SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): **August 4, 2015**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(IRS Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010
(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 2.02. Results of Operations and Financial Condition.

On August 4, 2015, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended June 30, 2015. In addition to disclosing results that are determined in accordance with Generally Accepted Accounting Principles (GAAP), the Company also discloses pro forma or non-GAAP results of operations, which are adjusted from GAAP to exclude non-cash compensation related to equity awards. The Company is presenting pro forma information excluding the effects of the non-cash compensation because the Company believes it is useful for investors in assessing the Company's operating results compared to the prior year. A copy of the release is furnished with this report as an exhibit pursuant to "Item 2.02. Results of Operations and Financial Condition" of Form 8-K in accordance with SEC Release Nos. 33-8216 and 34-47583.

The information in this Current Report on Form 8-K and the Exhibit attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1	Press Release dated August 4, 2015.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: August 4, 2015

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer

INDEX TO EXHIBITS

99.1	Press Release dated August 4, 2015.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR SECOND QUARTER 2015

- **Substantial Net Income Driven by More Than $180 Million in Revenue**
- **2015 Financial Guidance Significantly Improved**
- **Conference Call Webcast Tuesday, August 4, 11:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., August 4, 2015 – Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported net income of $35.6 million and $18.9 million for the three and six months ended June 30, 2015, respectively, compared to a net loss of $12.1 million and $43.4 million for the same periods in 2014. Isis' significantly improved financial results were driven primarily by the more than $90 million of revenue Isis earned in the second quarter related to the upfront payment from Bayer to license ISIS-FXI$_{Rx}$. Isis increased its cash position during the first half of 2015, ending June with more than $750 million in cash compared to approximately $730 million at December 31, 2014. The increase in the Company's cash position was primarily due to the more than $165 million in cash received from its partners in the first half of 2015.

"So far this year we have completed transactions that advance every element of our business. These transactions support our continued strong financial performance. However, their strategic value now and in the future is even more important. Yesterday, we announced an expansion of our strategic relationship with AstraZeneca that takes advantage of the breadth of our technology and provides us with a very strong partner to move forward with in the large and growing area of cardiometabolic and renal diseases. This strategic collaboration, which is valued at up to more than $4 billion, will continue to expand our technology in the kidney and builds on our positive oncology and drug delivery collaborations. Early in the year, we initiated a new collaboration with J&J that also enables us to expand the reach of our antisense technology. With J&J, we are focusing on the local treatment of inflammatory disease in the GI track, capitalizing on J&J's expertise in this area. In May, we licensed ISIS-FXI$_{Rx}$ to Bayer, a leader in the development and commercialization of antithrombotic drugs. Bayer plans to advance ISIS-FXI$_{Rx}$ with a robust development plan designed to maximize the value of the drug. The completion of these unique collaborations since the beginning of the year, each of which is already providing substantial added value to Isis, is an unparalleled achievement," said B. Lynne Parshall, chief operating officer of Isis Pharmaceuticals. "Moreover, at the beginning of the year, we created Akcea, a wholly owned subsidiary, to develop and commercialize our suite of lipid drugs. The Akcea team is making excellent progress in building a high-quality team and preparing to commercialize volanesorsen. The importance of the Akcea portfolio of drugs to provide new treatments for patients with inadequately treated lipid disorders is reflected in the fact that this portfolio has been the subject of three articles in two major medical journals, The Lancet and The New England Journal of Medicine. This is a testament to the ability of antisense technology to approach targets that are not easily approachable with other therapeutic modalities and to rapidly identify potent and specific inhibitors to newly discovered targets that play key roles in disease."

"In addition, our other collaborations continue to yield successes. We reported positive top line conclusions from the FOCUS FH study of KYNAMRO. We initiated the first clinical study on ISIS-HTT$_{Rx}$ in patients with Huntington's disease in our Roche collaboration. And, we are conducting Phase 3 trials for two separate indications in our Biogen collaboration with ISIS-SMN$_{Rx}$. We are encouraged by the maturing data from this program, and we continue to have constructive interations with regulatory agencies. By the end of the year, we expect that our drug, ISIS-TTR$_{Rx}$, which we are developing with GSK, will also be in Phase 3 clinical trials for two separate indications," continued Ms. Parshall.

“Our continued strong financial performance so far this year has been driven by the successes across all areas of our business. We reported significant operating and net income for our second quarter and the first six months of this year due in large part to the more than $90 million in revenue we earned from our license of ISIS-FXI$_{Rx}$ to Bayer in May. Moreover, we have earned more than $180 million in revenue from milestone and other payments for our partnered programs and drugs. As these programs advance, we have the potential to generate even more revenue and cash from milestone payments this year. Additionally, so far this year, we have generated nearly $300 million from our partners, including the $65 million upfront fee from AstraZeneca that we will receive upon Hart-Scott-Rodino clearance. It is important to note that the cash we receive significantly underestimates the financial value of our partnerships as our partners are contributing substantial resources to our collaborations. AstraZeneca, Bayer, Biogen and GSK are all conducting research and/or development in parallel with the work we are conducting. In addition, Biogen and GSK are preparing to commercialize ISIS-SMN$_{Rx}$ and ISIS-TTR$_{Rx}$, respectively. These are activities that we benefit from, for which our partners bear the expense,” said Elizabeth L. Hougen, chief financial officer of Isis Pharmaceuticals.

“Because of our strong financial performance in the first half of this year, we expect to substantially improve upon our year-end guidance. We are reducing our projected pro forma NOL by more than 40 percent to a pro forma NOL in the low $30 million range. We are also projecting to end the year with more than $750 million in cash, which is an increase over our original cash guidance of more than $120 million and a modest increase over our 2014 year end cash balance. Our improved guidance reflects the revenue and cash from our new AstraZeneca transaction and the $33 million in milestone payments we have achieved so far in the third quarter. Our revised guidance also reflects the many opportunities we have to generate revenue and cash throughout the second half of this year although we do not anticipate that any one event will contribute as much revenue as our Bayer license. In addition, as we move forward, we expect our expenses to increase as our Phase 3 drugs continue to progress and we continue to advance and expand our pipeline. Of particular importance, our expenses for Akcea will increase as they continue to build the commercial infrastructure and advance the pre-commercialization activities necessary to successfully launch volanesorsen within the next couple of years,” concluded Ms. Hougen.

Financial Results

All pro forma amounts referred to in this press release exclude non-cash compensation expense related to equity awards. Please refer to the reconciliation of pro forma and GAAP measures, which is provided later in this release.

Revenue

Revenue for the three and six months ended June 30, 2015 was $120.4 million and $183.0 million, respectively, compared to $57.1 million and $85.2 million for the same periods in 2014. Isis recognized $91.2 million in connection with its recently completed exclusive license agreement with Bayer in the second quarter of 2015. Isis also earned $57 million in revenue from milestone payments from its partners in the first half of 2015, which primarily consisted of:

- $41 million from Biogen including payments for advancing ISIS-SMN$_{Rx}$ in late-stage clinical development, for advancing ISIS-BIIB4$_{Rx}$ into development and for validating two new undisclosed targets for neurological disorders; and
- $15 million from GSK for advancing the Phase 3 study of ISIS-TTR$_{Rx}$.

Isis' revenue in the first half of 2015 also included $26.0 million in revenue from the amortization of upfront fees and manufacturing services performed for its partners.

Already in the third quarter of 2015, Isis has earned $33 million from milestone payments from Roche for the initiation of a Phase 1/2 study for ISIS-HTT_{Rx} and from Biogen for continuing to advance ISIS-SMN_{Rx}. Isis also expects to earn approximately $5 million over the second half of 2015 from the amortization of the upfront payment from its new AstraZeneca collaboration.

Isis' revenue fluctuates based on the nature and timing of payments under agreements with its partners and consists primarily of revenue from the amortization of upfront fees, milestone payments and license fees.

Operating Expenses

Isis is conducting more later-stage clinical trials in 2015 than it did in 2014, including the continuation of its Phase 3 programs for ISIS-TTR_{Rx}, ISIS-SMN_{Rx} and volanesorsen. As such, Isis' pro forma operating expenses of $62.2 million and $120.8 million for the three and six months ended June 30, 2015, respectively, were higher than the $56.0 million and $106.8 million in the same periods in 2014. On a GAAP basis, Isis' operating expenses for the three and six months ended June 30, 2015 were $75.8 million and $147.7 million, respectively, compared to $63.7 million and $121.6 million for the same periods in 2014. Isis' operating expenses on a GAAP basis included non-cash compensation expense related to equity awards, which increased in the first half of 2015 compared to the same period in 2014. As Isis' Phase 3 programs continue to progress in the second half of the year, the costs associated with these programs will increase compared to the first half of 2015. Additionally, Isis' operating expenses in the second half of the year will increase due to Akcea expenses to prepare for the commercial launch of volanesorsen.

Net Income (Loss)

Isis reported net income of $35.6 million and $18.9 million, for the three and six months ended June 30, 2015, respectively, compared to a net loss of $12.1 million and $43.4 million for the same periods in 2014. Basic net income per share for the three and six months ended June 30, 2015 was $0.30 and $0.16, respectively, compared to a basic net loss per share of $0.10 and $0.37 for the same periods in 2014. Diluted net income per share for the three and six months ended June 30, 2015 was $0.29 and $0.15, respectively, compared to a diluted net loss of $0.10 and $0.37 for the same periods in 2014. Isis' net income in the first half of 2015 was primarily due to the revenue the Company earned from its exclusive license agreement with Bayer for ISIS-FXI_{Rx}.

Balance Sheet

As of June 30, 2015, Isis had cash, cash equivalents and short-term investments of $754.9 million compared to $728.8 million at December 31, 2014. Isis' working capital was $753.3 million at June 30, 2015 compared to $721.3 million at December 31, 2014. The increase in the Company's cash and working capital primarily relates to the more than $165 million the Company received from its partners, including the $100 million up-front payment Isis received from Bayer. Isis' cash balance at June 30, 2015 did not include nearly $100 million, which is comprised of payments Isis has generated to date in the third quarter.

Business Highlights

"We believe that the second half of the year will be equally productive with a number of pipeline activities that should continue to provide value to Isis and its shareholders. From our lipid franchise, we plan to report data from our Phase 2 study on our novel Lp(a)-lowering drug. The importance of therapies to specifically reduce Lp(a) and the promise of Akcea's drug to do so was highlighted in a recent Lancet article and points to patients' need for a specific Lp(a) lowering medicine. We have numerous clinical trial initiations planned, including the Phase 3 study in cardiomyopathy being conducted by GSK and the Phase 3 study evaluating volanesorsen in patients with familial partial lipodystrophy. This second Phase 3 study for volanesorsen is designed to support bringing this important drug to the market for these patients who have an ultra-rare orphan disease and who are in need of effective new therapies. And of course, we expect to continue to add new drugs to our pipeline this year," concluded Ms. Parshall.

Corporate Highlights (*2015 second quarter and subsequent activities*)

- Isis licensed ISIS-FXI$_{Rx}$ to Bayer to develop and commercialize ISIS-FXI$_{Rx}$ for the prevention of thrombosis.
  - Isis generated a $100 million upfront payment from Bayer and is eligible to earn up to $275 million in additional payments, including a $55 million milestone payment upon advancement of the program following completion of the planned Phase 2 study.
  - Isis is eligible to receive tiered royalties in the low to high 20 percent range on gross margins of ISIS-FXI$_{Rx}$.
- Isis and AstraZeneca formed a multi-year collaboration to discover and develop novel antisense drugs primarily focused on treating cardiovascular, metabolic and kidney diseases.
  - In total, Isis has the potential to earn up to more than $4 billion in license fees and milestone payments.
    - Isis will receive a $65 million upfront payment from AstraZeneca and is eligible to earn substantial development and regulatory milestone payments and license fees. Isis is eligible to earn a payment of $25-30 million under this collaboration next year upon identification of the first drug candidate to move into development.
    - Isis is also eligible to earn tiered double digit royalties on annual net sales for each of the programs.
    - This transaction is subject to clearance under the Hart-Scott-Rodino Antitrust Improvements Act.
- To date this year, Isis has generated nearly $300 million in payments from its partners.

Drug Development Highlights *(2015 second quarter and subsequent activities)*

- Isis reported positive clinical results from KYNAMRO, ISIS-SMN$_{Rx}$ and ISIS-TTR$_{Rx}$. These data exemplify the broad applicability and potential for antisense drugs to provide therapeutic benefit for many different diseases.
  - Isis reported that the FOCUS FH study evaluating KYNAMRO in patients with severe heterozygous familial hypercholesterolemia met its primary endpoint with a statistically significant reduction of LDL-Cholesterol. Genzyme and Isis plan to report the full data from this study at an upcoming medical meeting.
  - Isis presented positive results based on an April 17, 2015 data analysis from the ongoing open-label Phase 2 clinical study of ISIS-SMN$_{Rx}$ in infants with Type I spinal muscular atrophy. The data reported showed continued increases in median event-free survival and muscle function scores as well as achievement of developmental milestones.
  - Isis provided an update based on a May 15, 2015 data analysis in children with spinal muscular atrophy who have completed the open-label, Phase 2 multiple-dose study of ISIS-SMN$_{Rx}$ and are continuing to receive treatment in an open-label extension study. Consistent with earlier observations, increases in muscle function scores and additional motor function tests were observed in children treated with ISIS-SMN$_{Rx}$.
  - Dr. Merrill Benson, an investigator of ISIS-TTR$_{Rx}$, reported positive data from an investigator-initiated study in patients with TTR amyloid-related cardiomyopathy. In this study, Dr. Benson observed apparent stabilization of cardiac disease after six months of treatment with ISIS-TTR$_{Rx}$ with no progression of cardiac disease. Patients also experienced up to 88 percent reduction in TTR after nine months of dosing compared to baseline.
  - Isis reported positive results from an ongoing open-label extension study of ISIS-TTR$_{Rx}$ in patients with familial amyloid polyneuropathy (FAP). In the open-label study after thirteen weeks of treatment with ISIS-TTR$_{Rx}$, TTR protein was reduced up to 92 percent with a median reduction of 78 percent in patients with FAP compared to their baseline TTR levels at entry into the Phase 3 study.

- Isis reported positive Phase 2 data for ISIS-GCCR$_{Rx}$ in patients with type 2 diabetes. In this study after six weeks of treatment with ISIS-GCCR$_{Rx}$, patients achieved improvements in multiple measures of glucose control with trends toward improvements in insulin sensitivity.

· Isis published clinical data from its novel lipid drugs, volanesorsen and ISIS-APO(a)$_{Rx}$, in the New England Journal of Medicine and The Lancet, respectively, two prestigious medical journals. These data highlight the significant interest from the medical community in Isis' lipid drugs and the significance of the clinical data from these programs.

· Volanesorsen was granted orphan drug designation from the US FDA for the treatment of patients with familial chylomicronemia syndrome.

· Isis continued to advance its pipeline of drugs.
  - Isis initiated a Phase 1/2 study of ISIS-HTT$_{Rx}$ in patients with Huntington's disease (HD). ISIS-HTT$_{Rx}$ has been granted orphan drug designation by the European Medicines Agency for the treatment of patients with HD.
  - Isis initiated a Phase 2 study to evaluate the safety and activity of ISIS-FGFR4$_{Rx}$ in patients who are obese.

Conference Call

At 11:30 a.m. Eastern Time today, August 4, 2015, Isis will conduct a live webcast conference call to discuss this earnings release and related activities. Interested parties may listen to the call by dialing 877-443-5662 or access the webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

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 38 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®, 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 volanesorsen, a drug Isis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with familial chylomicronemia syndrome and familial partial lipodystrophy; ISIS-TTR$_{Rx}$, a drug Isis is developing with GSK to treat patients with the polyneuropathy and cardiomyopathy forms of TTR amyloidosis; and ISIS-SMN$_{Rx}$, a drug Isis is developing with Biogen 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.

FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis Pharmaceuticals' financial position and outlook, Isis' business, the business of Akcea Therapeutics, Inc., a subsidiary of Isis Pharmaceuticals, and the therapeutic and commercial potential of Isis' technologies and products, including KYNAMRO, ISIS-SMN$_{Rx}$, ISIS-TTR$_{Rx}$ and volanesorsen, in development. 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, 2014, and its most recent quarterly report on Form 10-Q, which are on file with the SEC.

Copies of this 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.

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ISIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Data)

	Three months ended, June 30,		Six months ended, June 30,	
	2015	2014	2015	2014
Revenue:	(unaudited)		(unaudited)	
Research and development revenue under collaborative agreements	$ 119,658	$ 56,628	181,551	$ 76,177
Licensing and royalty revenue	770	448	1,461	9,060
Total revenue	120,428	57,076	183,012	85,237
Expenses:				
Research, development and patent expenses	68,007	59,264	132,454	112,712
General and administrative	7,775	4,462	15,241	8,842
Total operating expenses	75,782	63,726	147,695	121,554
Income (loss) from operations	44,646	(6,650)	35,317	(36,317)
Other income (expense):				
Investment income	917	671	1,761	1,328
Interest expense	(9,127)	(4,961)	(18,148)	(9,904)
Gain (loss) on investments, net	1	(260)	1	137
Income (loss) before income tax benefit	36,437	(11,200)	18,931	(44,756)
Income tax benefit (expense)	(789)	(881)	-	1,395
Net income (loss)	35,648	$ (12,081)	18,931	$ (43,361)
Basic net income (loss) per share	$ 0.30	$ (0.10)	$ 0.16	$ (0.37)
Diluted net income (loss) per share	$ 0.29	$ (0.10)	$ 0.15	$ (0.37)
Shares used in computing basic net income (loss) per share	119,742	117,588	119,348	117,359
Shares used in computing diluted net income (loss) per share	127,779	117,588	124,061	117,359

Isis Pharmaceuticals, Inc.
Reconciliation of GAAP to Pro Forma Basis:
Condensed Consolidated Operating Expenses, (Income) Loss From Operations, and Net Loss
(In Thousands)

	Three months ended, June 30,		Six months ended, June 30,	
	2015	2014	2015	2014
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 75,782	$ 63,726	$ 147,695	$ 121,554
Excluding compensation expense related to equity awards	(13,605)	(7,708)	(26,910)	(14,777)
Pro forma operating expenses	$ 62,177	$ 56,018	$ 120,785	$ 106,777
As reported income (loss) from operations according to GAAP	$ 44,646	$ (6,650)	$ 35,317	$ (36,317)
Excluding compensation expense related to equity awards	(13,605)	(7,708)	(26,910)	(14,777)
Pro forma income (loss) from operations	$ 58,251	$ 1,058	$ 62,227	$ (21,540)
As reported net income (loss) according to GAAP	$ 35,648	$ (12,081)	$ 18,931	$ (43,361)
Excluding compensation expense related to equity awards	(13,605)	(7,708)	(26,910)	(14,777)
Pro forma net income (loss)	$ 49,253	$ (4,373)	$ 45,841	$ (28,584)

Reconciliation of GAAP to Pro Forma Basis

As illustrated in the Selected Financial Information in this press release, pro forma operating expenses, pro forma income (loss) from operations, and pro forma net income (loss) were adjusted from GAAP to exclude compensation expense related to equity awards, which are non-cash. Isis has regularly reported non-GAAP measures for operating results as pro forma results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Isis reports these pro forma results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Isis' pro forma results is consistent with how Isis' management internally evaluates the performance of its operations.

Isis Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(In Thousands)

	June 30, 2015 (unaudited)	December 31, 2014
Assets:		
Cash, cash equivalents and short-term investments	$ 754,934	$ 728,832
Investment in Regulus Therapeutics Inc.	60,604	81,881
Other current assets	39,914	25,884
Property, plant and equipment, net	89,692	88,958
Other assets	31,114	30,254
Total assets	$ 976,258	$ 955,809
Liabilities and stockholders' equity:		
Other current liabilities	$ 43,847	$ 63,619
Current portion of deferred contract revenue	58,285	51,713
1% convertible senior notes	337,158	327,486
2 3/4% convertible senior notes	49,160	48,014
Long-term obligations, less current portion	79,360	79,400
Long-term deferred contract revenue	108,128	127,797
Stockholders' equity	300,320	257,780
Total liabilities and stockholders' equity	$ 976,258	$ 955,809

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