic sci-
ence and target discovery to translational research and drug discovery.

The Defeat Pediatric Brain Tumors Research Collaborative is currently the only effort in the field of pediatric neuro-oncology that is taking on all of these areas at once in a multifaceted, coordinated, and integrated approach. In this way, duplication of research endeavors is reduced and synergies and expertise in the field is maximized.

The preclinical research within the Defeat Pediatric Brain Tumors Research Collaborative then aims to leverage and collaborative with the clinical trial infrastructure developed by the Pacific Pediatric Neuro-Oncology Consortium for early phase clinical studies and for reverse-translation, whereby human clinical data may inform and guide new discoveries and preclinical studies.

**Simultaneous, Not Sequential**

In addition to its end-to-end scope, the Defeat Pediatric Brain Tumors Research Collaborative will address the key areas of preclinical research (noted above) at the same time, with leading researchers from each particular area (target discovery/genomics/molecular biology; preclinical modeling; biomarker identification and validation; drug screening; and clinical trial operations) working in their zone of expertise simultaneously.

Benefits to this unique approach to conducting research are:

- The pace of translation is accelerated from discovery to drug screening, as all the facets of preclinical research are happening at once across multiple teams, instead in sequential order by individual labs and the “hand-off” of work to move findings from one Core to another will be more efficient and faster; and
- The expertise of multiple, leading pediatric brain tumor researchers is utilized in precisely their area of prowess, as no one lab has the materials, expertise, and experience to undertake all of these projects alone.

**Multiple Core Model**

To achieve the ambitious aims of the Defeat Pediatric Brain Tumors Research Collaborative, the scientific plan is to structure research projects into multiple, integrated “Core” nodes, all of which will closely collaborate to enable scientific translation:
• **Discovery Core (Molecular Diagnostics & Target Discovery)**
  o Led by Dr. Stefan Pfister, German Cancer Research Center
  o Seeks to “decode” the role histone mutations and other molecular alterations play in driving and maintaining proliferation of pHGG cells, as well as drug resistance, in order to identify drugable targets
  o Works in combination with the Biomarker Core to interrogate clinical samples obtained from patients to identify novel drug targets as well as stratify patients into multiple molecular subgroups for molecular-based therapies

• **Biomarker Core (Identification & Validation - Tissue & Serum)**
  o Led by Dr. Nada Jabado, Montreal Children’s Hospital
  o Seeks to identify and validate predictive biomarkers for pHGG in human tumor tissue samples that can help stratify patients for biomarker-informed treatments and trials, as well as to identify and validate biomarkers in body fluids that can be used as surrogate diagnostic, prognostic, and therapeutic tools (as many pHGGs are extremely difficult to biopsy)
  o Uses molecular profiling data and characterizations obtained from the Preclinical Modeling & Drug Screening and Discovery cores to develop companion diagnostics for the clinical setting

• **Preclinical Modeling & Drug Screening Core**
  o Led by Dr. Suzanne Baker, St. Jude Children’s Research Hospital
  o Seeks to extensively characterize the molecular features and in vivo and in vitro growth properties of models of pHGGs for drug screening and identify compounds that inhibit growth of pHGGs in large (thousands of compounds and drugs) unbiased screens
  o Works in combination with the Discovery Core to perform thorough characterization of clinical trial samples throughout the course of the Defeat Pediatric Brain Tumors Research Collaborative, in order to further delineate driver events and cooperating mutations in molecular subgroups.
  o Intends to identify top candidate compounds that demonstrate promising safety and efficacy in preclinical studies to advance to clinical studies

• **Smart Trials (N-of-1 clinical trials)**
  o Collaboration with the Pacific Pediatric Neuro-Oncology Consortium to treat pHGG patients in an N-of-1 clinical trial setting by matching individual patients to targeted investigational agents on the basis of the molecular profile of the patient’s tumor
  o To use what’s learned in the clinical setting and enable Cores to investigate patient tumor samples after treatment to identify biomarkers of response, potential resistance mechanisms/biomarkers, and design combination therapies (reverse translation) that will enter the “preclinical phase” for validation prior to clinical application

**Scientific Process**

The impressive collective expertise of members in this Collaborative covers tumor biology; model systems; genomic and epigenomic data generation and analysis; drug screening; histone biology and function; and clinical experience. Throughout the Collaborative, there will be cross-talk and cross-interactions between all team members and sharing of datasets, expertise and material. This remarkable joint effort – being led by top researchers in the field who have played roles in many of the seminal scientific studies to date in pHGG can lead to improved clinical trials and, ultimately, treatments for pediatric high-grade gliomas patients.

In the end, the Defeat Pediatric Brain Tumors Research Collaborative seeks to fundamentally transform the trajectory of the pediatric high-grade glioma research and clinical settings by creating:

• New and trusted preclinical models for testing that can more faithfully predict clinical efficacy in human patients and incentivize the pharmaceutical industry to provide compounds and agents to researchers, as well as launch more pediatric high-grade glioma trials;
• A research platform that creates a system of tested and validated compounds to feed phase 1 clinical trials;
• A collaborative research model that is scalable across the pediatric cancer spectrum and that discovers new knowledge applicable to the fight against all pediatric brain tumors; and
• A new standard of care that deploys effective drugs to dramatically extend the survival of children with high-grade gliomas.

Ultimately, this work aims not only to directly produce new candidates for clinical trials on its own, but also to create incentives for industry to take on increased R&D efforts in the pediatric brain tumor space, by establishing and illuminating an optimal preclinical-to-clinical research model which companies can follow.
Project Impact: A Campaign to Defeat Pediatric Brain Tumors

Media Contacts & Spokespersons Available

Media Contacts

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• Michael Antonellis, National Brain Tumor Society – mantonellis@braintumor.org, 617-393-2841
• Lisa Rivero, Feinstein Kean Healthcare – lisa.rivero@fkhealth.com, 617-761-6746

Spokespersons Available

• David Arons, JD - NBTS CEO – Chair of the National Cancer Institute’s National Council of Research Advocates; Member, Blue Ribbon Panel, National Cancer Moonshot Initiative; cancer/scientific policy expert

• Dr. Suzanne Baker, PhD – Director of the Brain Tumor Research Division, Co-Leader of the Neurobiology & Brain Tumor Program, and Endowed Chair in Brain Tumor Research at St. Jude Children’s Research Hospital; Principle Investigator within the Defeat Pediatric Brain Tumors Research Collaborative

• Dr. Ann Kingston, PhD – NBTS Director of Research & Scientific Policy (NBTS employee, in-house scientific expert; has degrees in biochem & immunology; experience in academic research, as well as in the pharmaceutical industry)

• Dr. Roger Packer, MD – Scientific Director of Defeat Pediatric Brain Tumor Research Collaborative; leading researcher/doctor/expert on pediatric brain tumors

• Raphaël Rousseau, MD, PhD – Group Medical Director / Global Franchise Head, Pediatrics, Genentech, a member of the Roche Group

• Cord Schlobohm – Vice Chair of the National Brain Tumor Society Board of Directors; lost daughter to pediatric high-grade glioma; recently served as a patient advocate on the Peer-Reviewed Cancer Research Program of the Department of Defense’s Congressionally Directed Medical Research Program.

• Danielle Leach – Senior Director of Advocacy & Government Relations, St. Baldrick’s Foundation; and mother of son who died of pediatric high-grade glioma

• More parents/families as needed

• Additional St. Baldrick’s Foundation Executives, as requested