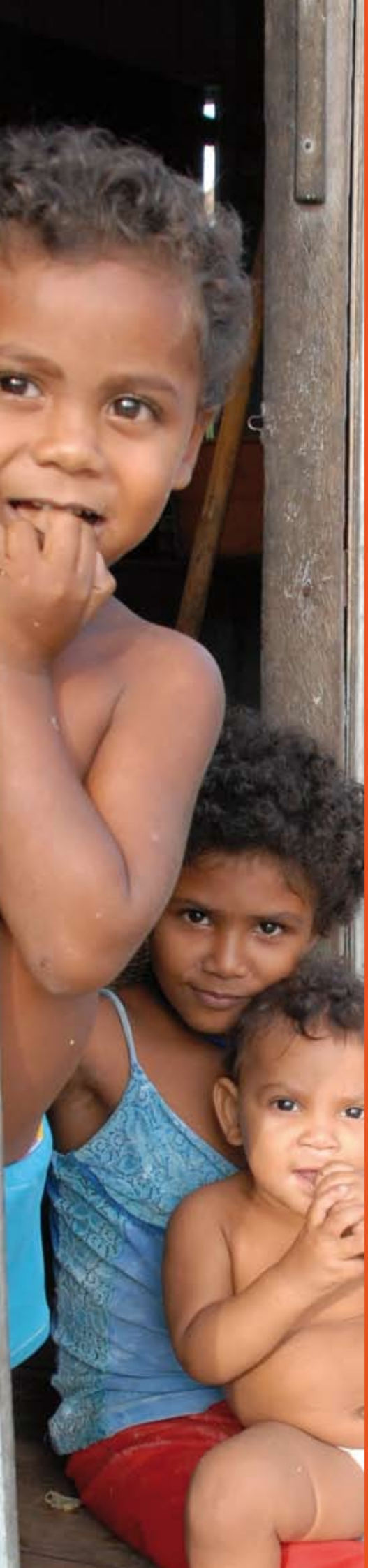

Stakeholders' Meeting 2008

New York City, USA
June 26

DNDi
Drugs for Neglected Diseases *initiative*

Dear Stakeholders:

Welcome on behalf of DND*i* to our 1st Annual DND*i* Stakeholders' Meeting. This exciting event brings together the key stakeholders, partners, and Friends of DND*i* to discuss the progress made and the challenges ahead in the landscape of drug research and development for neglected diseases.

By bringing together our stakeholders and partners in the field, we will have the opportunity to examine DND*i*'s activities in drug discovery, clinical development, access, and capacity strengthening. During our full day of discussions, we invite you to actively participate by sharing your knowledge and experience.

We will provide updates on our projects and platforms, with news on advances in our R&D efforts for visceral leishmaniasis (VL), human African trypanosomiasis (HAT, sleeping sickness), and Chagas disease. With regards to our malaria projects, we will provide a one year follow-up on ASAQ, DND*i*'s first product, made available in 2007, as well as an update on the recent launch of DND*i*'s second product, ASMQ.

In addition to DND*i* staff and board members, we are honored to have distinguished guests from industry, public institutions, donor groups, and fellow product development partnerships (PDPs). We look forward to keynote addresses by Dr. Richard Rockefeller and Professor Adel Mahmoud during the evening symposium.

The evening will be capped with the launch of DND*i* North America, a registered 501(c) non-profit organization and regional support office of DND*i*. DND*i* North America, located in downtown New York City, will support DND*i*'s scientific, advocacy, and fundraising efforts in the region. The evening's presentations and panel discussions will focus on innovative strategies to further research and advocate for sustained support in the fight against neglected diseases.

We are pleased that you could join us for what promises to be a riveting exchange of knowledge and wisdom aimed at breaking down the barriers to neglected disease research to bring treatments to patients in the field.

Best regards,

Bernard Pecoul, MD, MPH
Executive Director
DND*i*

Marcel Tanner
Chair, Board of Directors
DND*i*

Thanks to Our Donors!

DND*i*'s efforts in R&D and advocacy for neglected diseases over the last five years were made possible by our donors. Each of the public institutions, private foundations, and individuals below is a Stakeholder who shares in DND*i*'s vision and mission. DND*i* wishes to acknowledge and thank our donors for their support.

- Bill & Melinda Gates Foundation
- Canton of Geneva, Switzerland
- Department for International Development (DFID), United Kingdom
- Dutch Ministry of Foreign Affairs (DGIS)
- European Union – Framework Partnership 5 and 6
- French Development Agency (AFD)
- French Ministry of Foreign and European Affairs (MAEE)
- Médecins Sans Frontières, International
- Region of Tuscany, Italy
- Sasakawa Peace Foundation, Japan
- Spanish Agency for International Cooperation (AECI)
- Swiss Development and Cooperation Agency (DDC)
- United States National Institutes of Health – National Institute of Allergy and Infectious Diseases (NIAID)
- Other Private Foundations and Individuals

In order to achieve its objectives of building a robust pipeline and delivering 6-8 new treatments by 2014, DND*i* needs further support from public and private donors. DND*i* seeks diverse funding – including grants, sponsorships, monetary donations, in-kind contributions, and legacies – from individuals, governments, public institutions, companies, foundations, NGOs, and other sources. DND*i* also accepts donations of core funding to the organization, earmarked support for a specific project, or a contribution to several projects pertaining to one or multiple diseases.

To join our efforts to develop new medicines for those most in need, please contact DND*i*'s Fundraising Manager at +41.22.906.9240 or supportdndi@dndi.org.

Agenda of the Day

The DND*i* Stakeholders' Meeting, hosted at the New York Academy of Sciences, comprises both closed day sessions, to spur discussions and exchange knowledge on neglected diseases, and a public evening session, to advocate for support and launch DND*i* North America.

Day Sessions

Morning Session 1 - DND*i* Strategy, Chaired by Marcel Tanner

After the welcoming remarks of the New York Academy of Sciences President, DND*i*'s Chair of the Board will inaugurate the 1st Annual DND*i* Stakeholders' Meeting. To immediately capture DND*i*'s 'raison d' être,' Dr. Monique Wasunna, a medical researcher from the field, will give her perspective on the needs of patients suffering from neglected diseases. DND*i*'s Executive Director and Director of Research & Development will then frame the organization's strategy for 2008 as it strives to develop treatments to answer the needs of the most neglected.

Morning Session 2 - Discovery Efforts, Chaired by Ben Shapiro and Julio Urbina

Highlighting DND*i*'s drug discovery efforts and work to build a robust portfolio, two of DND*i*'s partners in lead optimization consortia, Scynexis and Advinus, will take the stage to discuss the synergies possible through linking research efforts across industry, academia, and the public sector. A panel discussion will follow, featuring experts from each sector, giving the audience an opportunity to learn more about product development partnerships (PDPs).

Afternoon Session - Clinical Efforts, Chaired by Carlos Morel and Lalit Kant

Experts in human African trypanosomiasis, leishmaniasis, and Chagas disease will present on the challenges of conducting clinical trials in neglected disease-endemic countries. The Vice-President of sanofi-aventis will also give an industry perspective on working with a PDP to research, develop, and launch a drug – showcasing ASAQ. To end the day sessions, a second panel of experts will discuss and invite questions on conducting clinical research and capacity building for neglected diseases.

In the evening session, amid a larger public audience, DND*i* will launch the initiative's new North America office. Under the session's theme of "Developing New Treatments for the Most Neglected through Global Research Partnerships," a series of prestigious speakers will engage in discussions to advocate uniting the global research community and ensuring a sustained commitment in the fight against neglected diseases.

Morning Session 1 - DND*i* Strategy: Chairs and Speakers

Chair:

Marcel Tanner, PhD, Director, Swiss Tropical Institute, Basel, Switzerland; Chair, DND*i* Board

Marcel Tanner obtained a PhD in medical biology from the University of Basel and an MPH from the University of London. He is Director of the Swiss Tropical Institute and Professor of Epidemiology and Medical Parasitology at the University of Basel and at the Federal Institute of Technology. Since 1977, his research has ranged from basic research on cell biology and immunology on malaria, schistosomiasis, trypanosomiasis, and filariasis to epidemiological and public health research on risk assessment, vulnerability, health impact, and district health planning. He has published over 400 original research papers as well as numerous book chapters and reviews. He also acts as an advisor for various national and international agencies/bodies and on boards/committees, including WHO/STAC-TDR, DND*i*, CHNRI, and INCLEN-Trust.

Speakers:

Ellis Rubinstein, President and Chief Executive Officer, The New York Academy of Sciences, New York, New York, USA

Mr. Rubinstein came to the Academy after more than 13 years with the American Association for the Advancement of Science (AAAS), where he served as Editor of Science magazine from 1993-2002. Prior to Science, Mr. Rubinstein was Editor of *The Scientist* and a Senior Editor at *Newsweek*. During his three decades as a journalist and editor, he was thrice honoured by National Magazine Awards - the Pulitzer Prizes of the periodical industry. He is a Fellow of the AAAS and a member of the IEEE and the National Association of Science Writers. Mr. Rubinstein has honorary degrees in Communications from Hallym University in South Korea and in Science from the University of Medicine and Dentistry of New Jersey. He holds a Bachelor's degree from the University of California, Berkeley.

Monique Wasunna, MD, Acting Director, Kenya Medical Research Institute (KEMRI), Nairobi, Kenya; Head, DND*i* Africa, Nairobi, Kenya

Dr. Wasunna is the Acting Director of KEMRI and Director of the Centre for Clinical Research. She is a physician who has specialized in Tropical Medicine and Infectious Disease. Dr. Wasunna has vast experience in clinical research and is a trained WHO Clinical Monitor. Dr. Wasunna has a special interest in neglected diseases and is coordinating DND*i's* activities throughout Africa. A founding member and former Chair of the Leishmaniasis East Africa Platform (LEAP), Dr. Wasunna's research interests have been primarily focused on clinical trials in visceral leishmaniasis (VL), as well as HIV and malaria. In addition to DND*i* and LEAP, she has collaborated with TDR and GlaxoSmithKline (GSK).

Bernard Pécoul, MD, MPH, Executive Director, DND*i*, Geneva, Switzerland

Dr. Pécoul's has led DND*i* since its founding in 2003. DND*i* and its partners have built the largest and most robust R&D portfolio ever for three of the most neglected diseases (leishmaniasis, human African trypanosomiasis, and Chagas disease), and launched ASAQ and ASMQ, two low-cost, non-patented antimalarial combinations. Dr. Pécoul played a key role in the formation of DND*i* as part of the Access to Essential Medicines Campaign of Médecins Sans Frontières (MSF). Prior to his involvement with the campaign, Dr. Pécoul was Executive Director of MSF-France, co-founder of Epicentre, and a MSF field physician in Africa, Latin America, and Asia. Dr. Pécoul obtained his MD from the University of Clermont Ferrand and his MPH from Tulane University.

Shing Chang, PhD, R&D Director, DND*i*, Geneva, Switzerland
Dr. Chang is responsible for building DND*i*'s project portfolio and advancing the discovery and development of new treatments for neglected diseases. Prior to DND*i*, Dr. Chang was a pharmaceutical industry executive: serving as Senior Vice President, Drug Discovery and Chief Scientific Officer at ICOS Corporation; holding various management positions at Abbott Laboratories in diagnostics and pharmaceutical research, including seven years as Divisional Vice President, Infectious Disease Research, in the global pharmaceutical research and development division; and rising to Vice President, Preclinical and Development at Cetus Corporation after joining initially as one of its first molecular biologists. Dr. Chang completed post-doctoral fellowships at the University of Wisconsin and Stanford University. He received his PhD in Molecular Biology and Biochemistry from the University of California, Santa Barbara, and his BS in Biology from Fu-Jen Catholic University in Taiwan.

Morning Session 2 – Discovery: Chairs, Speakers, and Panelists

Chairs:

Ben Shapiro, MD, Partner, PureTech Ventures, Boston, Massachusetts, USA; formerly Executive Vice President, Merck; Chair of the Board, DND*i* North America
Prior to his role with PureTech and as a consultant, Dr. Shapiro was Executive Vice President, Worldwide Licensing and External Research at Merck Research laboratories. Previously at Merck, he held the position of Executive Vice President, Worldwide Basic Research. Prior to entering the pharmaceutical industry, Dr. Shapiro was Professor and Chairman of the Department of Biochemistry at the University of Washington. He also held the position of Chief, Section on Cellular Differentiation in the Laboratory of Biochemistry at the US National Institutes of Health (NIH) and was a visiting scientist at the Institut Pasteur earlier in his career. Dr. Shapiro presently serves on Boards of several biotechnology companies and non-profit organizations. Dr. Shapiro received his MD from Jefferson Medical College in the USA.

Julio Urbina, PhD, Professor, Physical Chemistry and Biophysics, Central University of Venezuela and Head of the Biological Chemistry Research Group, Venezuelan Institute for Scientific Investigations, Caracas, Venezuela; Chair, DND*i* Scientific Advisory Committee
As a Professor and researcher at the Universidad Central de Venezuela from 1975 to 2006 and head of the Biological Chemistry Research Group, Venezuelan Institute for Scientific Investigations from 1991 to 2006, Dr. Urbina's work focused on the study of the structure and function of biological membranes and enzymes with the aim of identifying rational drug targets. He has published over 120 articles in peer-reviewed scientific journals in these areas. Dr. Urbina received a Simon Guggenheim Fellowship in 1996, the Lorenzo Mendoza Fleury Prize in 1997 and was a Howard Hughes Medical Institute International Scientific Research Scholar from 2000 to 2005. Dr. Urbina earned a Licenciado Degree in Biology from the Central University in Venezuela (1970) and a PhD in Physical Chemistry from the Massachusetts Institute of Technology (1975).

Speakers:

Yves Ribeill, PhD, President and CEO, SCYNEXIS, Research Triangle Park, North Carolina, USA
Prior to organizing SCYNEXIS, Inc. in 2000, Dr. Yves Ribeill held various positions during a 20-year international pharmaceutical career with Aventis and its predecessor Rhone-Poulenc Rorer. His roles with those companies included Discovery Chemistry Group Leader for Anti-Viral Research and in the Central Nervous System Group in France. He later served as Director of Chemistry for the Anti-Infective Group. He was involved in all phases of the drug

discovery and development effort that resulted in the FDA approval of the anti-bacterial Synercid in 1999. Dr. Ribeill is the author of more than 26 publications and 15 patents. He is a member of the Scientific Advisory Committee of the World Health Organization (WHO). Dr. Ribeill has a PhD in Chemistry from the University of Montpellier in France.

Rashmi Barbhaiya, PhD, CEO, Advinus Therapeutics, Bangalore, India
Dr. Barbhaiya is a pharmaceutical executive with extensive global experience in handling diverse aspects of drug discovery and development. Previous positions held by Dr. Barbhaiya include: President of Research and Development, Ranbaxy Research Laboratories, New Delhi, India and Vice President, Pharmaceutical Research Institute, Bristol-Meyers Squibb (BMS), Princeton, NJ. In his 21 years with BMS and 2.5 years with Ranbaxy, Dr. Barbhaiya has been instrumental in the discovery and development of numerous new drugs and drug delivery products. Dr. Barbhaiya has authored over 140 publications covering a broad range of therapeutic areas. He completed his post-doctoral training at the University of Florida and the University of Wisconsin after obtaining his PhD in Clinical Pharmacology from St. Bartholomew's Hospital Medical College, University of London.

Els Torreele, PhD, Senior Project Manager, DND*i*, Geneva, Switzerland
Having joined DND*i* in July 2003 as a founding team member, Dr. Torreele currently manages a number of discovery, preclinical and clinical development projects for African sleeping sickness. As an academic scientist, Dr. Torreele became involved in neglected disease issues in 1999 and assumed the role of Coordinator and Chair of the Drugs for Neglected Diseases Working Group (DND-WG) of the Access to Essential Medicines Campaign of MSF. Prior to joining MSF, she served as R&D Coordinator in the Department of Immunology, Parasitology & Ultrastructure at the Flanders Interuniversity Institute for Biotechnology of Brussels University. Els Torreele graduated as a Bio-Engineer and obtained a PhD in Applied Biological Sciences (Cell Biology and Immunology) from the Free University Brussels (VUB).

Panelists:
Cy Bacchi, PhD, Research Professor, Haskins Labs, Pace University, New York, New York, USA
Dr. Bacchi has been Professor of Biology at Pace University in New York City since 1968. From 1977 to 2006, he served as Director of the Haskins Laboratories at Pace University. His research has focused on the metabolism of African trypanosomes and the identification of new leads for human African trypanosomiasis (HAT) chemotherapy. Through his research into polyamine synthesis, Dr. Bacchi discovered DL- -difluoromethylornithine's (DFMO, eflornithine) activity against the *Trypanosoma brucei* parasite. Eflornithine is the only new drug clinically approved for HAT since 1950. From 1985 to 1989, he and the Kenya Trypanosomiasis Research Institute were co-investigators on a USAID grant.

Chris Hentschel, PhD, President and CEO, Medicines for Malaria Venture (MMV), Geneva, Switzerland
Dr. Hentschel, President and CEO of MMV since its inception in 1999, is a bio-pharmaceutical executive with more than 20 years of international R&D and technology transfer management experience in both the private and public sectors. He serves as a non-executive Director of a number of biotechnology companies, as an Advisor to a European venture capital fund, and as a Senior Research Fellow of the Wharton Business School's Emerging Technology Program. He is a member of the Supervisory Board of the Global Medical Forum in Zurich and the High-level Advisory Panel for Global Health Innovations Project, Saïd Business School, Oxford as well as an alternate Member of the Executive Committee of the Roll Back Malaria (RBM) Partnership representing the product development constituency.

Mel Spigelman, Director, Research and Development, Global Alliance for TB Drug Development (TB Alliance), New York, New York, USA
Dr. Spigelman is the Director of Research and Development at TB Alliance, with responsibility for the management of the R&D discovery and development portfolio. He received his medical degree from Mount Sinai School of Medicine. After completing training and obtaining Board Certifications in Internal Medicine, Medical Oncology and Preventive Medicine, he conducted basic research in CNS pharmacology and tumor biology, and clinical research in a variety of malignancies. He received the American Cancer Society Clinical Oncology Career Development Award (1985-1988). In 1989, Dr. Spigelman joined Knoll Pharmaceutical Company. Assuming the role of Vice President of R&D in 1991, he directed all R&D activities for Knoll for the next decade. Dr. Spigelman is also currently a Venture Partner with Wellington Partners.

Alan Magill, MD, FACP, Director Division Experimental Therapeutics, Walter Reed Army Institute of Research (WRAIR), Rockville, Maryland, USA
Colonel Magill has spent the last 15 years developing new generations of vaccines, diagnostics, and drugs directed against malaria and leishmaniasis. Dr. Magill previously served as the Head of Parasitology at the Naval Medical Research Center Detachment (NMRCD) in Lima, Peru, and as the Head of Clinical Research for the Malaria Vaccine Development Unit of the U.S. National Institutes of Health (NIH). He holds academic appointments at the US Uniformed Services University of the Health Sciences (USUHS) and the Gorgas Course in Clinical Tropical Medicine in Lima, Peru. He has authored more than 50 peer-reviewed publications, 90 abstracts, and ten book chapters. Dr. Magill received his MD from the USUHS and is board-certified in internal medicine and infectious diseases.

Afternoon Session – Clinical: Chairs, Speakers, and Panelists

Chairs:
Carlos Morel, MD, DSc, Director, Center for Technological Development in Health (CDTS), Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil
Dr. Morel is the Director of CDTS and a Senior Researcher at the Oswaldo Cruz Foundation, an institution to which he has devoted thirty years of his distinguished career. His is a renowned expert on Chagas disease and a strong advocate for neglected disease research. Maintaining his affiliations with Fiocruz, he served from 1998 to 2004 as the Director of TDR (UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases). Prior to his work at Fiocruz, Dr. Morel was an Associate Professor with the Institute of Biology of the University of Brasilia, and earlier, an Assistant Professor with the University's Faculty of Medicine. Dr. Morel received his MD from the Federal University of Pernambuco (UFPE) and his DSc in Biophysics and Molecular Biology from the Federal University of Rio de Janeiro.

Lalit Kant, MD, Head, Division of Epidemiology & Communicable Diseases, Indian Council of Medical Research (ICMR), New Delhi, India
Dr. Kant is an MD in Public Health and has a Masters degree in Communicable Disease Epidemiology. He heads the Division of Epidemiology & Communicable Diseases at the Indian Council of Medical Research. He has also headed the Division of International Health. ICMR, as a founding partner, has been on the Board of DNDi since 2003.

Speakers:

Constantin Miaka Mia Bilenge, MD, Secretary General, Ministry of Health, Democratic Republic of Congo and Special Advisor, National HAT Control Programme, Kinshasa, Democratic Republic of the Congo

Dr. Bilenge is a medical doctor with decades of experience in study, treatment, and advocacy for greater attention to neglected diseases such as malaria and sleeping sickness. He has also been engaged in conducting clinical research on therapeutics for sleeping sickness. Currently serving as Secretary General in the Ministry of Health of the Democratic Republic of the Congo, Dr. Bilenge also acts as Special Advisor to the National HAT Control Programme. Dr. Bilenge has served on the Board of the Roll Back Malaria Partnership and is a member of MotherNewBorNet,

Shyam Sundar, Professor of Medicine, Institute of Medical Sciences, Banaras Hindu University, India; Director, Kala Azar Medical Clinic, Muzaffurpur, India

Prof Sundar is Professor of Medicine at the Institute of Medical Sciences, Banaras Hindu University, where he uses immunological and molecular biology techniques to study the mechanisms of drug resistance of visceral leishmaniasis (VL). Having established a hospital which is at the forefront of the diagnosis and treatment of the disease in Muzaffarpur in the Indian state of Bihar, Prof Sundar has been involved in the study and treatment of VL for two decades, and has published over 250 papers on this subject.

Sergio Sosa-Estani, MD, MPH, PhD, Head, Service of Epidemiology, National Center for Research on Endemic Diseases (CeNDIE), ANLIS "Dr. Carlos G. Malbrán", Ministry of Health, Buenos Aires, Argentina

Dr. Sergio Sosa-Estani is a researcher at IECS in the team for Maternal and Child Health Research and a Professor of the Master of Clinical and Health Care Effectiveness, University of Buenos Aires. Dr. Sosa-Estani has conducted epidemiological and clinical research on tropical endemic diseases, re-emerging and emerging diseases. Having authored over 50 peer-reviewed scientific articles, reviews, book chapters, and two theses, Dr. Sosa-Estani has carried out research on Chagas disease, leishmaniasis, HIV-AIDS, Hantavirus, and others. A medical surgeon graduating from the University of Córdoba, Dr Sosa-Estani also has a Master of Public Health, a PhD in Medicine, and was a post-doctoral fellow at the School of Public Health and Tropical Medicine, Tulane University, USA.

Robert Sebbag, MD, Vice President, Access to Medicines, sanofi-aventis, Paris, France

In his current role, Dr. Sebbag implements the company's access to medicine strategy for the Southern Hemisphere. Prior to joining sanofi-aventis, Dr. Sebbag worked with the European Pharmaceutical Industry Association (EFPIA) to create a communications platform for pharmaceutical companies operating in Europe. Prior to that, he was Senior Vice President of Communications for the vaccine company Aventis Pasteur (today known as sanofi pasteur). In addition to his industry activities, Dr. Sebbag also teaches public health, focusing on tropical parasitic diseases, within the Paris hospital system. He is active within the French Red Cross and has participated in numerous health missions in the Southern Hemisphere. Dr. Sebbag is a Doctor of Medicine with specialties in tropical parasitic diseases and psychiatry.

Panelists:

Victoria Hale, PhD, Founder and Chair, Institute for OneWorld Health (iOWH), San Francisco, California, USA

Dr. Hale founded the Institute for OneWorld Health, a non-profit pharmaceutical company developing medicines for neglected diseases, and served as its CEO through 2007. Dr. Hale established her expertise in all stages of biopharmaceutical drug development at

Genentech, Inc., and at the Center for Drug Evaluation and Research of the US Food and Drug Administration (FDA). She presently maintains an Adjunct Associate Professorship in Biopharmaceutical Sciences at the University of California, San Francisco (UCSF), is an Advisor to the World Health Organization (WHO) for building ethical review capacity in the developing world, and has served as an expert reviewer to the National Institutes of Health (NIH) on the topic of biodiversity. Dr. Hale has received numerous awards and distinctions for her public health and business achievements with iOWH Dr. Hale received her PhD in Pharmaceutical Chemistry from the University of California, San Francisco.

Jean Jannin, MD, MPH, Coordinator, Innovative & Intensified Disease Management, Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

As Director of the Innovative & Intensified Disease Management Unit at WHO, Dr. Jannin, among other duties, is responsible for the control programmes against human African trypanosomiasis, leishmaniasis, Chagas disease, Buruli Ulcer, and Yaws. In addition to his role at WHO, Dr. Jannin is currently Inspector General of Public Health at the French Ministry of Health. Prior to joining WHO in 1995, Dr. Jannin worked for over a decade in preventive medicine in Africa treating tuberculosis, leprosy, schistosomisis, and sleeping sickness. Notably, he was the head of the sleeping sickness national program in Congo. Dr Jannin has both degrees in medicine and public health, and is a graduate of the French National School of Public Health and the Institute of Political Sciences.

Dawson Mbulamberi, MB CHB, M. Trop. Med., Assistant Commissioner, Health Services (Vector-borne Disease Control), Ministry of Health, Kampala, Uganda

Prior to his present role as the Assistant Commissioner for Vector-Borne Disease Control, Dr. Mbulamberi was the Assistant Commissioner of Health Services responsible for the CDC Malaria and Human African Trypanosomiasis Control Programme. From 1993-1997, he also served as the Director of the National Sleeping Sickness Control Programme with the Uganda Ministry of Health. Dr. Mbulamberi has devoted much of his career to combating sleeping sickness; he designed and established the Uganda National Programme for the control of human African trypanosomiasis and thereafter managed the programme for 13 years. Dr. Mbulamberi received his Bachelor's degree in Medicine, Bachelor's degree in Surgery, his Postgraduate Diploma in Public Health from the Makerere University Medical School in Uganda, and his Master's degree in Tropical Medicine from the Liverpool School of Tropical Medicine.

Manica Balasegaram, MD, Senior Project Manager, DND*i*, Geneva, Switzerland

Dr. Balasegaram manages DND*i*'s clinical research projects for the treatment of visceral leishmaniasis in East Africa. Prior to joining DNDi, he was Head of the Manson Unit, a medical research and implementation unit of Médecins Sans Frontières (MSF) – UK and worked in the field in Uganda, Sudan, the Republic of Congo, Ethiopia, India and Bangladesh. Dr. Balasegaram has clinical experience in tropical medicine including malaria, sleeping sickness, and visceral leishmaniasis. He was the Principal Investigator at Um el Kher, one of the two Sudan sites involved in the DND*i* paromomycin trial for the treatment of visceral leishmaniasis. He is currently completing a Masters in Public Health in Developing Countries at the London School of Hygiene and Tropical Medicine.

The Organization: Best Science for the Most Neglected Diseases

Background

Tropical diseases such as malaria, leishmaniasis, lymphatic filariasis, Chagas disease, human African trypanosomiasis (HAT), dengue fever, and schistomiasis continue to cause significant morbidity and mortality worldwide. These disabling and/or life threatening diseases represent an enduring unmet medical need and are collectively called "neglected diseases." Of the 1,556 new drugs approved between 1975 and 2004, only 21 (1.3%) were specifically developed for tropical diseases and tuberculosis, even though these diseases account for 11.4% of the global disease burden.

Although the R&D landscape has significantly changed for neglected diseases since 2000, there is an urgent need for new, field-adapted drugs to treat visceral leishmaniasis (VL), human African trypanosomiasis (HAT or sleeping sickness), and Chagas disease. A potentially fatal disease, VL is present in 62 countries, with 200 million people at risk and 500,000 new cases each year. Therapeutic options for VL are limited as there are significant drawbacks like route of administration, toxicity, or cost. HAT, a fatal disease if not treated, threatens more than 50 million people in 36 countries and has limited treatment options. For Chagas disease, which infects approximately 8 million and puts 100 million at risk in Central and South America, safer and more effective drugs adapted to patient needs are needed to treat both the acute and chronic phases of the disease.

Mission

Founded in 2003, DND*i* (Drugs for Neglected Diseases *initiative*) drew Founding Partners primarily from the public sector in neglected disease-endemic countries: the Oswaldo Cruz Foundation/Farmanguinhos in Brazil, the Indian Council for Medical Research (ICMR), the Kenya Medical Research Institute (KEMRI), and the Ministry of Health in Malaysia, along with Médecins Sans Frontières/Doctors Without Borders, the Institut Pasteur, and the UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases (TDR) as permanent observer. Today, DND*i* consists of a small team of permanent staff in Geneva and five regional support offices in Kenya, India, Brazil, Malaysia, and the USA, and two project support offices in the Democratic Republic of the Congo and Japan.

Collaborative Mode of Operation

DND*i* follows the virtual research model adopted by other product development partnerships (PDPs) whereby most research is outsourced and actively managed by DND*i* personnel. As an integral part of its mission, DND*i* utilizes South-South and North-South collaborations in working with R&D partners. While using and supporting existing capacity in countries where the diseases are endemic, DND*i* helps to build additional capacity in a sustainable manner through technology transfer in the field of drug R&D for neglected diseases. This includes early-stage access to molecules, pharmaceutical and clinical development, and working closely with control programs through, for example, the Leishmaniasis East Africa Platform (LEAP) and Human African Trypanosomiasis (HAT) platforms.

Regional Networks

DND*i* has built regional networks of scientists and clinicians actively involved in the research of new drugs for neglected diseases in Asia, Africa, and Latin America, as well as in the conduct of clinical trials in endemic countries.

To learn more about DND*i*'s activities, please visit www.dndi.org or contact info@dndi.org.

DND*i*: Current Highlights as of June 2008

DND*i* has 21 projects in its portfolio: ten discovery, four preclinical, five clinical, and two post-registration projects. Discovery projects include consolidated screening efforts which feed into disease-specific lead optimization programs. In the first half of 2008, DND*i* was honored to receive the **Goodwin Award** from the University of Siena for its Social Entrepreneurial Approach for the Most Neglected, and was also given the Médaille d'Or (Gold Medal) by La Société de Pathologie Exotique of France.

MALARIA

- ✓ **New fixed-dose combination of artesunate and amodiaquine (ASAQ) for treatment of malaria in sub-Saharan Africa launched in March 2007**
  - The ASAQ combination is available in 21 countries, with approximately 1.5 million treatments sold in the public market at a 'no-profit, no-loss' price of US$0.50 cents for 3-day pediatric treatment and US$1.00 for a 3-day adult treatment
  - Good Manufacturing Practice (GMP) certification has been granted and WHO pre-qualification is pending

- ✓ **New fixed-dose combination of artesunate and mefloquine (ASMQ)**
  - Successfully registered in Brazil in March 2008
  - Used by Brazilian national authorities as part of an ongoing intervention study, in which more than 25,000 patients were treated

VISCERAL LEISHMANIASIS (VL)

- ✓ **Lead Optimization Partnership established** with Indian partners which focuses on progressing molecules proven to to be safe and active against VL in early-stage screening research through the first steps of regulatory safety assessment in the preclinical phase

- ✓ **VL Combination Trial** to test drugs such as miltefosine, paromomycin, and liposomal amphotericin B to provide a shorter treatment regime & avoid resistance commenced recruitment in May 2008 in India

- ✓ **More than 1,000 patients included in a multi-center trial in East Africa testing paromomycin for the treatment of VL**

- ✓ **Leishmaniasis East Africa Platform (LEAP) for capacity strengthening**
  - Trained five trial site teams and three trial monitors
  - Established Data Safety Monitoring Board (DSMB)
  - New hospital lab at Kassab, Sudan
  - Two dedicated clinical research wards in Ethiopia
  - Trial coordination and data management offices at KEMRI, Kenya

HUMAN AFRICAN TRYPANOSOMIASIS (HAT)

- ✓ **Lead Optimization Partnership established** which focuses on progressing molecules proven to to be safe and active against HAT in early-stage screening research through the first steps of regulatory safety assessment in the preclinical phase

- ✓ **Fexinidazole finishing preclinical studies for the treatment of sleeping sickness with the objective to enter first-in-human phase I trials in Q1 2009**

- ✓ **Clinical trial of nifurtimox-eflornithine co-administration for the treatment of sleeping sickness showed promising interim safety data**
  - Médecins Sans Frontières (MSF) treatment program for African sleeping sickness has found that a new combination treatment using the drugs nifurtimox and eflornithine holds promise and deserves further evaluation
  - Data from all six sites of the multi-center NECT study, which is currently conducting patient follow-up, should be available at the end of 2008; a WHO recommendation is expected for the combination in 2009

- ✓ **Since 2005, the HAT Platform has been providing training** to platform members in Angola, DRC, Republic of Congo, Uganda and Sudan on treatment of HAT patients and the conduct of clinical trials, including good clinical practice
  - Good Clinical Practice (GCP) training in Nairobi and clinical monitor training in Kampala
  - Four training sessions conducted for Ethics Committee members
  - Annual Platform in Nairobi (2006) and Khartoum (2007); six monthly steering committee meetings, and interim meetings Luanda (2006), Basel (2007), and Kampala (June 2008); three HAT platform newsletters published
  - HAT Platform member participation in various scientific congresses

CHAGAS DISEASE

- ✓ **Lead Optimization Partnership established with partners in Australia and Brazil** focused on progressing molecules proven to to be safe and active against Chagas in early-stage screening research through the first steps of regulatory safety assessment in the preclinical phase

- ✓ **A project launched to investigate therapeutic switching potential of the azole class, which are well-known anti-fungals**

- ✓ **Partnership with LaFepe to develop pediatric formulation of benznidazole**

DND*i* Board in 2008

Since DND*i*'s inception in 2003, seven key stakeholders have helped to give life to the initiative. DND*i*'s original Board members each represent one of DND*i*'s Founding Partners, as highlighted below, and represent excellence in neglected disease research and patient care. Drawn primarily from the public sector in neglected disease-endemic countries, they have continued to serve as a backbone of DND*i* by providing their expert advice, the benefit of their experience, and key project participation.

- The Indian Council for Medical Research (ICMR), founded in 1949, is one of the oldest medical research bodies in the world. Its activities are focused on the formulation, coordination, and promotion of biomedical research.
- The Institut Pasteur, created in 1887, is a non-profit private foundation which contributes to the prevention and treatment of disease, primarily infectious diseases, through research, education, and public health activities.
- The Kenya Medical Research Institute (KEMRI), founded in 1979, is one of the leading health research institutions in Africa. Its activities focus on infectious and parasitic diseases, and on public health and biotechnology research.
- The Malaysian Ministry of Health is dedicated to activities and construction of partnerships to reduce the health, social, and economic burden of communicable diseases, and to promote public health.
- Médecins Sans Frontières/Doctors Without Borders, the international humanitarian organization, was founded in 1971 to deliver emergency aid to people affected by armed conflict, epidemics, natural or manmade disasters, or exclusion from healthcare in more than 70 countries.
- The Oswaldo Cruz Foundation (Fiocruz), founded in 1900, is the most prominent science and technology health institution in Latin America. Its activities are focused on research, education, healthcare, and production of vaccines, drugs, reagents, and diagnostic kits.
- The Special Programme for Research and Training in Tropical Diseases (TDR), established in 1975 and co-sponsored by the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP), the World Bank and the World Health Organization (WHO), aims to help coordinate, support, and influence global efforts to combat major diseases of the poor and disadvantaged. TDR is a permanent observer of DND*i*'s activities.
- In 2006, the DND*i* Board welcomed Paulina Tindana of the Navrongo Health Research Centre in Ghana as a patient representative to the Board.

DND*i* Welcomes New Board Members Bennett Shapiro & Gill Samuels in June 2008

Bennett M. Shapiro, Chair of the DND*i* North America Board, is an accomplished scientist and executive whose career encompasses academia, the public health sector, the pharmaceutical industry, and biotechnology entrepreneurship. Dr. Shapiro is very familiar with DND*i*, having served on DND*i*'s Scientific Advisory Committee since its inception in 2003. Dr. Shapiro presently serves on several Boards of biotechnology companies and non-profit organizations.

Gill Samuels, a physiologist and neuropharmacologist by training, joins the DND*i* Board of Directors after a distinguished career as a scientist and pharmaceutical executive. She most recently served as Pfizer's Executive Director of Science Policy and Scientific Affairs for Europe. Prior to her position in Science Policy, Dr. Samuels directed Pfizer's Cardiovascular Biology, contributing to the discovery of several new medicines. Dr. Samuels currently acts as Chair of the Foundation Council of the Global Forum for Health Research.