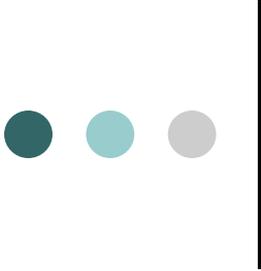


GTSAB REPORT

Recombinant DNA Advisory Committee

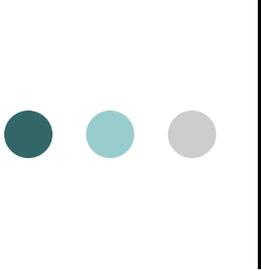
December 7, 2010





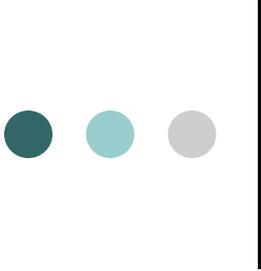
Protocols Submitted for 4th Quarter

- **16 submissions total**
 - **12 Protocols Not Selected:**
 - 8 are oncology protocols
 - 2 for monogenic diseases
 - 1 for critical limb ischemia
 - 1 for an infectious disease
 - Vectors:
 - 2 plasmid
 - 1 *Listeria monocytogenes*
 - 4 retrovirus
 - 1 adeno-associated
 - 4 lentivirus



MIC1 Submissions 4th Quarter 2010

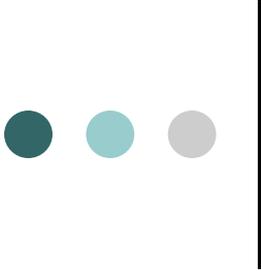
- **5 Protocols submitted MIC1s to OBA indicating enrollment**
- **2 Protocols were reviewed by the RAC at public meetings: protocols #0401-622 and #0906-977**
 - **Issues raised following RAC review of 0906-977 were previously addressed (December 2009 MIC1s)**



Adenylyl Cyclase VI Gene Transfer for Congestive Heart Failure

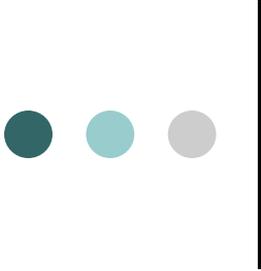
(#0401-622 reviewed March 2004)

- **Pre-clinical toxicology and biodistribution studies completed.**
- **Dose-limiting toxicities and stopping rules added.**
- **RAC had questioned need for placebo group at lower doses where clinical effects unlikely. PI believes placebo control for all doses needed for statistical power to determine efficacy, monitoring of adverse events and in order to conduct a placebo controlled trial must do so throughout all cohorts.**



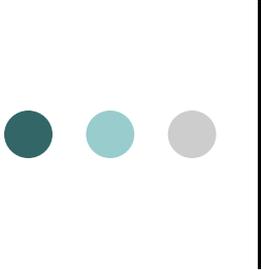
Serious Adverse Events

- **11 serious adverse events were reviewed by the GTSAB from 6 protocols, including initial and follow-up reports. No reports need additional discussion.**



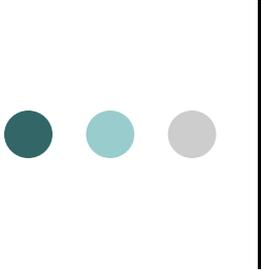
GlaxoSmithKline (GSK) to Collaborate on Gene Transfer for Rare Diseases

- GSK and Telethon Foundation, Italy and the San Raffaele Scientific Institute, Milan have announced a strategic alliance to develop treatments to address rare genetic disorders, using gene transfer carried out on stem cells (ex-vivo).**



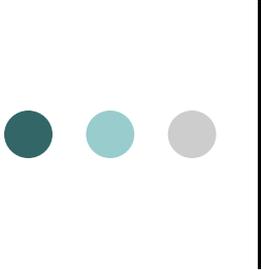
Collaboration on Gene Transfer for Rare Diseases

- **Telethon Foundation is one of the largest biomedical charities in Italy whose mission is to advance biomedical research for genetic diseases.**
- **The San Raffaele Scientific Institute is the largest private Italian Institute that carries out biomedical research and clinical trials.**
 - **It is recognized by the Italian Ministry of Health as a Center of Excellence and a University Research Hospital.**



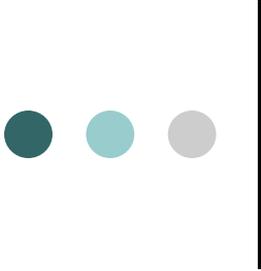
Collaboration on Gene Transfer for Rare Diseases

- **The San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET) is a joint venture between the Telethon Foundation and the San Raffaele Scientific Institute.**
- **Founded in 1995, the focus is on basic research and experimental protocols for gene and cell therapy of inherited diseases, in particular congenital immunodeficiencies, lysosomal storage diseases and blood disorders.**



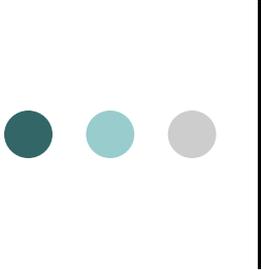
Collaboration on Gene Transfer for Rare Diseases

- **The Fondazione Telethon received an upfront \$15 million from GSK and is eligible to receive further payments upon successful completion of a number of predetermined development milestones.**
- **GSK gained an exclusive license to develop and commercialize an investigational gene therapy based on gamma-retrovirus vectors for ADA Severe Combined Immune Deficiency (ADA-SCID).**



Collaboration on Gene Transfer for Rare Diseases

- In addition, GSK gained rights to option lentiviral-based gene therapy products that HSR-TIGET has been working on for:
 - Metachromatic leukodystrophy (MLD)
 - Wiskott-Aldrich Syndrome (WAS)
 - Beta-thalassemia
 - Muccopolysaccharoidosis type 1 (MPS-I)
 - Globoid leukodystrophy (GLD)
 - Chronic granulomatous disorder (CGD)
- Clinical trials for WAS and MLD were initiated at HSR-TIGET last spring.



Collaboration on Gene Transfer for Rare Diseases

- **HSR-TIGET remains responsible of the pre-clinical and clinical testing of these new therapies until Proof of Concept (in term of safety and efficacy) is achieved in clinical trials.**
- **Once the Proof of Concept is reached, GSK will have the option to acquire exclusive rights to the development and commercialization of the therapy for that disease.**
- **GSK will assist in addressing regulatory and manufacturing issues.**

Original Article: Brief Report

Stem-Cell Gene Therapy for the Wiskott–Aldrich Syndrome

Kaan Boztug, M.D., Manfred Schmidt, Ph.D., Adrian Schwarzer, M.D., Pinaki P. Banerjee, Ph.D., Inés Avedillo Díez, Ph.D., Ricardo A. Dewey, Ph.D., Marie Böhm, M.Sc., Ali Nowrouzi, Ph.D., Claudia R. Ball, Ph.D., Hanno Glimm, M.D., Sonja Naundorf, M.Sc., Klaus Köhlcke, Ph.D., Rainer Blasczyk, M.D., Irina Kondratenko, M.D., László Maródi, M.D., Jordan S. Orange, M.D., Ph.D., Christof von Kalle, M.D., and Christoph Klein, M.D., Ph.D.

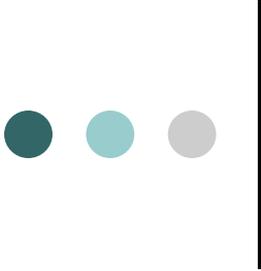
Study Overview

The authors report the long-term (up to 3 years) correction of the Wiskott–Aldrich syndrome in two patients through retroviral infection of CD34+ hematopoietic cells after busulfan-induced transient myelosuppression

N Engl J Med
Volume 363(20):1918-1927
November 11, 2010



The NEW ENGLAND
JOURNAL of MEDICINE



Acute T cell Leukemia reported in Wiskott-Aldrich Syndrome Trial

- **On the same day of publication of the New England Journal Article, these researchers reported in press release that although they have succeeded in correcting symptoms in 9 of 10 subjects enrolled in this trial (one subject did not receive sufficient cells), one subject, who had clinical benefit has developed an acute T cell leukemia related to the treatment.**