Summary of Strategic Planning Meeting

The Children’s Tumor Foundation formulated a research strategic plan in 2006 and again in 2011. These plans have been instrumental in guiding CTF research initiatives over the past decade. The NF research landscape has evolved significantly since the last plan was formulated. There have been important technological advances, such as the availability of affordable whole genome sequencing and new approaches to development of model systems. Additional groups interested in funding NF research are now exploring research opportunities. The pharmaceutical industry has expressed interest in partnering in the development of therapies for relatively rare conditions like NF. Given these changes, and the need to periodically re-evaluate the CTF research portfolio, a strategic planning retreat was held at the Airlie Conference Center, September 20-21. This report summarizes the major conclusions from this retreat.

Principles

1. The Children’s Tumor Foundation (CTF) research program is focused on finding effective treatments that will prevent, reverse, or manage the complications of NF1, NF2, and schwannomatosis and improve the quality of life of those affected with these disorders. Its mission is summarized as “Drive Research. Expand Knowledge. Advance Care.”

2. The CTF been particularly effective as a convener of communities with an interest in NF, including patients, clinicians, researchers, and funders, and as a catalyst, though not always the sole or even the major funder, of research initiatives. CTF may not have the financial or scientific resources to singlehandedly advance the field, but no other group has the passion and focus on advancing treatments for NF that CTF has, and therefore CTF is the critical partner.

3. The CTF has played a major role in attracting young investigators to focus on NF; this role is particularly important at a time when research funding for young investigators is difficult to secure.

4. The efforts of the CTF are most effective if leveraged in partnership with other organizations, including the NIH, Department of Defense, other funding groups such as the Neurofibromatosis Therapeutic Acceleration Project and the FasterCures NF initiative, as well as the pharmaceutical and biotechnology industries, and coordinated with the FDA.

5. The CTF research agenda should be inspirational, yet must set priorities in light of available resources.

Accelerating Neurofibromatosis Research

1. **Identification of New Therapeutic Targets.** Major progress has been made in preclinical and clinical testing of drugs that target the Ras signaling pathway in NF1. The precise mechanisms whereby loss of NF gene function leads to the various features of NF1, NF2, and
schwannomatosis remains largely unknown, however. The overall function of the various gene products and their interactions with other cellular proteins are likewise mostly unknown. A better understanding of the pathway from loss of function of the NF genes to the development of tumors and other aspects of the NF phenotype will reveal additional therapeutic targets.

2. **Develop Innovative Therapeutic Approaches.** As the list of therapeutic targets increases, there will be an increasing need to perform robust preclinical studies, including the use of combinations of therapeutic agents. Moreover, there are emerging innovative approaches to drug discovery and development that could lead to entirely novel approaches to therapy at the level of the gene, the gene product, the cellular signaling pathway, and intercellular communications. The full armamentarium of drug development should be applied to the problem of treatment of NF, including both approaches that may be successful in the near future and others that may take much longer to bring to practicality. New model systems may be needed to expand the approach to preclinical testing.

3. **Develop Approaches to Early Diagnosis and Prediction of Specific Manifestations.** Patient care would be vastly improved if an individualized plan of surveillance for complications could be implemented. This would enable more prompt diagnosis for those with complications at a point where treatment might be more effective; it would also obviate the need for costly surveillance for those not at risk, significantly improving their quality of life. The full power of biomarkers, using technologies such as genomics and imaging, as well as more systematic study of patient outcomes and study of tissue specimens should be harnessed to this end.

**The CTF Opportunity**

The CTF should continuously monitor the neurofibromatosis research landscape and be prepared to change its allocation of resources to respond to the most pressing problems and take advantage of the most compelling opportunities. Major funding priorities are as follows:

1. The NF Conference is the focal point for exchange of ideas between clinicians, investigators, and patients interested in NF. As such, it is a flagship effort for CTF that should remain a priority.
2. CTF should maintain its commitment to funding of young investigators, who are a critical source of future talent to advance NF research.
3. The Synodos initiatives have been particularly effective in bringing together a diverse group of investigators to work on problems in NF. Additional RFAs should be issued to address specific research problems with the goal of identification of new therapeutic targets for all forms of NF.
4. The preclinical consortium plays a critical function in testing new therapeutic approaches, and will have an expanded role as new drug combinations are available for testing. It is unlikely that this role will be taken up by other funding entities, but there are major opportunities for development of funding partnerships, especially with the pharmaceutical industry, that should be pursued.
5. CTF is not able to fund major clinical trials on its own, but it can play an important role by contributing funding to facilitate corollary endpoints in trials. In some cases, this funding can fill critical gaps that enable trials to go forward that might otherwise not be possible to complete.
6. Access to carefully collected and curated tissue from NF patients remains a critical need, but requires substantial investments in infrastructure. CTF should seek partners in supporting the biobank, especially the NIH through NCATS and the network of CTSAs at academic institutions, which should be able to provide much of the needed infrastructure.

7. The CTF should lead a discussion on how to develop targeted studies of biomarkers for major complications of the disorder. It will not be able to fund such studies on its own, but should seek partners to provide funding and can play a role in supplemental funding to these studies.

8. The NF Registry can play an important role in data collection and patient engagement, though its value to the community may not have been adequately articulated. Aside from maintaining the registry, CTF should seek innovative approaches to collection of patient-related data and patient engagement. These efforts should be done together with other funding partners.

9. The NF Clinic Network can play an important role in standardization and improvement in the quality of patient care. A two-tier system should be employed, including a small number of centers of excellence and a larger number of programs with a willingness to see NF patients, though with less commitment to advancing research. The centers could be a rich source of patient data and tissue collection and could help formulate standards of clinical care. Additional funding partners would be necessary to adequately support this effort.