OSCIENT PHARMACEUTICALS CORP
Form 10-K
February 06, 2008
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark one)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2007

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission file number: 0-10824

OSCIENT PHARMACEUTICALS CORPORATION

(Exact name of registrant as specified in its charter)

Massachusetts	**04-2297484**
(State or other jurisdiction of incorporation or organization)	**(IRS employer identification number)**
1000 Winter Street, Suite 2200	
Waltham, Massachusetts	**02451**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number: (781) 398-2300

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $.10 Par Value	**NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act:

None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨ Accelerated filer x Non-accelerated filer ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

As of June 30, 2007, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was $56,587,564 as reported on the NASDAQ Global Market. The number of shares outstanding of the registrant s common stock as of February 1, 2008 was 13,764,113.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s proxy statement for use at its 2008 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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Oscient Pharmaceuticals Corporation

ANNUAL REPORT

ON FORM 10-K

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PART I

Forward-Looking Statements

Certain statements contained herein related to future operating losses and our potential for profitability, the sufficiency of our cash resources, future revenues and sales of ANTARA and FACTIVE, our discount and rebate programs for ANTARA and FACTIVE, possible partnering or other strategic opportunities for the continued development of Ramoplanin, potential marketing approval of FACTIVE in the European Union, as well as other statements related to the progress and timing of product development, present or future licensing, collaborative or financing arrangements or that otherwise relate to future periods, are forward-looking statements as defined by the Private Securities Litigation Reform Act of 1995. These statements represent, among other things, the expectations, beliefs, plans and objectives of management and/or assumptions underlying or judgments concerning the future financial performance and other matters discussed in this document. The words may, will, should, plan, believe, estimate, intend, anticipate, project, and expect and similar expressions are intended to identify forward-looking stateme forward-looking statements involve certain risks, estimates, assumptions, and uncertainties with respect to future revenues, cash flows, expenses and the cost of capital, among other things.

Some of the important risk factors that could cause our actual results to differ materially from those expressed in our forward-looking statements are included under the heading Risk Factors in this Form 10-K. We encourage you to read these risks carefully. We caution investors not to place significant reliance on the forward-looking statements contained in this report. These statements, like all statements in this report, speak only as of the date of this report (unless another date is indicated) and we undertake no obligation to update or revise forward-looking statements.

Item 1. Business

OVERVIEW

Oscient Pharmaceuticals Corporation (we , us , or the Company) is a commercial-stage pharmaceutical company marketing Food and Drug Administration (FDA)-approved products in the United States. Our strategy is to grow the sales of our existing products and to gain access to new products via transactions, including acquisition, in-licensing and co-promotion. We have developed a commercial infrastructure, including a national sales force calling on targeted primary care physicians, cardiologists, endocrinologists and pulmonologists in the United States.

We currently market two products: ANTARA® (fenofibrate) capsules, a cardiovascular product, and FACTIVE® (gemifloxacin mesylate) tablets, a fluoroquinolone antibiotic. ANTARA is approved by the FDA to treat hypercholesterolemia (high blood cholesterol) and hypertriglyceridemia (high triglycerides) in combination with a healthy diet. We license the rights to ANTARA from Ethypharm S.A. of France (Ethypharm) and began promoting ANTARA in late August 2006. In 2007, ANTARA generated approximately $59 million in net revenues. FACTIVE is indicated for the treatment of community-acquired pneumonia of mild to moderate severity, or CAP, and acute bacterial exacerbations of chronic bronchitis, or AECB. We license the rights to gemifloxacin, the active ingredient in FACTIVE tablets, from LG Life Sciences of the Republic of Korea (LG Life Sciences) and launched FACTIVE in the U.S. market in September 2004. In 2007, FACTIVE generated approximately $20 million in net revenues.

Additionally, we have a novel, late-stage antibiotic candidate, Ramoplanin for the treatment of *Clostridium difficile*-associated disease, or CDAD. We have made the strategic decision to concentrate our financial resources on building our revenues for products promoted to community-based physicians in the United States and are currently seeking to out-license, co-develop or sell the rights to Ramoplanin to a partner.

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ANTARA

The Fenofibrate and Cholesterol-Treatment Markets

Nearly 37 million Americans have total cholesterol values above recommended levels and heart disease remains the number one cause of death in the U.S. Abnormal cholesterol and lipid levels, known as dyslipidemia, can lead to the development of atherosclerosis, a dangerous hardening of blood vessels and a primary cause of coronary heart disease. Managing cholesterol levels is a complex undertaking and several therapeutic options are available to treat different types of abnormalities. Statins are the standard of care for lowering high levels of LDL-C (low density lipoprotein cholesterol). Fenofibrate products have demonstrated their utility in managing atherogenic dyslipidemia or mixed dyslipidemia (also known as lipid abnormalities) which are characterized by high triglycerides, low HDL-C (high density lipoprotein cholesterol), high levels of remnant-like particle cholesterol and a high proportion of cholesterol carried by small, dense LDL particles. Other drugs commonly used to treat lipid abnormalities include niacin and omega-3 fatty acids.

In 2007, total U.S. sales of fenofibrate products were approximately $1.7 billion, a 12% increase over 2006 sales. The fenofibrate market has experienced a 25% average annual growth in sales since 2003.

Indications and Efficacy

ANTARA is a once-daily formulation of fenofibrate approved for use in combination with a diet restricted in saturated fat and cholesterol to reduce elevated LDL-C (bad cholesterol), triglyceride and apolipoprotein B (free floating fats in the blood) levels and to increase HDL-C (good cholesterol) in adult patients with high cholesterol or an abnormal concentration of lipids in the blood. Fenofibrate products work primarily to lower triglycerides and increase HDL-C. ANTARA received FDA approval in November 2004 and is approved and marketed in 43 mg and 130 mg doses. The predominantly prescribed dose is 130 mg while the 43 mg dose is generally used for titration and in patients with impaired renal function. ANTARA was approved based in part on demonstrating its bioequivalence to Abbott Laboratories fenofibrate product Tricor®, meaning that, under FDA guidelines, the bioequivalence of the two products does not differ significantly when the two products are given under similar conditions. ANTARA was also studied in the Triglyceride Reduction in Metabolic Syndrome study, known as TRIMS, to measure the impact of ANTARA on cholesterol levels in patients with multiple cardiovascular risk factors and to assess the use of ANTARA without regard to meals.

In the treatment of hypercholesterolemia, ANTARA is approved as adjunctive therapy to diet to reduce elevated LDL-C, total cholesterol (total-C), triglycerides and apolipoprotein B (apo B) and to increase HDL-C in adult patients with primary hypercholesterolemia or mixed dyslipidemia. The effects of fenofibrate at a dose equivalent to 130 mg ANTARA per day were assessed in four randomized, placebo-controlled, double-blind, parallel-group studies. Fenofibrate therapy lowered LDL-C, total-C, and the LDL-C/HDL-C ratio. In these studies, fenofibrate therapy also lowered triglycerides, raised HDL-C and significantly reduced apo B as compared with placebo.

ANTARA is also indicated as an adjunctive therapy to diet for the treatment of hypertriglyceridemia, which affects an estimated 10% of American men over the age of 30 and 10% of American women over the age of 55. In clinical studies, the effects of fenofibrate on serum triglycerides were studied in two randomized, double-blind, placebo-controlled clinical trials of 147 hypertriglyceridemic patients for eight weeks. In patients with hypertriglyceridemia, treatment with fenofibrate at dosages equivalent to 130 mg ANTARA per day effectively decreased very low density lipoprotein (VLDL) triglycerides and VLDL cholesterol.

Mechanism of Action: ANTARA increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). The resulting decrease in triglycerides produces an alteration in the size and composition of LDL from small, dense particles (which are thought to be atherogenic due to their susceptibility to oxidation), to large

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buoyant particles. These larger particles have a greater affinity for cholesterol receptors and are catabolized rapidly. ANTARA also activates PPAR-alpha, which induces an increase in the synthesis of apoproteins A-I, A-II and HDL-cholesterol.

Competitive Advantages: The TRIMS study produced exclusive clinical data for ANTARA. In the study, ANTARA was evaluated in patients with elevated triglyceride levels and multiple cardiovascular risk factors. Of the 146 patients studied, 70% had hypertension and 32% had diabetes. The double-blind, placebo-controlled trial measured levels of total cholesterol, triglycerides, HDLs and LDLs, as well as other types of cholesterol, during eight weeks of therapy. In the study, ANTARA demonstrated the ability to reduce triglyceride and increase HDL-C levels after two weeks of therapy. At the end of therapy, patients treated with ANTARA had a statistically significant 37% reduction in their triglyceride levels and a statistically significant 14% increase in their HDL levels. ANTARA is distributed in 130 mg and 43 mg formulations, as compared to the 145 mg and 48 mg formulations of Tricor, which is marketed by Abbott Laboratories.

License Agreement

On August 18, 2006, we acquired the rights to ANTARA in the Unites States from Reliant Pharmaceuticals Inc. (Reliant) for $78.0 million plus approximately $4.3 million for ANTARA inventory, excluding estimated transaction costs. Under the terms of our acquisition of ANTARA, we assumed certain of Reliant s liabilities related to ANTARA, including obligations to make certain royalty and milestone payments on sales of ANTARA, and we were assigned rights to an exclusive license from Ethypharm S.A. (Ethypharm). In order to maintain the exclusivity of our rights, we must achieve minimum annual sales in the United States until February 2012 or alternatively compensate Ethypharm for any shortfall. During the term of the agreement with Ethypharm, we are obligated to pay a royalty on net sales of ANTARA in the U.S., including a royalty on other fenofibrate monotherapy products in formulations and dosage forms that may be substantially similar or identical to ANTARA developed by us. The license term expires in February 2020 and, absent notice of termination by either party, automatically renews for consecutive periods of two (2) years each. Under the terms of the agreement, at our option, Ethypharm is obligated to manufacture and deliver to us finished ANTARA capsules or to deliver bulk product to us for encapsulation and packaging. Ethypharm has a right of first refusal on any divestiture of the ANTARA rights by us. Additional Oscient obligations under the Ethypharm agreement include using commercially reasonable efforts to maintain a sales force of at least 150 representatives through February 2008 and funding a portion of the active pharmaceutical ingredient safety stock that Ethypharm is required to maintain.

Pursuant to the terms of our acquisition of ANTARA from Reliant, we also acquired the New Drug Application, or NDA, and the Investigational New Drug application, or IND, covering the ANTARA products in the United States, clinical data, inventory, the ANTARA® trademark in the United States and certain related contracts and licenses covering intellectual property rights related to the ANTARA products. We also assumed certain of Reliant s liabilities related to the ANTARA products.

We are not required to pay Reliant a royalty on the sale of the ANTARA products; however, we are required to pay a low single-digit royalty to Reliant for a specified time period on net sales of any line extensions and improvements to the ANTARA products which we develop, which include all products containing fenofibrate as their active pharmaceutical ingredient. We do not currently pay royalties to Reliant. We also agreed that we would not, at any time prior to August 2016, develop or sell any product in the United States that is a combination of fenofibrate and an omega-3 compound without the prior written consent of Reliant. On December 19, 2007, Reliant was acquired by GlaxoSmithKline.

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FACTIVE

Infectious Diseases Market

Infectious diseases represent the second leading cause of death worldwide accounting for over 14 million deaths each year, with lower respiratory tract infections alone causing 3.9 million deaths annually. Bacterial infections are the ninth leading cause of death in the U.S. Sales of antibiotics in the U.S. totaled $14 billion in 2007. Within the antibiotic market, fluoroquinolones, a product class with close to $3.9 billion in annual sales in the U.S. in 2007, have been gaining market share at the expense of older classes of antibiotics, according to Wolters Kluwer, a leading provider of pharmaceutical market data. This is a trend that is expected to continue as resistance to older antibiotic classes increases.

The principal classes of antibiotics include beta-lactams, fluoroquinolones, macrolides, tetracyclines, aminoglycosides, glycopeptides and trimethoprim combinations. Bacterial resistance to existing antibiotics has increased in recent years, leading to bacterial infection recurrences, treatment failures and higher costs. These factors have fueled a growing need for more effective products in existing antibiotic classes, as well as for products with new mechanisms of action.

Acute Bacterial Exacerbations of Chronic Bronchitis: Chronic bronchitis is a health problem associated with significant morbidity and mortality. It is estimated that chronic bronchitis affects approximately 9 million adults in the United States. Patients with chronic bronchitis are prone to frequent exacerbations, characterized by increased cough and other symptoms of respiratory distress. Longitudinal studies have estimated that 1 to 4 exacerbations occur each year in patients with chronic bronchitis; studies estimate that two-thirds are caused by bacteria. Exacerbations are estimated to account for approximately 12 million physician visits per year in the U.S. Antibiotic therapy, the standard treatment for acute bacterial exacerbations of chronic bronchitis, or AECB, is typically effective in reducing the course of illness for patients. Fluoroquinolones are frequently used to treat AECB due to their activity versus *Haemophilus influenzae* and *Moraxella catarrhalis,* two of the most common causes of these infections. Newer fluoroquinolones have enhanced activity versus *Streptococcus pneumoniae,* or *S. pneumoniae,* another common cause of these infections.

Community-Acquired Pneumonia: Community-acquired pneumonia, or CAP, is a common and serious illness in the United States. Of the estimated 4 to 5 million cases per year of CAP, nearly 1 million cases occur in patients over the age of 65. CAP cases result in approximately 10 million physician visits and as many as 1 million hospitalizations annually. Antibiotics are the mainstay of treatment for most patients with pneumonia, and where possible, antibiotic treatment should be specific to the pathogen responsible for the infection on a case by case basis. However, since the responsible pathogen is not identified in a high proportion of patients with CAP, physicians usually take an empiric approach to treatment in the first instance. Over the last decade, resistance to penicillins and macrolides has increased significantly, and in many cases, fluoroquinolones are now recommended as a first line of therapy due to their efficacy against a wide range of respiratory pathogens, including many antibiotic resistant strains. The most recent treatment guidelines from the Infectious Diseases Society of America and the American Thoracic Society recommend fluoroquinolones as a first-line treatment for certain higher-risk patients with CAP and as therapy for treating patients with pneumonia in geographic regions of the U.S. with high levels of macrolide-resistant *S. pneumoniae*.

Indications and Efficacy

FACTIVE is a member of the fluoroquinolone class of antibiotics. In April 2003, FACTIVE was approved by the FDA for the five-day treatment of AECB and seven-day treatment of CAP of mild to moderate severity. In July 2003, FACTIVE was also approved by the FDA to treat CAP caused by multi-drug resistant *S. pneumoniae*, a growing clinical concern. Multi-drug resistant *S. pneumoniae*, or MDRSP, is defined as *S. pneumoniae* resistant to two or more of the following antibiotics: penicillin, second-generation cephalosporins (such as cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole. In May 2007, FACTIVE was approved by the FDA for the five-day treatment of CAP.

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FACTIVE has potent *in vitro* activity against a wide range of Gram-positive, Gram-negative and atypical pathogens, including key respiratory pathogens, such as *S. pneumoniae, H. influenzae* and *M. catarrhalis.* FACTIVE is bactericidal at clinically achievable concentrations. Gemifloxacin, the active ingredient in FACTIVE, has minimum inhibitory concentrations, or MICs, as low as 0.032 µg/ml for *S. pneumoniae*. In clinical trials, FACTIVE has been administered to approximately 8,000 patients and had a good overall safety and tolerability profile. FACTIVE has been the subject of over 200 scientific publications and has been mentioned in nearly 300 scientific articles. Among the research published are data from a study involving 438 subjects indicating that a statistically significant higher percentage of patients treated with FACTIVE (71%) remained free of AECB recurrences than those treated with a comparator agent (58.5%) over a six-month period following treatment.

Mechanism of Action: FACTIVE tablets act by inhibiting bacterial DNA synthesis through the inhibition of both DNA gyrase and topoisomerase IV, two enzymes essential for bacterial growth and survival. Strains of *S. pneumoniae* showing mutations in both DNA gyrase and topoisomerase IV (double mutants) are resistant to most fluoroquinolones. Since gemifloxacin has the ability to inhibit both target enzymes at therapeutically relevant drug levels, some of these *S. pneumoniae* double mutants remain susceptible to FACTIVE. FACTIVE is also active against many strains of *S. pneumoniae* that are resistant to other classes of antibiotics.

Clinical Efficacy: The clinical development program for FACTIVE included 19 Phase III trials in respiratory tract infections. FACTIVE was studied for the treatment of acute bacterial exacerbations of chronic bronchitis in three pivotal, non-inferiority, double-blind, randomized, active-controlled clinical trials using 320 mg once daily for five-days. In these principal Phase III AECB studies, FACTIVE given once daily for five-days was at least as effective as the comparators given for seven-days, with clinical response rates in the FACTIVE arms ranging from 85.4% to 93.6%. FACTIVE was also studied for the treatment of CAP in three double-blind, randomized, active-controlled clinical studies, one open, active-controlled study, and two uncontrolled studies. The results of these studies showed that gemifloxacin was effective in the treatment of mild to moderate CAP.

Safety and Tolerability: FACTIVE tablets have been studied in approximately 8,000 patients in clinical trials and we estimate that to date, nearly 795,000 prescriptions have been written for FACTIVE since its launch in September 2004. In clinical trials, the incidence of adverse events reported for FACTIVE tablets was low and comparable to comparator drugs, namely beta-lactam antibiotics, macrolides and other fluoroquinolones. Most adverse events were described as mild to moderate. The most common adverse events reported in FACTIVE clinical trials were diarrhea, rash and nausea. In clinical trials across all durations of therapy, rash was reported in 2.8% of patients receiving gemifloxacin and was more commonly observed in patients with treatment durations greater than seven-days and patients less than 40 years of age, particularly females. In clinical trials conducted in 3,696 patients treated with five-days of FACTIVE therapy, the rate of rash reported was 1.1% vs. 0.7% for comparator antibiotics. Since the launch of the drug, the post-marketing adverse events reported have been consistent with those observed in the clinical development program, and with the fluoroquinolone class as a whole.

Competitive Advantages: We believe the competitive advantages of FACTIVE tablets include:

- FACTIVE has been shown in *in vitro* studies to be active against many bacterial isolates resistant to other classes of antibiotics.
- FACTIVE is the most active fluoroquinolone against *S. pneumoniae*, one of the most prevalent pathogens found in lower respiratory tract infections, compared to the currently marketed fluoroquinolones (MIC_{90} 0.032 µg/mL).
- FACTIVE has a dual mechanism of action in bacteria, targeting two enzymes essential for bacterial growth and survival at therapeutically relevant drug levels, and as a result we believe FACTIVE has low potential for generating bacterial resistance.
- FACTIVE can be dosed once daily, with short courses of therapy (five-days) for both AECB and CAP.

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FACTIVE is effective in the treatment of CAP due to penicillin-resistant *S. pneumoniae* and due to MDRSP. In clinical trials, of 22 patients with MDRSP treated with FACTIVE for seven-days, 19 (87%) achieved both clinical and bacteriological success at follow-up.

FACTIVE achieves high concentration levels in lung and bronchial tissues and in secretions.

FACTIVE has composition of matter patent protection which extends into 2018, longer than the composition of matter patent protection for any currently marketed fluoroquinolone or other antibiotic widely used to treat respiratory tract infections.

Post-Marketing Commitments: As a post-marketing commitment to the FDA, we completed a Phase IV trial of FACTIVE. This prospective, randomized study examined the activity of FACTIVE tablets (5,000 patients) versus an active comparator (2,500 patients) in treating patients with mild to moderate CAP or AECB. The study included patients of different ethnicities so that safety information in populations not substantially represented in the existing clinical trial program could be collected, specifically as it relates to rash. This Phase IV trial was initiated in the fall of 2004 and was completed in January 2007. In connection with the approval of FACTIVE tablets, the FDA has also required us to perform a utilization study to obtain data on the prescribing patterns and use of FACTIVE tablets for the first three years after initial marketing in the U.S. As part of this requirement, we furnish interim reports to the FDA describing the number of prescriptions issued, including refills and the diagnoses for which the prescriptions are dispensed. The final report of the utilization study is scheduled for submission in the first half of 2008. In the future, we need only to provide the FDA with annual reports containing safety information.

Additional Development of FACTIVE

Five-Day Treatment of CAP: We completed a clinical trial to demonstrate that a five-day course of FACTIVE for the treatment of mild to moderate CAP is as effective as the previously approved seven-day course of treatment. On September 21, 2006, we received an approvable letter from the FDA for the supplemental New Drug Application (sNDA) seeking approval for the five-day treatment of CAP with FACTIVE tablets. In accordance with the letter, we provided clarification and additional interpretation regarding certain data included in the application to assist the FDA in its evaluation. On May 1, 2007, the FDA approved FACTIVE for the five-day treatment of CAP.

In the five-day CAP clinical trial, a five-day course of therapy with FACTIVE was shown to be as effective as the FDA-approved seven-day course of treatment, with both arms displaying excellent clinical response rates. Further, data showed that the bacteriological and radiologic success rates with five-days of therapy were also non-inferior to the success rates with seven-days of therapy. The multicenter, randomized, double-blind study enrolled 510 patients with CAP, with 469 patients comprising the per protocol group. Investigators measured clinical and bacteriological response at end of therapy as well as clinical, bacteriological and radiologic response at follow-up (two to three weeks post therapy). Clinical response at follow-up, the primary endpoint, in the per protocol group was 95% for the five-day treatment arm and 92% for the seven-day treatment arm (95% CI: -1.48, 7.42), demonstrating non-inferiority between the two groups. Further, clinical response at end of therapy in the per protocol group was 96% for the five-day group and 96% for the seven-day group (95% CI: -3.85, 3.42). The study also yielded encouraging results for bacteriological response. Bacteriological response in the per protocol population was 91% for the five-day and seven-day groups at follow-up (95% CI: -6.89, 7.93) and 94% for the five-day group and 96% for the seven-day group (95% CI: -8.27, 3.25) at end of therapy. The study demonstrated radiologic response at follow-up in the per protocol population of 98% for the five-day arm and 93% for the seven-day arm (95% CI: 0.35, 7.91). FACTIVE was well-tolerated in the study, with a low withdrawal rate due to adverse events: 1.2% for the five-day group and 2.0% for the seven-day group. The most common adverse event reported was a laboratory finding of elevated liver enzymes (increased ALT and increased AST). Analysis of all ALT/AST values demonstrated that the elevations were significantly associated with baseline ALT levels (elevated in many patients) with no significance or association with a particular treatment group. There was also no evidence of symptomatic hepatic events. In addition, the rate of drug-related rash in both treatment groups was low: 0.4% for the five-day arm and 2.8% for the seven-day arm. There were no withdrawals due to rash.

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Acute Bacterial Sinusitis: As part of the FACTIVE development program, several studies relating to acute bacterial sinusitis, or ABS, were completed, and, in November 2005, we filed an sNDA for ABS. In September 2006, the FDA s Anti-Infective Drugs Advisory Committee voted not to recommend approval of this sNDA. In November 2006, we voluntarily withdrew our sNDA seeking approval of the ABS indication.

FACTIVE IV: An intravenous formulation of gemifloxacin has also been studied. If we elect to further pursue such a formulation, additional formulation development will be necessary before initiating a bioequivalence study.

License Agreement with LG Life Sciences

We license the rights to gemifloxacin, the active ingredient in FACTIVE tablets, from LG Life Sciences. We have the rights to commercialize gemifloxacin in North America, France, Germany, the United Kingdom, Luxembourg, Ireland, Italy, Spain, Portugal, Belgium, the Netherlands, Austria, Greece, Sweden, Denmark, Finland, Norway, Iceland, Switzerland, Andorra, Monaco, San Marino, Vatican City, Poland, Czech Republic, Slovakia, Slovenia, Hungary, Estonia, Latvia, Lithuania, Liechtenstein, Malta, Cyprus, Romania, Bulgaria, Croatia, Serbia and Montenegro, Bosnia and Herzegovina, Albania and the Former Yugoslav Republic of Macedonia. The term of the agreement with respect to each country extends at least through the life of the patents covering gemifloxacin in such country. In the United States, the last of the currently issued patents for composition of matter expires in 2018. The patent term could extend further in countries outside of the U.S. depending upon several factors, including whether we obtain patent extensions and the timing of our commercial sale of the product in a particular country.

Under the terms of the agreement, LG Life Sciences has agreed to supply and we are obligated to purchase from LG Life Sciences all of our anticipated commercial requirements for the FACTIVE active pharmaceutical ingredient, or API. LG Life Sciences currently supplies the FACTIVE API from its manufacturing facility in South Korea.

The agreement with LG Life Sciences also requires that we achieve a minimum gross sales level of $30 million from our licensed territories over a 12-month period of time starting on the third anniversary from the launch of FACTIVE in the U.S. in 2004 which, if not met, LG Life Sciences could elect to terminate the agreement and have the technology be returned to LG Life Sciences. Under this agreement, we are responsible, at our expense and through consultation with LG Life Sciences, for the clinical and commercial development of gemifloxacin in the countries covered by the license, including the conduct of clinical trials, the filing of drug approval applications with the FDA and other applicable regulatory authorities and the marketing, distribution and sale of gemifloxacin in our territory.

We are obligated to pay a royalty on sales of FACTIVE in North America and the territories covered by the license in Europe. These royalty obligations expire with respect to each country covered by the agreement on the later of (i) the expiration of the patents covering FACTIVE in such country or (ii) the expiration of data exclusivity in Mexico, Canada or the European Union respectively, or 2014 in the U.S. We are also obligated to make aggregate milestone payments of up to approximately $40 million (not including payments to LG Life Sciences previously made pursuant to up-front obligations or achievements of certain milestones) including milestone payments required by the amendments described below upon achievement of additional regulatory approvals and sales thresholds.

Collaborations and Partnerships for FACTIVE

Pfizer, S.A. de C.V. On February 6, 2006, we entered into a Sublicensing and Distribution Agreement with Pfizer, S.A. de C.V. (Pfizer Mexico), pursuant to which we sublicensed our rights to market FACTIVE tablets in Mexico to Pfizer Mexico. In exchange for those rights, Pfizer Mexico has made an up-front payment and has agreed to pay milestone payments upon obtaining certain regulatory approvals and sales goals, as well as

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royalties on future sales. The up-front payment is being recognized as revenue over the term of our continuing obligations under the agreement. These royalty rates are subject to reduction upon expiration of certain patents in Mexico for FACTIVE or if a generic form of gemifloxacin has a material impact on Pfizer Mexico s sales volumes in Mexico. Pfizer Mexico is obligated to exclusively purchase from us, and we must exclusively supply, all API for FACTIVE. The agreement with Pfizer Mexico may be terminated by either party upon the occurrence of certain termination events, including Pfizer Mexico s right to terminate at any time after the first anniversary of launch of FACTIVE tablets in Mexico upon nine months prior written notice. Upon termination, Pfizer Mexico is obligated to assign any and all rights to regulatory approvals in Mexico to us or our designee.

In October 2006, Pfizer Mexico launched its promotion and marketing of FACTIVE-5 in Mexico for the five-day treatment of acute bacterial exacerbations of chronic bronchitis (AECB), acute bacterial sinusitis (ABS) and community-acquired pneumonia (CAP).

Abbott Laboratories Ltd. On August 9, 2006, we granted the commercialization rights to FACTIVE tablets in Canada to Abbott Laboratories, Ltd. (Abbott Canada), the Canadian affiliate of Abbott. In exchange for those rights, Abbott Canada agreed to a transfer price on product purchases and to make certain payments to us upon achievement of certain regulatory and sales milestones. FACTIVE tablets are currently approved in Canada for the five-day treatment of AECB. We subsequently amended the agreement on January 31, 2008 whereby Abbott Canada s development and commercialization obligations were substantially reduced. In accordance with the terms of the amendment, Abbott Canada will continue to maintain FACTIVE tablets in its current product price list and it will continue to pay us a transfer price on FACTIVE tablets purchases. Abbott Canada is not required to pursue the CAP and ABS indications. Additionally, the amendment provides that we can terminate the agreement at any time with prior notice to Abbott Canada and Abbott Canada can terminate with prior notice to us after November 30, 2008.

Menarini International Operation Luxembourg SA. We entered into a License, Supply and Marketing Agreement with Menarini International Operation Luxembourg SA (Menarini), a wholly-owned subsidiary of Menarini Industrie Farmaceutiche Riunite S.r.l. dated December 28, 2006, whereby we sublicensed our rights to sell FACTIVE tablets in the European Union to Menarini. Under the terms of our agreement, Menarini is responsible for obtaining regulatory approval for FACTIVE in the European Union, and Oscient has agreed to reimburse Menarini for expenses associated with such regulatory development up to an agreed limit. Menarini has also paid us an up-front payment which is being recognized over the term of our continuing obligations under the agreement of approximately thirty-three months. Menarini has also agreed to pay us milestone payments upon obtaining certain regulatory and reimbursement approvals and upon achieving certain annual net sales goals, which could total up to $23.0 million, if all the milestones are achieved. Menarini will pay us a transfer price on purchases of the active pharmaceutical ingredient, or API, for FACTIVE, which is determined based on a percentage of quarterly sales of FACTIVE by Menarini in Europe. Menarini is also obligated to exclusively purchase from us, and we must exclusively supply, all API for FACTIVE to be sold in Europe for the earlier of (i) the expiration of the life of certain patents covering the product or (ii) expiration of data exclusivity. Our agreement with Menarini may be terminated by either party upon the occurrence of certain termination events, including Menarini s right to terminate if the European regulatory authorities do not recommend approval of FACTIVE at various stages of the approval process with a package insert, or label, that meets certain requirements as to the safety, dosing and indications for which FACTIVE may be prescribed. Menarini may also terminate the agreement if it does not receive approval for reimbursement from European member countries that is above a certain minimum price per tablet. Upon termination, Menarini is obligated to assign any and all rights to regulatory approvals in the European Union to Oscient or its designee.

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RAMOPLANIN

***Clostridium difficile*-Associated Disease (CDAD)**

CDAD, a serious form of colitis caused by toxins produced by the Gram-positive bacterium *Clostridium difficile* (*C. difficile*), is the most commonly recognized microbial cause of diarrhea, resulting from high rates of colonization in hospitalized patients and the frequent use of antimicrobials. About 3% of healthy adults and 16 to 35% of hospital patients are colonized with *C. difficile* either prior to or during admission. Because it is a spore-forming bacterium, *C. difficile* is readily spread from person to person, especially in the hospital and nursing home environment. Under certain conditions, such as extended antibiotic therapy and gastrointestinal surgery, *C. difficile* can colonize the gut and release toxins, leading to bowel inflammation and severe diarrhea. Severe cases can occur and involve the development of fulminant colitis (severe inflammation of the colon); such occurrences can be life threatening, especially in elderly or immunocompromised populations.

Over 400,000 patients are treated in U.S. hospitals each year for CDAD. CDAD is associated with an average increased hospital stay of 3.6 days and an average increase in hospital costs of over $3,600 per patient. It is estimated that the annual increase in hospital costs attributable to CDAD exceeds $1 billion in the U.S.

Two studies published in *The New England Journal of Medicine* in December 2005 describe a new strain of *C. difficile,* one that produces 16 to 23 times more toxins *in vitro* than do other strains, thus potentially contributing to its virulence. The very high incidence and mortality rates are of particular concern with this new strain. Data support the concept that this highly virulent strain is causing epidemic disease at certain locations and is associated with more frequent and more severe disease.

Current therapies for the treatment of CDAD include oral metronidazole and oral vancomycin. However, recent relapse rates have increased to 28%. The use of oral vancomycin has been associated with the emergence of vancomycin-resistant organisms, including vancomycin-resistant enterococci, or VRE. Resistance has also been reported for metronidazole.

Ramoplanin Overview

In October 2001, we in-licensed U.S. and Canadian rights to Ramoplanin from Vicuron Pharmaceuticals Inc., or Vicuron, a wholly-owned subsidiary of Pfizer Inc., and on February 3, 2006, acquired worldwide rights from Vicuron, assuming full control of Ramoplanin manufacturing, development and commercialization. Ramoplanin is a novel glycolipodepsipeptide antibiotic produced by fermentation of the bacteria *Actinoplanes*, with activity against Gram-positive aerobic and anaerobic microorganisms. In preclinical studies, Ramoplanin has been shown to be bactericidal against most Gram-positive species, including methicillin-resistant staphylococci, VRE and *C. difficile,* including the recent epidemic strains. Ramoplanin inhibits the bacterial cell wall peptidoglycan biosynthesis with a mechanism different from that of vancomycin, teicoplanin or other cell wall-synthesis inhibitors. No evidence of cross-resistance between Ramoplanin and other glycopeptide antibiotics has been observed *in vitro* to date. Ramoplanin has a unique profile that may make it particularly well-suited for killing bacteria in the GI tract.

In 2004, we completed a Phase II trial to assess the safety and efficacy of Ramoplanin in the treatment of CDAD. The open-label study enrolled 87 patients in 24 U.S. sites. The trial compared two doses of Ramoplanin (200 mg and 400 mg twice daily) to vancomycin (125 mg four times daily). Both agents were administered for ten days, during which data on Ramoplanin was collected to measure safety and efficacy. The primary endpoint of the study was response rate at the test-of-cure visit, 7 to 14 days post-therapy. For this trial, the response rates were 60% for Ramoplanin 200 mg, 71% for Ramoplanin 400 mg, and 78% for vancomycin 125 mg in the clinically evaluable population. While the study did not meet its primary endpoint, non-inferiority at the test-of-cure visit, the response rates for all three arms were comparable. A potentially more clinically relevant endpoint, response at the end of therapy, was also assessed. At the end of therapy, the response rates were 83% for Ramoplanin 200 mg, 85% for Ramoplanin 400 mg and 86% for vancomycin 125 mg.

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We agreed with the FDA to a Special Protocol Assessment regarding the specific components of a Phase III program that, if completed successfully, would support regulatory approval for the indication. On January 8, 2008, the United States Patent and Trademark Office (USPTO) issued us a patent relating to methods of use of Ramoplanin for the treatment of CDAD.

Potential Competitive Advantages: We believe the potential competitive advantages of Ramoplanin are:

- Ramoplanin belongs to a novel class of antibiotics and there have been no observed cases of bacterial resistance or cross-resistance with other antibiotics to date.
- Ramoplanin is orally administered, but not absorbed into the bloodstream, so it concentrates and exerts its killing effects in the GI tract.
- Its bactericidal effect may result in lower potential for bacteria to develop resistance.
- Ramoplanin has a Gram-positive spectrum of activity and low potency against Gram-negative anaerobes that normally colonize the GI tract making it less likely that its use will result in the overgrowth of other opportunistic organisms or in the elimination of normal, healthy bacteria.
- Along with its activity against *C. difficile,* Ramoplanin has demonstrated *in vitro* activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and VRE. Both organisms are associated with causing serious infections.

Acquisition of Expanded Rights: In exchange for the assignment of the rights for Ramoplanin under the acquisition agreement with Pfizer, we made a one-time, up-front payment to Pfizer and agreed to make additional milestone payments for regulatory filings and approvals in various countries. We will also pay mid-single-digit to low double-digit royalties to Pfizer on net sales of Ramoplanin dependent upon the territory.

With the acquisition of ANTARA, we have made the strategic decision to concentrate our financial resources on building our revenues for products promoted to community-based physicians in the United States and are currently seeking to out-license, co-develop or sell our rights to Ramoplanin to a partner. There can be no assurance that we will be able to license or divest Ramoplanin to a partner on acceptable terms, or at all.

SALES AND MARKETING

We market ANTARA and FACTIVE through our sales and marketing organization in the U.S, which is currently comprised of approximately 270 field sales personnel, including sales representatives, district managers and regional sales directors. Sales and marketing functions are located at our New Jersey office. Our sales representatives focus on community-based physicians and opinion leaders who are potential high prescribers of fluoroquinolones and/or fenofibrate products. We have also built a team of professionals with experience in insurance and government reimbursement, medical affairs and marketing. Our strategy is to continue to leverage our existing commercial infrastructure through the acquisition, in-license or co-promotion of additional marketed products to market to community-based physicians in the United States. Longer term, we anticipate expanding our commercial infrastructure to reach additional physicians.

Our strategy includes granting commercialization rights to FACTIVE tablets in territories outside of the U.S. to third parties to leverage the additional resources that a pharmaceutical marketing partner with expertise in such countries can provide. Thus, we have partnered with following entities:

- On February 6, 2006, we sublicensed our rights to sell FACTIVE tablets in Mexico to Pfizer, S.A. de C.V. (Pfizer Mexico), the largest pharmaceutical company in Mexico. Pfizer Mexico is commercializing FACTIVE for community-acquired pneumonia, acute bacterial exacerbations of chronic bronchitis and acute bacterial sinusitis with three national field sales forces and one specialty field sales

force.

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On August 9, 2006, we granted the commercialization rights to FACTIVE tablets in Canada to Abbott Laboratories, Ltd. (Abbott Canada), the Canadian affiliate of Abbott; however, on January 31, 2008, we amended the agreement whereby Abbott Canada s obligations to commercialize FACTIVE tablets were substantially reduced.

On December 27, 2006, we sublicensed our rights to sell FACTIVE tablets in Europe to Menarini International Operation Luxembourg SA (Menarini), the second largest primary care pharmaceutical company in Europe. Menarini is responsible for obtaining regulatory approval for FACTIVE in Europe and will leverage its regulatory and marketing experience to pursue approval and launch of FACTIVE in Europe.

COMPETITION

The pharmaceutical industry generally is characterized by rapidly evolving technology and intense competition. Our competitors include pharmaceutical and biotechnology companies both in the United States and abroad. Many of our competitors have substantially greater capital resources, facilities and human resources than we do.

Competition with respect to our products and product candidates is and will be based on, among other things:

our sales and marketing expertise,

our clinical trial results and post marketing experience,

our ability to obtain appropriate regulatory approvals for our product candidates in a cost-efficient and timely manner and subsequently remain in regulatory compliance,

our ability to secure adequate reimbursement for our products from public and private healthcare payors,

our ability to attract and retain qualified personnel,

our ability to obtain patent protection and defend our patent challenges,

our ability to in-license product candidates for clinical development,

our ability to gain access to new products via co-promotion or in-license agreements or product acquisitions,

our ability to secure sufficient capital resources to fund our clinical development and sales and marketing operations, and

our ability to secure sufficient capital resources to execute transactions to gain access to new products.

Because we rely primarily on in-licensing, co-promotion and acquisitions of products and product candidates to expand our portfolio, it is important to note that we may also face increasing competition for in-licensing, co-promotion and acquisition opportunities from leading pharmaceutical and biotechnology companies. We cannot be certain that we will be able to in-license product opportunities in the future or acquire new products.

ANTARA

ANTARA is a fenofibrate product approved by the FDA to treat hypercholesterolemia and hypertriglyceridemia in combination with a healthy diet. The marketing of branded versions of fenofibrate could reduce our net sales of ANTARA and adversely impact our revenues. The primary competition for ANTARA in the fenofibrate market is Tricor, a product manufactured by Abbott Laboratories, which accounted for approximately 92% of U.S. fenofibrate sales for the twelve month period ended December 31, 2007. ANTARA also competes with Triglide®, a fenofibrate marketed by Sciele Pharma, Inc., which accounted for approximately 2% of U.S. fenofibrate sales for the twelve month period ended December 31, 2007.

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Additionally, ANTARA competes with Lipofen, a 150 mg fenofibrate product, which was recently launched and is currently being marketed by ProEthic Pharmaceuticals, Inc. LifeCycle Pharma A/S recently announced the FDA approval of their 120 mg branded fenofibrate product, which had been filed with the FDA in late 2006 referencing ANTARA in accordance with the provisions of section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. LifeCycle Pharma granted Sciele Pharmaceuticals rights to market its fenofibrate product in North America, which when launched can also be expected to compete with ANTARA.

Several generic versions of fenofibrate in varying doses are also available for the treatment of dyslipidemias. Revenues from these products accounted for approximately 2% of total U.S. sales of fenofibrate products in 2007. In May 2005, Teva Pharmaceutical Industries, Ltd. (Teva) obtained FDA approval to market a generic version of Abbott Laboratories 160 mg Tricor tablet (which is no longer marketed or sold). In addition, Solvay S.A., Abbott Laboratories partner announced on January 23, 2008, that Teva had filed an Abbreviated New Drug Application (ANDA) with a Paragraph IV certification seeking the approval of a generic version of Tricor 145 mg. If a generic version of Abbott Laboratories Tricor 145 mg product is approved by the FDA, the percentage of total revenues attributable to generic fenofibrate products would likely increase. There are also several other FDA-approved products and products in development for similar indications as ANTARA which could compete with ANTARA, including statins, omega-3 fatty acids, niacin, ezetimibe and fixed-dose, combination products.

The growth of any of these branded products or the marketing of generic fenofibrate products could result in a decrease in ANTARA sales, create pressure on the price at which we are able to sell ANTARA, reduce our profit margins, reduce our net sales of ANTARA and adversely impact our revenues.

FACTIVE

FACTIVE tablets are approved for the treatment of community-acquired pneumonia of mild to moderate severity and acute bacterial exacerbations of chronic bronchitis. There are several classes of antibiotics that are primary competitors for the treatment of these indications, including other fluoroquinolones (levofloxacin, ciprofloxacin and moxifloxacin), macrolides (clarithromycin and azithromycin) and penicillins (amoxicillin/clavulanate potassium).

Many generic antibiotics are also currently prescribed to treat these infections. Moreover, a number of the antibiotic products that are competitors of FACTIVE tablets have composition of matter patents which have gone or will be going off patent at dates ranging from 2003 to 2016. As these competitors lose patent protection, their manufacturers will likely decrease their promotional efforts. However, makers of generic drugs will likely begin to produce some of these competing products and this could result in pressure on the price at which we are able to sell FACTIVE tablets and reduce our profit margins.

Ramoplanin

Ramoplanin is in clinical development for the treatment of CDAD. We are aware of two products currently utilized in the marketplace: Vancocin® pulvules (vancomycin), a product marketed by ViroPharma Inc., and metronidazole, a generic product, for treatment of this indication. We are also aware of several other companies with products in development for the treatment of CDAD.

Legacy Assets

Our alliance-related product development programs are all in preclinical stages, and it is therefore not possible to identify any product profiles or competitors for these product development programs at this time. Our industry is very competitive and it therefore is likely that if and when product candidates from our early stage internal programs or our alliance programs reach the clinical development stage or are commercialized for sale, these products will also face competition.

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GOVERNMENT REGULATION

Regulation by governmental entities in the United States and other countries will be a significant factor in the development, manufacturing, distribution and marketing of any product candidates that we develop or commercialize. The extent to which such regulation may apply to us and our licensees will vary depending on the nature of the product. Virtually all of our pharmaceutical products, including expanded uses of our pharmaceutical products, will require regulatory approval by governmental agencies prior to commercialization. In particular, the FDA in the United States and similar health authorities in foreign countries subject human therapeutic and vaccine products to rigorous preclinical and clinical testing, and require review and approval of extensive data in order to permit commercial marketing.

Virtually all aspects of our activities are regulated by federal and state statutes and regulations, and government agencies. The research, development, manufacturing, processing, packaging, labeling, distribution, sale, advertising, promotion, import and export of our products, and disposal of waste products arising from these activities, are subject to regulation by one or more federal agencies and their state equivalents, including the FDA, the Consumer Product Safety Commission, the Occupational Safety and Health Administration and the Environmental Protection Agency, as well as by state and local governments and governmental authorities in those foreign countries in which we or our partners operate.

Noncompliance with applicable regulatory policies or requirements of the FDA or other governmental authorities could subject us to enforcement actions, such as suspensions of product distribution, seizure of products, product recalls, civil monetary and other penalties, criminal prosecution and penalties, injunctions, whistleblower lawsuits, failure to approve pending drug product applications or total or partial suspension of product marketing approvals. Similar civil or criminal penalties could be imposed by other government agencies or the agencies of the states and localities in which our products are manufactured, sold or distributed, and could have ramifications for our contracts with government agencies. These enforcement actions would detract from management s ability to focus on our daily business and would have an adverse effect on the way we conduct our daily business, which could severely impact future profitability.

Product Approval

For innovative, or non-generic, new drugs, an FDA-approved new drug application, or NDA, is required before the drugs may be marketed in the United States. The NDA must contain data to demonstrate that the drug is safe and effective for its labeled uses, and that it will be manufactured to appropriate quality standards. In order to demonstrate safety and effectiveness, an NDA typically must include or reference preclinical data from animal and laboratory testing and clinical data from controlled trials in humans. For a new chemical entity, this generally means that lengthy, uncertain and rigorous pre-clinical and clinical testing must be conducted. For compounds that have a record of prior or current use, it may be possible to utilize existing data or medical literature and limited new testing to support an NDA. Any preclinical laboratory and animal testing must comply with FDA s good laboratory practice and other requirements. Clinical testing in human subjects must be conducted in accordance with FDA s good clinical practice and other requirements. In order to initiate a clinical trial, the sponsor must submit an investigational new drug application, or IND, to the FDA or meet one of the narrow exemptions that exist from the IND requirement. Clinical research must also be reviewed and approved by independent institutional review boards, or IRBs, at the sites where the research will take place, and the study subjects must provide informed consent. The FDA also regulates and typically inspects manufacturing facilities, equipment and processes used in the manufacturing of pharmaceutical products before granting approval to market any drug. Each NDA submission requires a substantial user fee payment, unless a waiver or exemption applies. FDA has committed generally to review and make a decision concerning approval on an NDA within 10 months, and on a new priority drug within six months. However, final FDA action on the NDA can take substantially longer, and where novel issues are presented there may be review and recommendation by an independent FDA advisory committee. The FDA can also refuse to file and review an NDA it deems incomplete or not properly reviewable.

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Clinical trial programs in humans generally follow a three-phase process. Typically, Phase I studies are conducted in small numbers of healthy volunteers or, on occasion, in patients afflicted with the target disease, to determine the metabolic and pharmacological action of the product candidate in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. In Phase II, studies are generally conducted in larger groups of patients having the target disease or condition in order to validate clinical endpoints, and to obtain preliminary data on the effectiveness of the product candidate and optimal dosing. This phase also helps determine further the safety profile of the product candidate. In Phase III, large-scale clinical trials are generally conducted in hundreds of patients having the target disease or condition to provide sufficient data for the statistical proof of effectiveness and safety of the product candidate as required by U.S. and foreign regulatory agencies.

The FDA can, and does, reject new drug applications, require additional clinical trials, grant approvals on only a restricted basis even when product candidates performed well in clinical trials, or require further studies as a condition of approval. In addition, the Food and Drug Administration Amendments Act of 2007 (FDAAA) permits the agency to require new drug applicants to submit a risk evaluation and mitigation strategy (REMS) if the agency determines that a REMS is necessary to ensure that the benefits of the drug outweigh the risks.

Generic drugs are approved through an abbreviated process based on the submission to FDA of an abbreviated new drug application, or ANDA. The ANDA must seek approval of a drug product that has the same active ingredient(s), dosage form, strength, route of administration, and labeling as a so-called reference listed drug approved under an NDA, although some limited exceptions may be permitted. The ANDA also generally contains limited clinical data to demonstrate that the product covered by the ANDA is absorbed in the body at the same rate and to the same extent as the reference listed drug. This is known as bioequivalence. In addition, the ANDA must contain information regarding the manufacturing processes and facilities that will be used to ensure product quality, and must contain certifications to patents listed with the FDA for the reference listed drug. Special procedures apply when an ANDA contains certifications stating that a listed patent is invalid or not infringed, and if the owner of the patent or the NDA for the reference listed drug brings a patent infringement suit within a specified time, an automatic stay bars FDA approval of the ANDA for a specified period of time pending resolution of the suit or other action by the court. The amount of testing and effort that is required to prepare and submit an ANDA is generally substantially less than that required for an NDA.

In addition to the NDA and ANDA procedures, there is an additional approval mechanism known as a 505(b)(2) application. A 505(b)(2) application is a form of an NDA where the applicant does not have a right to reference all or some of the data being relied upon for approval. Under current regulations and FDA policies, 505(b)(2) applications can be used where the applicant is relying in part on published literature or on findings of safety or effectiveness in another company s NDA. This might be done, for example, where the applicant is seeking approval for a new use for a drug that has already been approved for a different use or for a different formulation of the same drug that is already approved for the same use.

The use of 505(b)(2) applications is the subject of ongoing legal controversy, and it is thus not clear what the permitted use of a 505(b)(2) application might be in the future.

In European Union countries (where our partner, Menarini is currently attempting to gain marketing approval for certain indications of FACTIVE) and in Canada, regulatory requirements and approval processes are similar in principle to those in the United States and can be at least as rigorous, costly and uncertain. Additionally, depending on the type of drug for which an applicant is requesting approval, there are currently two potential tracks for marketing approval in European Union countries: the centralized procedure and a de-centralized process which requires requesting approval on a country-by-country basis. These review mechanisms may ultimately lead to approval in all European Union countries, but each method grants all participating countries some decision making authority in product approval.

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Post-Approval Requirements

Products on the market are subject to continual review by the FDA. If previously unknown problems are discovered or if there is a failure to comply with applicable regulatory requirements, the FDA may restrict the marketing of an approved product, cause the withdrawal of the product from the market, or under certain circumstances seek recalls, seizures, injunctions or criminal sanctions. For example, the FDA may require a change in labeling for an approved marketing application or additional studies for any marketed drug product if new information reveals questions about a drug s safety or effectiveness. In addition, changes to the product, the manufacturing methods or locations, or labeling are subject to additional FDA approval, which may or may not be received, and which may be subject to a lengthy FDA review process.

Manufacturing facilities that produce drugs are subject to extensive regulation both by the FDA, state and local governments, and foreign regulatory authorities. These laws and regulations require, among other things, that our facilities and the facilities of third parties, such as LG Life Sciences, Ethypharm S.A., Patheon Pharmaceuticals Inc. (our third party finished-product manufacturer for FACTIVE tablets) and Catalent Pharma Solutions (our third party packager of ANTARA capsules), be registered with the FDA and other regulatory authorities, comply with current good manufacturing practices requirements, and pass periodic inspections by the FDA and other regulators. Facilities in foreign countries may be subject to inspection by the FDA, local regulators or both. Current good manufacturing practices, or cGMP, require extensive recordkeeping, quality control, documentation and auditing to ensure that products meet applicable specifications. Failure to comply with these requirements can result in warning letters, requirements of remedial action, and, in the case of more serious failures, suspension of manufacturing, seizure, injunctions or recall of product and fines and other penalties. Compliance with these requirements can be time consuming, costly and can result in delays in product approval or product sales.

In addition to cGMP requirements, certain of our products must also be packaged with child-resistant and senior friendly packaging under the Poison Prevention Packaging Act and Consumer Product Safety Commission regulations. Products that do not comply with these requirements can be considered misbranded and subject to seizure, recall, monetary fines, and other penalties.

The distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. States require the registration of manufacturers and distributors who provide pharmaceuticals, including in certain states even if these manufacturers or distributors have no place of business within the state but satisfy other nexus requirements, for example, the shipment of products into such state. States also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that are requiring manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Both the PDMA and state laws limit the distribution of prescription drug product samples to licensed practitioners and impose other requirements to ensure accountability in the distribution of samples.

Other reporting and recordkeeping requirements also apply for marketed drugs, including for most products requirements to review and report cases of adverse events. Product advertising and promotion are subject to FDA and state regulation, including requirements that promotional claims conform to any applicable FDA approval, and be appropriately balanced and substantiated. We are also subject to various federal and state laws pertaining to health care fraud and abuse, including the anti-kickback provisions of the Social Security Act, the False Claims Act, the Veterans Healthcare Act, and the implementing regulations and policies of the United States Health and Human Services Office of Inspector General and United States Department of Justice, as well as similar state laws. Anti-kickback laws make it illegal for a prescription drug manufacturer or marketer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase, recommendation or prescription of a particular drug, covered by a federal healthcare program, unless

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one of several narrow safe harbors or other exceptions applies. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, for payment to third-party government payors, including Medicare and Medicaid, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

Similar laws apply in other countries, including anti-bribery prohibitions in the European Union and member countries of the European Union.

Other Regulatory and Compliance Requirements

Under the laws of the United States, the countries of the European Union and other nations, we and the institutions where we sponsor research are subject to obligations to ensure the protection of personal information of human subjects participating in our clinical trials. In the United States, these laws include the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, the implementing regulations of the United States Department of Health and Human Services, and state medical records privacy laws. We have instituted procedures that we believe will enable us to comply with these requirements and the contractual requirements of our data sources. The laws and regulations in this area are evolving and further regulation, if adopted, could affect the timing and the cost of future clinical development activities.

We are subject to the United States Foreign Corrupt Practices Act, which prohibits corporations and individuals from engaging in specified activities to obtain or retain business or to influence a person working in an official capacity. Under this act, it is illegal to pay, offer to pay, or authorize the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. Our present and future business has been and will continue to be subject to various other laws and regulations.

Pricing and Third-Party Reimbursement

In the United States and elsewhere, sales of therapeutic and other pharmaceutical products are dependent in part on the availability of reimbursement to the consumer from third party payors, such as government and private insurance plans. Increasingly, third party payors are challenging the prices charged for medical products and services. As a result, in the future, our products could be considered not cost effective or reimbursement to the consumer could become unavailable or could be insufficient to allow us to sell our products on a competitive and profitable basis. For example, in some foreign markets, pricing reimbursement or profitability of therapeutic and other pharmaceutical products is subject to governmental control. In Canada this practice has led to lower priced products than in the United States. As a result, importation of products from Canada into the United States may result in reduced product revenues. In the United States there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing reimbursement controls. For example, Congress may give the federal government authority to negotiate drug prices for the Medicare Part D outpatient prescription drug benefit. Currently under Part D, prices are negotiated by the manufacturer with individual Part D plan sponsors or their administrators. Medicare Part B provides separate reimbursement for a limited universe of prescription drugs (primarily physician administered drugs). Currently, reimbursement for most Part B drugs is set at 106% of average sales price (which a manufacturer must report quarterly). Congress may consider proposals to reduce reimbursement for Part B drugs.

In many foreign markets, including the countries in the European Union, pricing of pharmaceutical products is subject to governmental control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing controls. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effecte non-public information about the underlying share issuer, which we will not disclose to you. Moreover, if any of our affiliates is or becomes a creditor of the underlying share issuer, they may exercise any remedies against the underlying share issuer that are available to them without regard to your interests.

You will have no rights and will not receive dividends with respect to the underlying shares. You should understand that you will not receive any dividend payments under the securities. In addition, if any change to the underlying shares is proposed, such as an amendment to the underlying share issuer’s organizational documents, you will not have the right to vote on such change. Any such change may adversely affect the market price of the underlying shares.

Even if the underlying share issuer pays a dividend that it identifies as special or extraordinary, no adjustment will be required under the securities for that dividend unless it meets the criteria specified in the accompanying product supplement. In general, an adjustment will not be made under the terms of the securities for any cash dividend paid on the underlying shares unless the amount of the dividend per underlying share, together with any other dividends paid in the same fiscal quarter, exceeds the dividend paid per underlying share in the most recent fiscal quarter by an amount equal to at least 10% of the closing price of the underlying shares on the date of declaration of the dividend. Any dividend will reduce the closing price of the underlying shares by the amount of the dividend per underlying share. If the underlying share issuer pays any dividend for which an adjustment is not made under the terms of the securities, holders of the securities will be adversely affected. See "Description of the Securities—Certain Additional Terms for Securities Linked to Company Shares or ETF Shares—Dilution and Reorganization Adjustments—Certain Extraordinary Cash Dividends" in the accompanying product supplement.

The securities will not be adjusted for all events that could affect the price of the underlying shares. For example, we will not make any adjustment for ordinary dividends or extraordinary dividends that do not meet the criteria described above, partial tender offers or additional public offerings of the underlying shares. Moreover, the adjustments we do make may not fully offset the dilutive or adverse effect of the particular event. Investors in the securities may be adversely affected by such an event in a circumstance in which a direct holder of the underlying shares would not.

If the underlying shares are delisted, we may call the securities prior to maturity for an amount that may be less than the stated principal amount. If we exercise this call right, you will receive the amount described under "Description of the Securities—Certain Additional Terms for Securities Linked to Company Shares or ETF Shares—Delisting of Company Shares" in the accompanying product supplement. This amount may be less, and possibly significantly less, than the stated principal amount of the securities.

The securities may become linked to shares of an issuer other than the original underlying share issuer upon the occurrence of a reorganization event or upon the delisting of the underlying shares. For example, if the underlying share issuer enters into a merger agreement that provides for holders of underlying shares to receive stock of another entity, the stock of such other entity will become the underlying shares for all purposes of the securities upon consummation of the merger. Additionally, if the underlying shares are delisted and we do not exercise our call right, the calculation agent may, in its sole discretion, select shares of another issuer to be the underlying shares. See "Description of the Securities—Certain Additional Terms for Securities Linked to Company Shares or ETF Shares—Dilution and Reorganization Adjustments," and "—Delisting of Company Shares" in the accompanying product supplement.

The calculation agent, which is an affiliate of ours, will make important determinations with respect to the securities. If certain events occur, such as market disruption events, corporate events with respect to the underlying share issuer that may require a dilution adjustment or the delisting of the underlying shares, CGMI, as calculation agent, will be required to make discretionary judgments that could significantly affect your return on the securities. In making these judgments, the calculation agent's interests as an affiliate of ours could be adverse to your interests as a holder of the securities.

The U.S. federal tax consequences of an investment in the securities are unclear. There is no direct legal authority regarding the proper U.S. federal tax treatment of the securities, and we do not plan to request a ruling from the Internal Revenue Service (the "IRS"). Consequently, significant aspects of the tax treatment of the securities are uncertain, and the IRS or a court might not agree with the treatment of the securities as described in "United States

Federal Tax Considerations" below. If the IRS were successful in asserting an alternative treatment, the tax consequences of ownership and disposition of the securities might be materially and adversely affected. Moreover, as described in the accompanying product supplement under "United States Federal Tax Considerations," in 2007 the U.S. Treasury Department and the IRS released a notice requesting comments on various issues regarding the U.S. federal income tax treatment of "prepaid forward contracts" and similar instruments. While it is not clear whether the securities would be viewed as similar to the typical prepaid forward contract described in the notice, it is possible that any Treasury regulations or other guidance promulgated after consideration of these issues could materially and adversely affect the tax consequences of an investment in the securities, including the character and timing of income or loss recognized by U.S. investors, possibly with retroactive effect. You should read carefully the discussion under "United States Federal Tax Considerations" and "Risk Factors Relating to the Securities" in the accompanying product supplement and "United States Federal

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Tax Considerations" in this pricing supplement. You should also consult your tax adviser regarding the U.S. federal tax consequences of an investment in the securities, as well as tax consequences arising under the laws of any state, local or non-U.S. taxing jurisdiction.

Non-U.S. investors should note that persons having withholding responsibility in respect of the securities may withhold on any coupon payment paid to a non-U.S. investor, generally at a rate of 30%. To the extent that we have withholding responsibility in respect of the securities, we intend to so withhold.

In addition, Section 871(m) of the Internal Revenue Code of 1986, as amended (the "Code"), imposes a withholding tax of up to 30% on "dividend equivalents" paid or deemed paid to non-U.S. investors in respect of certain financial instruments linked to U.S. equities. In light of Treasury regulations, as modified by an IRS notice, that provide a general exemption for financial instruments issued prior to January 1, 2021 that do not have a "delta" of one, as of the date of this preliminary pricing supplement the securities should not be subject to withholding under Section 871(m). However, information about the application of Section 871(m) to the securities will be updated in the final pricing supplement. Moreover, the IRS could challenge a conclusion that the securities should not be subject to withholding under Section 871(m).

We will not be required to pay any additional amounts with respect to amounts withheld.

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Information About Verizon Communications Inc.

Verizon Communications Inc. is a provider of communications, information and entertainment products and services to consumers, businesses and government agencies. The underlying shares are registered under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Information provided to or filed with the SEC by the underlying share issuer pursuant to the Exchange Act can be located by reference to the SEC file number 001-08606 through the SEC's website at http://www.sec.gov. In addition, information regarding the underlying share issuer may be obtained from other sources including, but not limited to, press releases, newspaper articles and other publicly disseminated documents. The underlying shares trade on the New York Stock Exchange under the ticker symbol "VZ."

This pricing supplement relates only to the securities offered hereby and does not relate to the underlying shares or other securities of the underlying share issuer. We have derived all disclosures contained in this pricing supplement regarding the underlying shares and the underlying share issuer from the publicly available documents described above. In connection with the offering of the securities, none of Citigroup Global Markets Holdings Inc., Citigroup Inc. or CGMI has participated in the preparation of such documents or made any due diligence inquiry with respect to the underlying share issuer.

The securities represent obligations of Citigroup Global Markets Holdings Inc. (guaranteed by Citigroup Inc.) only. The underlying share issuer is not involved in any way in this offering and has no obligation relating to the securities or to holders of the securities.

Neither we nor any of our affiliates make any representation to you as to the performance of the underlying shares.

Historical Information

The graph below shows the closing price of the underlying shares for each day such price was available from January 2, 2013 to November 14, 2018. The table that follows shows the high and low closing prices of, and dividends paid on, the underlying shares for each quarter in that same period. We obtained the closing prices and other information below from Bloomberg L.P., without independent verification. If certain corporate transactions occurred during the

historical period shown below, including, but not limited to, spin-offs or mergers, then the closing prices of the underlying shares shown below for the period prior to the occurrence of any such transaction have been adjusted by Bloomberg L.P. as if any such transaction had occurred prior to the first day in the period shown below. You should not take the historical prices of the underlying shares as an indication of future performance.

Common Stock of Verizon Communications Inc. – Historical Closing Prices
January 2, 2013 to November 14, 2018

* The red line indicates the hypothetical downside threshold price of $44.205, assuming the closing price on November 14, 2018 was the initial share price.

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Common Stock of Verizon Communications Inc.	**High**	**Low**	**Dividends**
2013			
First Quarter	$49.48	$41.51	$0.51500
Second Quarter	$53.91	$48.30	$0.51500
Third Quarter	$51.49	$45.91	$0.51500
Fourth Quarter	$51.14	$46.05	$0.53000
2014			
First Quarter	$49.30	$45.98	$0.53000
Second Quarter	$50.05	$45.94	$0.53000
Third Quarter	$51.97	$48.40	$0.53000
Fourth Quarter	$51.50	$45.42	$0.55000
2015			
First Quarter	$49.81	$45.71	$0.55000
Second Quarter	$50.55	$46.61	$0.55000
Third Quarter	$48.10	$43.50	$0.55000
Fourth Quarter	$47.21	$42.84	$0.56500
2016			
First Quarter	$54.08	$44.15	$0.56500
Second Quarter	$55.84	$49.14	$0.56500
Third Quarter	$56.53	$51.20	$0.56500
Fourth Quarter	$53.74	$46.18	$0.57750
2017			
First Quarter	$54.64	$48.03	$0.57750
Second Quarter	$49.31	$44.41	$0.57750
Third Quarter	$49.90	$42.89	$0.57750
Fourth Quarter	$53.43	$44.11	$0.59000
2018			
First Quarter	$54.72	$46.29	$0.59000
Second Quarter	$51.57	$46.38	$0.59000
Third Quarter	$54.97	$50.42	$0.59000
Fourth Quarter (through November 14, 2018)	$58.94	$53.33	$0.60250

The closing price of the underlying shares on November 14, 2018 was $58.94.

We make no representation as to the amount of dividends, if any, that may be paid on the underlying shares in the future. In any event, as an investor in the securities, you will not be entitled to receive dividends, if any, that may be payable on the underlying shares.

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United States Federal Tax Considerations

You should read carefully the discussion under “United States Federal Tax Considerations” and “Risk Factors Relating to the Securities” in the accompanying product supplement and “Summary Risk Factors” in this pricing supplement.

Due to the lack of any controlling legal authority, there is substantial uncertainty regarding the U.S. federal tax consequences of an investment in the securities. In connection with any information reporting requirements we may have in respect of the securities under applicable law, we intend (in the absence of an administrative determination or judicial ruling to the contrary) to treat the securities for U.S. federal income tax purposes as prepaid forward contracts with associated coupon payments that will be treated as gross income to you at the time received or accrued in accordance with your regular method of tax accounting. In the opinion of our counsel, Davis Polk & Wardwell LLP, which is based on current market conditions, this treatment of the securities is reasonable under current law; however, our counsel has advised us that it is unable to conclude affirmatively that this treatment is more likely than not to be upheld, and that alternative treatments are possible.

Assuming this treatment of the securities is respected and subject to the discussion in “United States Federal Tax Considerations” in the accompanying product supplement, the following U.S. federal income tax consequences should result under current law:

- Any coupon payments on the securities should be taxable as ordinary income to you at the time received or accrued in accordance with your regular method of accounting for U.S. federal income tax purposes.

- Upon a sale or exchange of a security (including retirement at maturity), you should recognize capital gain or loss equal to the difference between the amount realized and your tax basis in the security. For this purpose, the amount realized does not include any coupon paid on retirement and may not include sale proceeds attributable to an accrued coupon, which may be treated as a coupon payment. Such gain or loss should be long-term capital gain or loss if you held the security for more than one year.

We do not plan to request a ruling from the IRS regarding the treatment of the securities, and the IRS or a court might not agree with the treatment described herein. In addition, the U.S. Treasury Department and the IRS have released a notice requesting comments on the U.S. federal income tax treatment of “prepaid forward contracts.” While it is not

clear whether the securities would be viewed as similar to the typical prepaid forward contract described in the notice, it is possible that any Treasury regulations or other guidance promulgated after consideration of these issues could materially and adversely affect the tax consequences of an investment in the securities, including the character and timing of income or loss, possibly with retroactive effect. You should consult your tax adviser regarding possible alternative tax treatments of the securities and potential consequences of the IRS notice.

Withholding Tax on Non-U.S. Holders. Because significant aspects of the tax treatment of the securities are uncertain, persons having withholding responsibility in respect of the securities may withhold on any coupon payment paid to Non-U.S. Holders (as defined in the accompanying product supplement), generally at a rate of 30%. To the extent that we have (or an affiliate of ours has) withholding responsibility in respect of the securities, we intend to so withhold. In order to claim an exemption from, or a reduction in, the 30% withholding, you may need to comply with certification requirements to establish that you are not a U.S. person and are eligible for such an exemption or reduction under an applicable tax treaty. You should consult your tax adviser regarding the tax treatment of the securities, including the possibility of obtaining a refund of any amounts withheld and the certification requirement described above.

Moreover, as discussed under “United States Federal Tax Considerations – Tax Consequences to Non-U.S. Holders – Possible Withholding Under Section 871(m) of the Code” in the accompanying product supplement, Section 871(m) of the Code and Treasury regulations promulgated thereunder (“Section 871(m)”) generally impose a 30% withholding tax on dividend equivalents paid or deemed paid to Non-U.S. Holders with respect to certain financial instruments linked to U.S. equities (“U.S. Underlying Equities”) or indices that include U.S. Underlying Equities. Section 871(m) generally applies to instruments that substantially replicate the economic performance of one or more U.S. Underlying Equities, as determined based on tests set forth in the applicable Treasury regulations (a “Specified Security”). However, the regulations, as modified by an IRS notice, exempt financial instruments issued prior to January 1, 2021 that do not have a “delta” of one. Based on the terms of the securities and representations provided by us, our counsel is of the opinion that the securities should not be treated as transactions that have a “delta” of one within the meaning of the regulations with respect to any U.S. Underlying Equity and, therefore, should not be Specified Securities subject to withholding tax under Section 871(m).

A determination that the securities are not subject to Section 871(m) is not binding on the IRS, and the IRS may disagree with this treatment. Moreover, Section 871(m) is complex and its application may depend on your particular circumstances. For example, if you enter into other transactions relating to a U.S. Underlying Equity, you could be subject to withholding tax or income tax liability under Section 871(m) even if the securities are not Specified Securities subject to Section 871(m) as a general matter. You should consult your tax adviser regarding the potential application of Section 871(m) to the securities.

This information is indicative and will be updated in the final pricing supplement or may otherwise be updated by us in writing from time to time. Non-U.S. Holders should be warned that Section 871(m) may apply to the securities based on circumstances as of the pricing date for the securities and, therefore, it is possible that the securities will be subject to withholding tax under Section 871(m).

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We will not be required to pay any additional amounts with respect to amounts withheld.

You should read the section entitled "United States Federal Tax Considerations" in the accompanying product supplement. The preceding discussion, when read in combination with that section, constitutes the full opinion of Davis Polk & Wardwell LLP regarding the material U.S. federal tax consequences of owning and disposing of the securities.

You should also consult your tax adviser regarding all aspects of the U.S. federal income and estate tax consequences of an investment in the securities and any tax consequences arising under the laws of any state, local or non-U.S. taxing jurisdiction.

Supplemental Plan of Distribution

CGMI, an affiliate of Citigroup Global Markets Holdings Inc. and the underwriter of the sale of the securities, is acting as principal and will receive an underwriting fee of $0.25 for each $10.00 security sold in this offering. From this underwriting fee, CGMI will pay selected dealers not affiliated with CGMI, including Morgan Stanley Wealth Management, and their financial advisors collectively a fixed selling concession of $0.20 for each $10.00 security they sell. In addition, Morgan Stanley Wealth Management will receive a structuring fee of $0.05 for each security they sell. For the avoidance of doubt, the fees and selling concessions described in this pricing supplement will not be rebated if the securities are automatically redeemed prior to maturity.

CGMI is an affiliate of ours. Accordingly, this offering will conform with the requirements addressing conflicts of interest when distributing the securities of an affiliate set forth in Rule 5121 of the Financial Industry Regulatory Authority. Client accounts over which Citigroup Inc. or its subsidiaries have investment discretion will not be permitted to purchase the securities, either directly or indirectly, without the prior written consent of the client.

Secondary market sales of securities typically settle two business days after the date on which the parties agree to the sale. Because the issue date for the securities is more than two business days after the pricing date, investors who wish to sell the securities at any time prior to the second business day preceding the issue date will be required to specify an

alternative settlement date for the secondary market sale to prevent a failed settlement. Investors should consult their own investment advisors in this regard.

See “Plan of Distribution; Conflicts of Interest” in the accompanying product supplement and “Plan of Distribution” in each of the accompanying prospectus supplement and prospectus for additional information.

A portion of the net proceeds from the sale of the securities will be used to hedge our obligations under the securities. We expect to hedge our obligations under the securities through CGMI or other of our affiliates. CGMI or such other of our affiliates may profit from this expected hedging activity even if the value of the securities declines. This hedging activity could affect the closing price of the underlying shares and, therefore, the value of and your return on the securities. For additional information on the ways in which our counterparties may hedge our obligations under the securities, see “Use of Proceeds and Hedging” in the accompanying prospectus.

Valuation of the Securities

CGMI calculated the estimated value of the securities set forth on the cover page of this pricing supplement based on proprietary pricing models. CGMI’s proprietary pricing models generated an estimated value for the securities by estimating the value of a hypothetical package of financial instruments that would replicate the payout on the securities, which consists of a fixed-income bond (the “bond component”) and one or more derivative instruments underlying the economic terms of the securities (the “derivative component”). CGMI calculated the estimated value of the bond component using a discount rate based on our internal funding rate. CGMI calculated the estimated value of the derivative component based on a proprietary derivative-pricing model, which generated a theoretical price for the instruments that constitute the derivative component based on various inputs, including the factors described under “Summary Risk Factors—The value of the securities prior to maturity will fluctuate based on many unpredictable factors” in this pricing supplement, but not including our or Citigroup Inc.’s creditworthiness. These inputs may be market-observable or may be based on assumptions made by CGMI in its discretionary judgment.

The estimated value of the securities is a function of the terms of the securities and the inputs to CGMI’s proprietary pricing models. As of the date of this preliminary pricing supplement, it is uncertain what the estimated value of the securities will be on the pricing date because certain terms of the securities have not yet been fixed and because it is uncertain what the values of the inputs to CGMI’s proprietary pricing models will be on the pricing date.

For a period of approximately three months following issuance of the securities, the price, if any, at which CGMI would be willing to buy the securities from investors, and the value that will be indicated for the securities on any brokerage account statements prepared by CGMI or its affiliates (which value CGMI may also publish through one or more financial information vendors), will reflect a temporary upward adjustment from the price or value that would otherwise be determined. This temporary upward adjustment represents a portion of the hedging profit expected to be realized by CGMI or its affiliates over the term of the securities. The amount of this temporary upward adjustment will decline to zero on a straight-line basis over the three-month temporary adjustment period. However, CGMI is not

obligated to buy the securities from investors at any time. See “Summary Risk Factors—The securities will not be listed on any securities exchange and you may not be able to sell them prior to maturity.”

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Certain Selling Restrictions

Prohibition of Sales to EEA Retail Investors

The securities may not be offered, sold or otherwise made available to any retail investor in the European Economic Area. For the purposes of this provision:

(a) the expression "retail investor" means a person who is one (or more) of the following:

(i) a retail client as defined in point (11) of Article 4(1) of Directive 2014/65/EU (as amended, "MiFID II"); or

(ii) a customer within the meaning of Directive 2002/92/EC, where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II; or

(iii) not a qualified investor as defined in Directive 2003/71/EC; and

(b) the expression "offer" includes the communication in any form and by any means of sufficient information on the terms of the offer and the securities offered so as to enable an investor to decide to purchase or subscribe the securities.

Contact

Clients of Morgan Stanley Wealth Management may contact their local Morgan Stanley branch office or the Morgan Stanley principal executive offices at 1585 Broadway, New York, New York 10036 (telephone number (212) 762-9666). All other clients may contact their local brokerage representative.