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23 July 2012 | News | By BioSpectrum Bureau

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Mumbai: The Drugs for Neglected Diseases initiative (DNDi), a not-for-profit research and development (R&D) organization, has signed a new collaboration with Indian drug manufacturer Cipla to develop and produce an improved first-line antiretroviral (ARV) combination therapy. The collaboration was signed on the eve of the XIX International AIDS Conference in Washington, DC.

The therapy will be specifically adapted to meet the treatment needs of infants and toddlers living with HIV/AIDS. Once delivered, this new paediatric ARV combination could help to accelerate the provision of care to the world's youngest children living with HIV/AIDS, who are at very high risk of dying without treatment. An estimated 3.4 million children have HIV/AIDS, but less than a quarter currently have access to antiretroviral therapy (ART), compared with 54 percent for adults. Without treatment, more than half of children with HIV/AIDS will die before their second birthday, and 80 percent will die before they turn five.

Current therapeutic options for HIV-positive infants and young children are insufficient in certain key circumstances. Although fixed-dose combination dissolvable 'baby pills' (for example Triomune Baby and Junior produced by Cipla in 2007) are used throughout most of Africa, they are not optimal for the youngest children who have very high levels of virus in their blood and have already been exposed to some of these drugs from their mother. An important alternative drug (lopinavir-ritonavir protease inhibitor) has been used mainly in South Africa, but has problems, including poor taste, impractical multiple liquid preparations that are cumbersome to transport, requirements for refrigeration, high cost, difficulties for caregivers to administer, and negative interactions with tuberculosis (TB) drugs.

The goal of the collaboration between DNDi and Cipla is to develop a 4-in-1 ARV combination product for HIV-infected children under the age of three years, including those who have been exposed to drugs while in the womb, and also those who are co-infected with TB.

Historically, major pharmaceutical companies have invested little in R&D specifically aimed at addressing the needs of young

children with HIV/AIDS largely because of the absence of a viable market: the virtual elimination of mother-to-child transmission of HIV in high-income countries means that nearly all HIV-positive children live in low- and middle-income countries, with over 90% in sub-Saharan Africa. The global strategy to eliminate new infant infections through prevention of mother-to-child transmission (PMTCT) by 2015 will be confronted with the reality that some children continue to be infected and urgently need access to early diagnosis and immediate ART with safe, potent, child-friendly treatment combinations.

"Cipla is fully committed to take its ARV work for children with HIV/AIDS a step further," said Dr Yusuf K Hamied, chairman and managing director of Cipla. "We have already been working with the Medical Research Council Clinical Trials Unit (MRC CTU) in the UK and their paediatric colleagues in Zambia and Uganda for several years, first producing several appropriate baby pill formulations for infants and children, and more recently we have produced a new sprinkle of lopinavir-ritonavir. Cipla and DNDi are now joining forces to produce further drug formulations for HIV-infected children in poor countries."

Within the new collaboration, Cipla will provide its lopinavir/ritonavir (LPV/r) 40-/10-mg sprinkle formulation ('Lopimune Sprinkles') and work with DNDi and other partners to test new combinations of HIV treatment for infants and young children. The initial data on the lopinavir-ritonavir sprinkle - being generated by Ugandan paediatricians and MRC CTU in partnership with Cipla (CHAPAS 2 trial) - will be essential for DNDi and its partners to develop an optimized first-line therapy in a fixed-dose combination of Lopimune Sprinkles, combined with one of two other powerful ARV drug combinations, abacavir/lamivudine (ABC/3TC) or zidovudine/lamivudine (AZT/3TC). Cipla will work to produce an appropriate 4-in-1 combination sachet product, in which the four ARV drugs will be in taste-masked, granular form, for easy mixing into food or liquids such as water, juice, or breast milk, with the aim of registering the drug by 2015.

"The lack of appropriate treatments for young children with HIV/AIDS has been devastating," noted Dr Unni Karunakara, president of MSF International. "This initiative responds to our call for attention and resources to be directed towards giving these kids the medicines, life, and dignity they deserve."

As the industrial partner, Cipla will take responsibility for production, registration, and distribution of the product and will thus retain all intellectual property (IP) related to the new formulations. Should Cipla opt out as industrial partner, DNDi will be granted non-exclusive, worldwide, royalty-free licences to the IP. In addition, the collaboration aims to bring the cost of the final ARV product in the public sector substantially lower than the cost of the products used separately. Cipla and DNDi will establish a detailed drug access and implementation plan to ensure delivery of the new product to patients.

"This partnership with Cipla and other collaborators provides us a critical path to developing better paediatric antiretroviral formulations for the youngest, most vulnerable patients living with HIV/AIDS," said Dr Bernard PÃ©coul, executive director of DNDi. "Young children living with - and dying from - HIV/AIDS deserve the best that science has to offer. We will concentrate our every effort to ensure that we get to the right treatment as soon as possible to save the lives of the over 600 HIV-positive children who die silently every day."