Complete Phase 2a Study of HIV-1 Investigational Maturation Inhibitor Demonstrates Positive Results for Therapy Designed to Attack Virus Differently Than Existing Treatments

Release Date:
Friday, October 23, 2015 9:30 am EDT

Terms:

Dateline City:
PRINCETON, N.J.

Complete proof-of-concept Phase 2a dataset of investigational HIV-1 Maturation Inhibitor presented at European AIDS Conference (EACS)

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) today announced overall antiviral activity and safety results from the three-part Phase 2a proof-of-concept study of BMS-955176, a novel investigational therapy designed to prevent the maturation of HIV-1. Presented today at the European AIDS Clinical Society's 15th European AIDS Conference (EACS) in Barcelona, the study findings support the continued development of BMS-955176, an investigational therapy from a potential new drug class that is designed to attack the HIV-1 virus differently than other available treatments.

BMS-955176 is a second-generation maturation inhibitor designed to inhibit one of the last steps of the HIV-1 viral lifecycle, which is theorized to disrupt the "maturation" of new virus particles and cause the release of immature HIV-1 particles that are unable to complete their lifecycle. The overall results of the study demonstrate BMS-955176's antiretroviral activity against the HIV-1 virus as both monotherapy and in combination with other antiretroviral medicines, and across patient subtypes (B, C), including those infected with the HIV-1 virus with changes in a critical protein ("Gag polymorphisms") that were not responsive to a previously investigated maturation inhibitor. Please refer to the “Study Design and Results” sections below for the specific data presented.

"Life-long management of HIV-1 infection requires sequencing of antiretroviral therapy to stay ahead of resistance and long-term tolerability challenges, and there is a need for new options for treatment-experienced patients," said Douglas Manion, M.D., head of Specialty Development, Bristol-Myers Squibb. "The overall findings of this proof-of-concept study confirm that BMS-955176 should be studied further in Phase 2b for patients in need of new antiretrovirals."

Maturation is one of the final steps in the HIV-1 lifecycle and occurs when the virus breaks connections between structural proteins. As a result, these proteins then undergo changes that produce fully mature infectious virus particles, which are released from cells with the ability to infect new CD4+ T-cells. BMS-955176 is designed to inhibit the last cleavage step in the HIV-1 maturation process, and thus potentially block the virus from becoming mature and infectious.

Thirty-four million people are infected with HIV-1 globally, and although the last twenty years have seen significant treatment advances, drug resistance, tolerability, and the potential for drug-drug interactions still present challenges. As the patient population ages and patients are on treatment longer, those developing resistance to existing regimens and classes, or who are unable to tolerate current available treatments, is increasing. This shift is driving a need for novel drug classes with innovative mechanisms of action and the potential to address these evolving needs. Bristol-Myers Squibb, a leader in the development of HIV-1 treatments for more than two decades, is centering its current HIV-1-related research and development on potential novel therapeutic options for treatment-experienced patients.

Today at EACS, Bristol-Myers Squibb presented new data from Part C of the randomized, multi-part trial evaluating the antiviral activity and safety of BMS-955176 administered as monotherapy in patients infected with HIV-1 subtype C, a type of the virus that has a higher prevalence of the naturally occurring changes in the Gag polyprotein (a critical protein for viral replication). Taken together, data from all three parts of the Phase 2a study support the further evaluation of BMS-955176 in broader global studies.

Part A Study Design & Results

Part A of the Phase 2a, randomized, multi-part trial evaluated BMS-955176 antiviral activity, safety, and exposure-response during 10 days of monotherapy in 40 HIV-1, subtype B-infected patients with HIV-1 RNA ≥5000 c/mL and CD4+ T-cell counts ≥200 cells/µL. Patients were randomized 1:1:1:1 to dose groups of 5, 10, 20 or 40 mg, and then 4:1 to receive an oral suspension of BMS-955176 (n=48) or placebo once daily (n=12) for 10 days. Twenty additional subjects were later randomized to 80 and 120 mg once-daily dose groups. The primary endpoint was change in HIV-1 RNA from baseline to Day 11, and safety and exposure-response were secondary endpoints. A summary of the data is below.
There were no deaths, serious adverse events (SAEs), adverse events (AEs) leading to discontinuation, grade 3-4 related AEs or clinically relevant grade 2-4 laboratory abnormalities. With all reported AEs except for G1-2 diarrhea in 4 subjects on BMS-955176, the same or greater percentage of subjects on placebo reported AEs as compared to subjects receiving BMS-955176. Subjects receiving placebo reported headache (42%), abnormal dreams (25%), night sweats (8%), and diarrhea (0%).

**Part B Study Design & Results**

In Part B of the trial, antiviral activity and safety of BMS-955176 administered with atazanavir ± ritonavir were evaluated and compared to a standard of care regimen of atazanavir and ritonavir plus tenofovir disoproxil fumarate/emtricitabine after 28 days of therapy. The study included 28 HIV-1, subtype B-infected patients with HIV-1 RNA ≥5000 c/mL and CD4+ T-cell counts ≥200 cells/µL who were randomized 2:2:2:1 to four treatment groups: BMS-955176 40 mg plus atazanavir 400 mg; BMS-955176 40 mg plus atazanavir 300 mg and ritonavir 100 mg; BMS-955176 80 mg plus atazanavir 400 mg; and a SOC control of atazanavir 300 mg and ritonavir 100 mg plus tenofovir disoproxyl fumarate 300 mg plus emtricitabine 200 mg in a fixed dose combination. Study endpoints included change in HIV-1 RNA from baseline to Day 28, change in HIV-1 RNA from baseline to the end of the study (Day 42) and safety. A summary of the data is below.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median change in HIV-1 RNA (log_{10} c/mL) on Day 29 (min, max)</th>
<th>Maximum median change in HIV-1 RNA (log_{10} c/mL) on Day 42 (min, max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS-955176 40 mg</td>
<td>-1.99 (-1.04, -3.32)</td>
<td>-2.20 (-1.24, -3.52)</td>
</tr>
<tr>
<td>BMS-955176 80 mg</td>
<td>-2.18 (-1.53, -2.68)</td>
<td>-2.23 (-1.87, -2.68)</td>
</tr>
<tr>
<td>Placebo</td>
<td>-2.22 (-1.83, -2.84)</td>
<td>-2.39 (-1.83, -3.04)</td>
</tr>
</tbody>
</table>

There were no deaths, SAEs or AEs leading to discontinuation. In addition, bilirubin levels were lower for patients receiving BMS-955176 plus unboosted atazanavir compared to patients receiving BMS-955176 40 mg plus boosted atazanavir or the standard of care. The most common AEs (≥10%) across all treatment groups included increased bilirubin levels (58%), headache (50%) and abnormal dreams (38%).

**Part C Study Design & Results**

Part C of the trial evaluated the antiviral activity and safety of BMS-955176 administered as monotherapy for 10 days. The study included 19 treatment-naïve or treatment-experienced patients (who had not previously received a protease inhibitor- or maturation inhibitor-containing regimen) infected with HIV-1 subtype C with plasma HIV-1 RNA ≥5,000 c/mL and CD4+ T-cell count ≥200 cells/µL. Patients were randomized to three dose groups: BMS-955176 40 mg (n=8), BMS-955176 120 mg (n=7), or placebo (n=4) once daily. The primary endpoint was the change in HIV-1 RNA from baseline to Day 11. A summary of the data is below.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median change in HIV-1 RNA (log_{10} c/mL) on Day 29 (min, max)</th>
<th>Maximum median change in HIV-1 RNA (log_{10} c/mL) on Day 42 (min, max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS-955176 40 mg</td>
<td>-1.66 (-1.19, -2.04)</td>
<td>-1.86 (-1.49, -2.37)</td>
</tr>
<tr>
<td>BMS-955176 80 mg</td>
<td>-2.18 (-1.53, -2.68)</td>
<td>-2.20 (-1.24, -3.52)</td>
</tr>
<tr>
<td>Placebo</td>
<td>-2.22 (-1.83, -2.84)</td>
<td>-2.39 (-1.83, -3.04)</td>
</tr>
</tbody>
</table>

There were no deaths, SAEs or AEs leading to discontinuation. In addition, bilirubin levels were lower for patients receiving BMS-955176 plus unboosted atazanavir compared to patients receiving BMS-955176 40 mg plus boosted atazanavir or the standard of care. The most common AEs (≥10%) across all treatment groups included increased bilirubin levels (58%), headache (50%) and abnormal dreams (38%).
<table>
<thead>
<tr>
<th></th>
<th>BMS-955176 40mg QD</th>
<th>BMS-955176 120mg QD</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>8</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td><strong>Median change</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>in</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HIV-1 RNA (log_{10} c/mL) on Day 11</strong></td>
<td>(-1.21, -0.93, -1.72)</td>
<td>(-1.03, 0.25, -1.88)</td>
<td>(0.001, 0.52, -1.21)</td>
</tr>
<tr>
<td><strong>Maximum median change</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>in</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HIV-1 RNA (log_{10} c/mL) on Day 24</strong></td>
<td>(-1.35, -1.04, -2.03)</td>
<td>(-1.26, -0.70, -2.02)</td>
<td>(-0.42, 0.22, -1.21)</td>
</tr>
</tbody>
</table>

There were no deaths, SAEs or AEs leading to discontinuation of treatment.

Two Phase 2b studies of BMS-955176 began in 2015 and are ongoing, including a traditional dose-finding study in treatment-naive patients and a study to evaluate an innovative nucleos(t)ide- and booster-sparing regimen in treatment-experienced patients.

**About Bristol Myers-Squibb’s HIV Portfolio**

For more than 20 years, Bristol-Myers Squibb has focused on delivering innovative medicines to help meet the needs of patients living with HIV-1. Our goal is to help individuals living with HIV-1 to live longer and healthier lives by achieving and maintaining viral suppression and by managing challenges associated with treatment resistance. We are investigating new ways to attack the HIV-1 virus - studies are ongoing involving this HIV-1 maturation inhibitor and another novel investigational therapy, an HIV-1 attachment inhibitor (BMS-663068).

**About Bristol-Myers Squibb**

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit [http://www.bms.com](http://www.bms.com) or follow us on Twitter at [http://twitter.com/bmsnews](http://twitter.com/bmsnews).

**Bristol-Myers Squibb Forward Looking Statement**

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that clinical trials of BMS-955176 will support regulatory filings, or that BMS-955176 will receive regulatory approval, or if approved, that it will become a commercially successful product. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb’s business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2014, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

**Language:**

English

**Contact:**

Bristol-Myers Squibb Company
Media:
Robert Perry, 609-419-5378
Cell: 407-492-4616
rob.perry@bms.com
or
Investors:
Ranya Dajani, 609-252-5330
ranya.dajani@bms.com
or
Bill Szablewski, 609-252-5894
william.szablewski@bms.com

**Ticker Slug:**

Ticker: BMY
Exchange: NYSE

demonstrates-positive