

## Once-Daily Dolutegravir is Non-Inferior to Twice-Daily Raltegravir in Treatment-Naïve Adults with HIV-1

- *Shionogi-ViiV Healthcare LLC present full 48-week data results from SPRING-2 Phase III study at International AIDS Conference*
  - *Findings support progression towards registration*
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**Washington, DC – 26 July, 2012** – Shionogi-ViiV Healthcare LLC today announced 48-week data from the SPRING-2 Phase III study, which is evaluating the investigational integrase inhibitor dolutegravir in treatment-naïve adults with HIV-1 infection. In this double-blind, double-dummy study, the proportion of study participants who were virologically suppressed (HIV-1 RNA <50 c/mL) was 88% for once-daily dolutegravir (DTG) and 85% for twice-daily raltegravir (RAL), with a 95% confidence interval for the difference, (-2.2% to +7.1%) meeting the 10% non-inferiority limit. Response rates were similar regardless of which dual nucleoside reverse transcriptase inhibitor (NRTI) therapy was used. For study participants with high baseline viral load (HIV-1 RNA >100,000 c/mL), the response rates were 82% for DTG vs. 75% for RAL. These data were presented at the XIX International AIDS Conference in Washington, DC.

Prespecified secondary analyses also supported non-inferiority of dolutegravir to raltegravir; the proportion of subjects without treatment-related discontinuations was 93% on dolutegravir and 92% on raltegravir. Median CD4 increases were also similar in both groups (+230 cells/mm<sup>3</sup>). Virologic failure occurred in 5% of DTG subjects and 7% of RAL subjects; neither genotypic integrase resistance mutations nor NRTI resistance mutations were detected in the DTG group vs. 1 subject and 4 subjects, respectively, who failed RAL.

The tolerability of dolutegravir was similar to that of raltegravir, with adverse events (AEs) leading to withdrawal at 2% in both arms. Commonly occurring AEs (10-15% of subjects on both arms) comprised nausea, headache, nasopharyngitis and diarrhoea. Grade 3 or higher liver enzymes (ALT) occurred in 2% of subjects in each group; no Grade 3 or higher elevation in serum creatinine (a measure of kidney function) occurred on either arm.

“These data offer compelling evidence for once-daily dolutegravir as an option that does not require a booster for first-line HIV treatment. Furthermore, the efficacy was similar regardless of which dual NRTI therapy was used with the core dolutegravir regimen,” said John Pottage, MD, Chief Scientific and Medical Officer, ViiV Healthcare. “There have been many recent incremental advances in the treatment of HIV, but we believe dolutegravir could be a significant step forward in how we approach the management of the disease.”

“These data from treatment-naïve subjects come from the first of four studies within our dolutegravir clinical programme. We are very pleased that in SPRING-2, we did not observe any genotypic resistance in treatment-naïve subjects treated with dolutegravir, which supports preclinical evidence that DTG has a high barrier to resistance. We continue to look forward to data from further studies in a variety of clinical settings—including treatment-experienced people living with HIV—to support regulatory submission later in 2012,” said Dr. Tsutae "Den" Nagata, Chief Medical Officer, Shionogi & Co., Ltd.

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SPRING-2 is the first of four Phase III studies that are due to be reported in 2012. Topline data from the clinical trial SINGLE (ING114467) were reported earlier this month and will be presented at an upcoming scientific meeting; results from VIKING-3 (ING112574) and SAILING (ING111762) will be received later this year and will allow further determination of the profile of dolutegravir. These studies are designed to support a future regulatory submission for dolutegravir.

## **SPRING-2 Study Design**

SPRING-2 (ING113086) is a Phase III, randomised, double-blind, double-dummy, multicentre, parallel group, non-inferiority study. The study included 822 HIV-1 infected treatment-naïve participants. The ongoing study compares the efficacy and safety of unboosted dolutegravir to raltegravir as part of an overall treatment regimen; both treatment arms are administered with investigator-selected dual nucleoside reverse transcriptase inhibitor therapy (either abacavir + lamivudine or tenofovir + emtricitabine).

The primary objective for SPRING-2 is to demonstrate the antiviral activity of dolutegravir 50mg administered once-daily compared to raltegravir 400mg administered twice-daily over 48 weeks. Secondary objectives include the assessment of antiviral activity of dolutegravir compared to raltegravir at 96 weeks, to compare the tolerability, long-term safety and antiviral and immunologic activity of dolutegravir to raltegravir, and to evaluate viral resistance in study participants experiencing virological failure.

## **About Dolutegravir**

S/GSK1349572 (dolutegravir) is an investigational integrase inhibitor (INI) currently in development by Shionogi-ViiV Healthcare LLC for the treatment of HIV. DTG, which is in phase III clinical development, is currently the only once-daily INI that does not require a pharmacologic booster. Integrase inhibitors block HIV replication by preventing the viral DNA from integrating into the genetic material of human immune cells (T-cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic infection.

## **About Shionogi-ViiV Healthcare LLC**

The Shionogi-ViiV Healthcare LLC is a joint venture between Shionogi & Co., Ltd. and ViiV Healthcare Ltd., a global company with a sole focus on HIV established in 2009 by GlaxoSmithKline and Pfizer, Inc. Dolutegravir is the lead compound in the Shionogi-ViiV Healthcare LLC partnership. Shionogi-ViiV Healthcare LLC is also developing another integrase inhibitor which is at an earlier stage of development.

## **About Shionogi & Co., Ltd.**

Headquartered in Osaka, Japan, Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to placing the highest value on patients. Shionogi's Research and Development currently targets three therapeutic areas: Infectious Diseases, Pain and Metabolic Syndrome. The Company is the originator of innovative medicines which have been successfully delivered to millions of patients worldwide. In addition, Shionogi is engaged in new research areas such as allergy and cancer. Contributing to the health of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit [www.shionogi.co.jp](http://www.shionogi.co.jp). For more information on Shionogi Inc. headquartered in Florham Park, NJ, please visit [www.shionogi.com](http://www.shionogi.com).

## **About ViiV Healthcare Ltd.**

ViiV Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV. The company's aim is to take a deeper and broader interest in HIV/AIDS than any company has done before and

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take a new approach to deliver effective and new HIV medicines as well as support communities affected by HIV. For more information on the company, its management, portfolio, pipeline and commitment, please visit [www.viivhealthcare.com](http://www.viivhealthcare.com).

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#### **GlaxoSmithKline Cautionary statement regarding forward-looking statements**

Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Factors that may affect GSK's operations are described under 'Risk factors' in the 'Financial review & risk' section in the company's Annual Report 2011 included as exhibit 15.2 to the company's Annual Report on Form 20-F for 2011.

**Pfizer disclosure notice:** Pfizer assumes no obligation to update any forward-looking statements contained in this release as a result of new information or future events or developments. This release contains forward-looking information about Pfizer, GlaxoSmithKline and ViiV Healthcare and about the prospects of the companies, including revenues from in-line products and the potential benefits of product candidates that will be contributed to that company, as well as the potential financial impact of the transaction. Such information involves substantial risks and uncertainties including, among other things, decisions by regulatory authorities

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regarding whether and when to approve any drug applications that have been or may be filed for such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates; and competitive developments.

A further list and description of risks and uncertainties can be found in Pfizer's Annual Report of Form 10-K for the fiscal year ended December 31, 2011 and in its reports on Form 10-Q and Form 8-K.

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