

# Isis Pharmaceuticals Significantly Improves Upon 2014 Financial Guidance

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## Strong Performance represents success of novel business strategy

CARLSBAD, Calif., Jan. 8, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that the Company expects to significantly improve upon its 2014 financial guidance. The Company expects to end 2014 with a pro forma net operating loss (NOL) in the mid to high teens and more than \$725 million in cash. The significantly improved financial performance of the Company in 2014 was a result of the successful execution of its business strategy, the maturation of its pipeline and the growing validation of antisense as a viable, efficient and effective drug discovery technology.



"The success of our drugs and our partnerships contributed significantly to our strong financial performance in 2014 and shows that our business model is working. During 2014, we received more than \$220 million in payments from our partners, including more than \$150 million from milestone payments. We also took advantage of favorable market conditions to further strengthen our balance sheet by selling a portion of our Regulus stock for more than \$20 million and by refinancing the majority of our outstanding convertible debt, obtaining a very favorable interest rate while reducing the potential dilution from the convertible notes," said Elizabeth L. Hougen, chief financial officer at Isis Pharmaceuticals. "Because of our strong financial performance throughout the year, we expect to end 2014 with more than \$725 million in cash, substantially exceeding our year-end cash guidance by more than \$150 million. We also expect to end 2014 with a pro forma NOL in the mid to high teens, which represents a nearly 70% improvement over our original guidance of a pro forma NOL in the low \$50 million range."

"Our strong performance in 2014 is a product of our unique business strategy, which we designed to maximize the value of the products we are developing and to ensure continuing technology leadership. We reported positive clinical data from 15 of the 18 clinical studies that read out in 2014 and our pipeline continued to mature with 7 drugs in Phase 3 studies and 15 drugs in Phase 2 studies by the end of the year. Our partnered programs were also very successful this year as evidenced by the significant value and number of milestone payments we received from partners. Our partnerships not only bring in money, they also allow us to take advantage of partner expertise to expand the applications of our antisense technology. Earlier this week we announced a new partnership with Janssen, which allows us to expand the reach of our technology with Janssen's pharmaceuticals expertise and expertise in autoimmune diseases to develop antisense drugs to treat autoimmune diseases in the gastrointestinal tract," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals. "We have also continued to evolve our business strategy, which should allow us to create even more value in the drugs in our pipeline. We have formed Akcea Therapeutics, a wholly owned subsidiary focused on the development and commercialization of our lipid drugs and recently hired Paula Soteropoulos as Akcea's chief executive officer. Paula's expertise in commercializing drugs for cardiovascular and severe and rare diseases should be very valuable as we continue to advance the drugs in our lipid franchise. And finally, we have added further senior commercial leadership to the Isis management team with the addition of Sarah Boyce, our new chief business officer. Sarah's business expertise should bring valuable global perspective to our ongoing and future programs."

### ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in RNA-targeted technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 33 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, including neurological disorders, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO<sup>®</sup>, in the United States and other countries for the treatment of patients with homozygous FH. Isis has numerous drugs in Phase 3 development in severe/rare diseases and cardiovascular diseases. These include ISIS-APOCIII<sub>RX</sub>, a drug Isis is developing through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with severely high triglycerides, such as patients with familial chylomicronemia syndrome; ISIS-TTR<sub>RX</sub>, a drug Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN<sub>RX</sub>, a drug Isis is developing with Biogen Idec to treat infants and children with spinal muscular atrophy, a severe and rare neuromuscular disease. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

### ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis Pharmaceuticals and Isis' business. Financial projections provided in this press release are unaudited and subject to change. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2013, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

Isis Pharmaceuticals<sup>®</sup> is a registered trademark of Isis Pharmaceuticals, Inc. Akcea Therapeutics<sup>™</sup> is a trademark of Isis Pharmaceuticals, Inc. Regulus Therapeutics<sup>™</sup> is a trademark of Regulus Therapeutics Inc. KYNAMRO<sup>®</sup> is a registered trademark of Genzyme Corporation.

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