

## New INSIGHT Governance Structure

Following a strategic planning process last year, INSIGHT's new vision is "to reduce the global burden of HIV and other infectious diseases" and our mission is "to define optimal strategies for the management of HIV and other infectious diseases through a global clinical research network." In support of this vision and mission, three overall goals were defined: 1) enhance and sustain an efficient and effective organizational structure and model for the conduct of global clinical research in HIV and other infectious diseases; 2) develop and implement a globally relevant clinical research agenda in HIV and other infectious diseases, building on our experiences in HIV research; and 3) achieve recognition as a leader of global clinical research in HIV and other infectious diseases.

To move toward these goals, INSIGHT has transitioned to a new governance structure. A streamlined Executive Steering Committee (ESC) is focusing on expanding INSIGHT's funding base. The ESC is chaired by Jim Neaton and includes the principal investigators of the four International Coordinating Centers (ICCs), the INSIGHT Operations Center (CORE) director, and representatives from NIAID and DAIDS. Network governance responsibilities for science and operations have been assigned to two new committees: a Scientific Steering Committee (SSC) and an Operations Steering Committee (OSC).

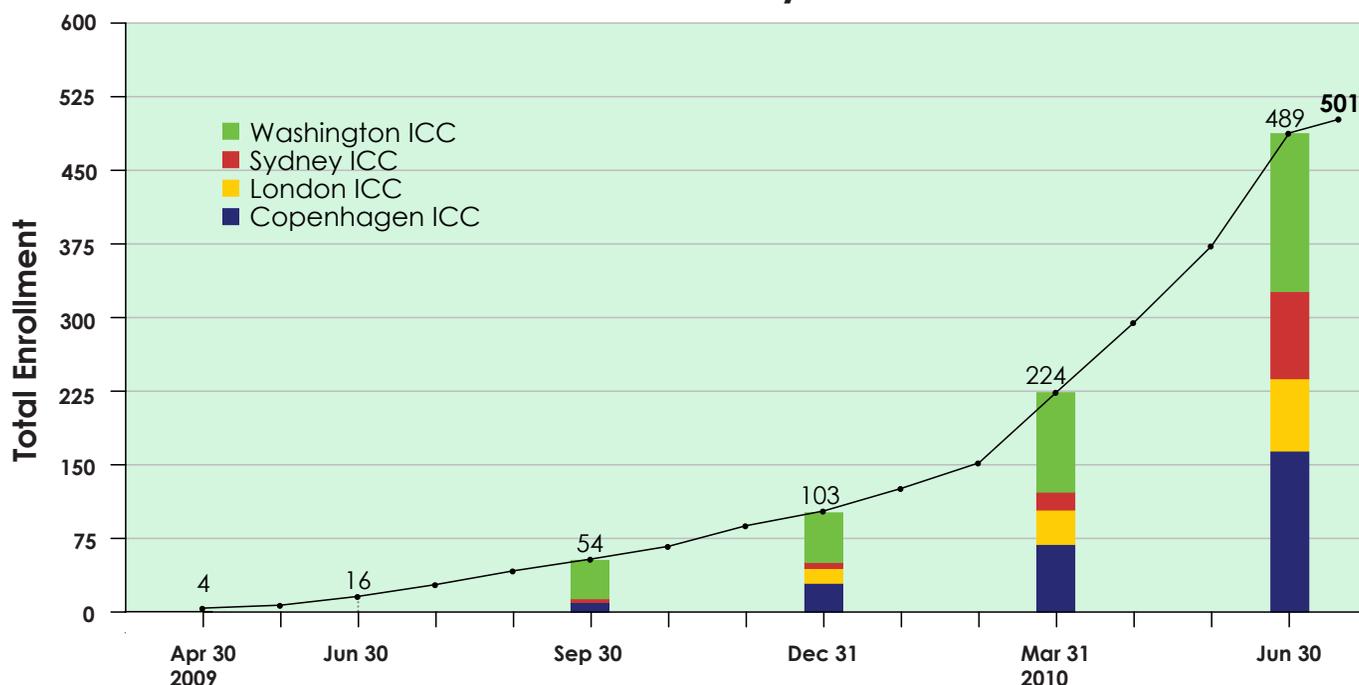
The SSC, chaired by Jens Lundgren, is responsible for formulating new scientific ideas, prioritizing INSIGHT's scientific agenda, and ensuring that INSIGHT's findings are disseminated rapidly and effectively. The SSC is supported by the INSIGHT Interest Groups and a committee secretariat. SSC membership includes senior research scientists, clinicians, and representatives from the Community Advisory Board (CAB), NIAID and DAIDS. The ESC membership is involved in all proceedings of the SSC.

The OSC, chaired by Sean Emery, is responsible for developing and implementing cross-protocol operating procedures and is supported by the Network Lab Group, the Quality and Performance Oversight Committee, and a committee secretariat. OSC membership includes clinicians and representatives from the ICCs, CAB, Statistical and Data Management Center, CORE, Network Lab, NIAID and DAIDS.

## START Enrollment Takes Off, Surpasses 500!

The idea of a study like START has been talked about, planned and anticipated for years. After overcoming impediments concerning sponsorship, acquisition of drug, and drug distribution, the most important HIV treatment trial is now underway. Nearly all of the 101 START sites participating in the pilot

**START Cumulative Enrollment as of 2 July 2010**



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## START (continued from page 1)

phase are now open to enrollment. Since March, the monthly enrollment rate has exceeded 70 patients, reached 116 in June, and is expected to continue to increase over the next 6 months. To fully enroll START in 3 years or less, a rate of at least 110 randomizations per month must be maintained.

Community involvement has been an important factor in expanding enrollment. While many potential participants may have opinions about whether they want to be on ART, they have recognized the uncertainty surrounding when to start ART. Investigators benefit from working closely with regional CABs or other local community organizations to distribute information about the START study question to the HIV community. ICCs and Site Coordinating Centers, as well as members of the INSIGHT CAB, have assisted investigators in making these key connections with organizations or publications in their areas.

One of the strengths of START is the valuable data being collected through its substudies. Five substudies are currently co-enrolling participants.

**Genomics** – Nearly 80% of sites are participating in the Genomics substudy, which has co-enrolled 94% of START participants at those sites.

**Informed Consent** – A large majority of sites (73%) are enrolling in the Informed Consent substudy. Thus far, 81% of the 447 substudy participants have completed the questionnaire that is the primary source of substudy data.

**Neurology** – About a third of the START sites participate in the Neurology substudy, and nearly 75% of the participants at these sites co-enroll.

**Arterial Elasticity** – The Arterial Elasticity substudy is taking place at 16 sites, and 62% of START participants at those sites co-enroll.

**Pulmonary** – The Pulmonary substudy has just opened at 18 sites, and 21 participants have enrolled; about half of all START sites ultimately plan to participate in this substudy.

A bone mineral density substudy is in the planning stages and will open later this year.

## Biomarker Research Update

Since completion of SMART, INSIGHT investigators have been studying the relationship of novel biomarkers with all-cause mortality, AIDS, cardiovascular disease and cancer. INSIGHT's stored specimen repositories include more than 500,000 samples. Combined with our large numbers of participants and clinical events, we are uniquely qualified to conduct this research, which has resulted in many publications and abstracts and continues to motivate new work.

Much of the new and ongoing work is being supported by funds made available for research by the American Recovery and Reinvestment Act (ARRA) of 2009. INSIGHT submitted two ARRA biomarker proposals to DAIDS. The first, "Biomarkers, Genes and Serious Non-AIDS Conditions," was awarded \$1.6 million in September 2009 and will continue through 31 August 2011. Using stored specimens from SMART and ESPRIT, the project is focused on the relationships between biomarkers, genetic traits, serious non-AIDS events, and the effects of ART. Laboratory work will expand knowledge about the effects of ART on coagulation markers, enable a number of studies on the predictors of chronic kidney disease (CKD) to be carried out, and develop a DNA bank to support multiple projects, including genetic traits associated with cardiovascular disease and CKD among HIV-infected participants.

A second ARRA proposal, "Biomarker Studies on the Pathogenesis of Non-AIDS Conditions Associated with HIV and Viral Hepatitis," was submitted in April 2010 for approximately \$1.4 million in funding and builds on the currently funded biomarker work using SMART and ESPRIT specimens. This grant proposal includes projects on the effect of ART on novel markers related to platelet activation, hepatitis co-infection and liver disease, the effects of HIV and HIV treatments on CKD and biomarkers of bone turnover, and studies of factors associated with vitamin D deficiency. Funding has been approved, and work is expected to begin in September.

For more information, see the following articles (available on the INSIGHT website):

- Kuller LH et al. PLoS Med 2008; 5[10]:e203.
- Duprez DA et al. Atherosclerosis 2009;207(2):524-529.
- Mocroft A et al. AIDS 2009; 23:71-82.
- Rodger AJ et al. J Infect Dis 2009; 200(6):973-983.
- Lampe FC et al. J Acquir Immun Defic Synd 2010; 54(3):275-284.
- Neuhaus J et al. J Infect Dis 2010; 201(12):1788-1795.