# Argos Therapeutics, Inc. (ARGS)

ASCO Takeaways- Immunotherapy in Renal Cell Carcinoma (RCC)

**MARKET OUTPERFORM** | Price: $6.95 | Target Price: $17.00

## MARKET DATA

| | |
|---|---|
| Price | $6.95 |
| 52-Week Range: | $7.97 - $13.74 |
| Shares Out. (M): | 19.0 |
| Market Cap ($M): | $132.1 |
| Average Daily Vol. (000): | 39.0 |
| Cash (M): | $83 |
| LT Debt (M): | $9 |

Source: Thomson Reuters and JMP Securities LLC

| FY DEC | | 2013A | 2014E | 2015E |
|---|---|---|---|---|
| Revenue ($M) | 1Q | $1.3 | $0.8A | -- |
| | 2Q | $1.5 | $0.8 | -- |
| | 3Q | $1.0 | $0.8 | -- |
| | 4Q | $0.7 | $0.3 | -- |
| | **FY** | **$4.4** | **$2.7** | **$0.2** |
| EPS | 1Q | ($34.19) | ($1.05)A | -- |
| | 2Q | ($29.91) | ($0.57) | -- |
| | 3Q | ($30.06) | ($0.59) | -- |
| | 4Q | ($36.19) | ($0.64) | -- |
| | **FY** | **($147.37)** | **($2.61)** | **($1.75)** |

Source: Company reports and JMP Securities LLC

## STOCK PRICE PERFORMANCE


## INVESTMENT HIGHLIGHTS

**Updates on potential future mRCC therapies suggest need and room for AGS-003; reiterating our Market Outperform rating and $17 price target on Argos Therapeutics.** Treatment with PD-1 or CTLA4 inhibitors are emerging as potential therapies in many cancers and preliminary data for these agents in metastatic renal cell carcinoma (mRCC) were presented at ASCO this week. A combination of a PD-1 with small molecule TKI inhibitors or a PD-1/CTLA4 combination have been looked at for first-line therapy- the population targeted for AGS-003. The body of data at ASCO lead us to believe that if the Phase III data for AGS-003 confirm the efficacy and safety observed in Phase II (doubling the effect of Sutent alone with no added toxicity), AGS-003 should be able to capture share first line with a first-mover advantage against a potential anti-PD-1/CTLA-4 combination. Argos's pivotal study, ADAPT, has enrolled about 150 patients so far with 100 more being screened and enrollment set to complete around year end. Our $17 price target is based on a risk-adjusted, NPV analysis with ~$15 attributed to AGS-003 in mRCC and ~$2 for AGS-003 in early-stage RCC; we do not include AGS-004 for HIV in our valuation at this time.

**Hope for immunotherapy in mRCC.** Renal cell cancer is known to respond to immunotherapy with IL-2 as the first approved treatment for the disease. Current first-line standard of care, tyrosine kinase inhibitor (TKI) Sutent, has been shown to lower Tregs in addition to its other functions. Therefore, anti-PD-1 and anti-CTLA4 therapies have been widely anticipated in this area. Our key takeaways from these early data are: 1) layering on a PD-1 to TKI therapy does not appear to add much efficacy, 2) combination therapy adds toxicities that may position it for the refractory population, 3) PD-1 monotherapy second line did not live up to expectations, and 4) PD-1 and ipilimumab combination therapy looks promising, but will small numbers (n=9) first line.

**Combination TKI efficacy similar to TKI therapy alone**. PFS for nivolumab (anti-PD-1) and Sutent was about 11.4 months; higher than recent 9.5-month data published for Sutent alone, but in a more favorable population; physicians at the meeting believe the PFS observed is in the range of Sutent alone. That being said, there was hope for delayed response to therapy and potentially a greater benefit in overall survival for the combination. We remind investors that in a higher-risk population than these studies, AGS-003 doubled both PFS and OS observed with Sutent alone (Figure 1).

**Nivolumab and Sutent combination leads to unexpected toxicities.** Treatment related adverse events for the combination were higher than expected for each therapy alone. Specifically, Grade 3/4 liver enzyme elevations and renal toxicities were higher than anticipated, including one Grade 3/4 acute liver failure (Figure 2). Physicians at the meeting expressed caution moving this combination forward and stressed that more work is needed to figure out dosing and timing of administration.

**Heather Behanna, PhD**
hbehanna@jmpsecurities.com
(312) 768-1795

**Michael G. King, Jr.**
mking@jmpsecurities.com
(212) 906-3520

**Nivolumab monotherapy may be positioned for refractory patients**. A dose-ranging study of nivolumab in mRCC patients demonstrated about a 25-month overall survival in refractory patients of varying risk (Figure 1). We estimate that this is in line with what would likely be expected for these patients on TKI therapy, although the median survival of 18.7 months for patients treated third and fourth line suggests a benefit for these patients.

**Nivolumab and ipilimumab data early, but promising**. mRCC patients were treated with nivolumab and ipilimumab in combination - about 20% were treatment naive. These data are early with the PFS not yet reached, although about 65% of patients are past six months without progression, suggesting this combination may work better than TKI therapy alone. We note that only nine of these patients were treatment naive and we do not know if they were favorable or poor risk patients, therefore, it is difficult to compare directly to AGS-003/Sutent. We see Argos with a first-mover advantage (nivo/ipi combination is planned, but not enrolling) and we await the Phase 3 data from each program to understand the profile and positioning of each combination.

**FIGURE 1. Overview of Efficacy Data**

| | TKI | Sutent | AGS-003 Sutent | Nivo Sutent | Nivo | Nivo Ipi |
|---|---|---|---|---|---|---|
| n | 1189 | 589 | 21 | 33 | 34 | 43 |
| First line (%) | 100% | 92% | 100% | 100% | 0% | 20% |
| Risk | | | | | | |
| Favorable | 0% | 25% | 0% | 24% | ~33% | 23% |
| Intermediate | 66% | 54% | 52% | 70% | ~50% | 76% |
| Poor | 34% | 19% | 48% | 0% | ~10% | 0% |
| PFS (months) | ~6 | 9.5 | 11.2 | 11.4 | ~4 | 65% at 6 months |
| OS (months) | 14.7 | n/a | 30.2 | n/a | 25.5 | n/a |

*Source: ASCO 2014*

**FIGURE 2. Treatment Related Adverse Events of Nivolumab and Sutent**

| | Sutent | | Sutent + Nivo | |
|---|---|---|---|---|
| | All | Grade 3/4 | All | Grade 3/4 |
| ALT elevation | 60% | 3% | 40% | 18% |
| AST elevation | 43% | 4% | 36% | 9% |
| Blood creatinine inc | 32% | 1% | 30% | 3% |
| Nephritis autoimmur | n/a | n/a | 3% | 3% |
| Acute renal failure | n/a | n/a | 12% | 3% |

*Source: ASCO 2014*

## Company Description

North Carolina-based Argos Therapeutics is a biopharmaceutical company focused on personalized immunotherapy for cancer and infectious disease. Its products are based in Argos's proprietary Arcelis platform with lead candidate AGS-003 in Phase III development for metastatic renal cell carcinoma in combination with Sutent as first line therapy. Argos is also developing AGS-004 for HIV eradication.

## Investment Risks

Clinical. Drug development is inherently risky and Argos's studies may not succeed. Argos is conducting a Phase III study based on a single arm Phase II trial, which carries various risks. It is possible that the study may not be powered properly to demonstrate a benefit of AGS-003. There is also risk that the combination of AGS-003 and Sutent will not outperform Sutent alone due to changes in patient population between Phase II and Phase III. Phase II data may be driven by factors outside of the mechanism of action of AGS-003 and may not translate into Phase III success. Manufacturing of AGS-003 may hinder enrollment rates, pushing out timelines to data. The company is also developing AGS-004 for HIV, an area where there has yet to be a successful vaccine. It is possible that AGS-004 will not succeed in allowing patients to discontinue anti-retroviral therapy.

Regulatory. AGS-003 pivotal study ADAPT is being conducted under a SPA with FDA; however, this does not guarantee approval. It is not known if the EMA will want more data, either clinical or on manufacturing before allowing Argos to file for EMA approval. For AGS-004, the regulatory path forward and potential commercial market is unclear. The timing of validation of automated manufacturing could lead to a delay in filing the BLA for AGS-003.

Commercial. Argos is developing personalized immunotherapies for cancer and infectious disease. The development of these products requires patient sample, either blood or tumor from surgery or biopsy, and patient cells obtained through leukapheresis. This may represent a paradigm shift in treatment and physicians may not be comfortable working these therapies into practice, creating commercial risk. Argos is finalizing automation of its manufacturing process; timing delays add risk to regulatory filing submissions. Unanticipated problems with automation may hinder Argos' ability to produce its therapies.

Competitive. Oncology drug development is competitive, with various companies bringing technologies forward that could make Argos's products obsolete. There are other targeted immunotherapies in development that, if successful, could be applied in RCC, adding direct competition to AGS-003.

Balance sheet. Following its IPO, Argos has cash to reach pivotal data; however, the company may seek additional equity financing, leading to dilution risk for shareholders. The company may seek debt financing for AGS-003 manufacturing facilities.

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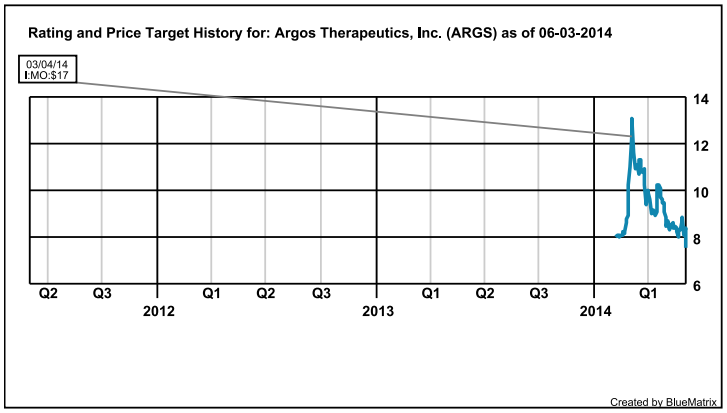
| JMP Rating | Regulatory Equivalent | # Co's Under Coverage | *% of Total* | Regulatory Equivalent | # Co's Under Coverage | *% of Total* | # Co's Receiving IB Services in Past 12 Months | *% of Co's With This Rating* |
|---|---|---|---|---|---|---|---|---|
| MARKET OUTPERFORM | Buy | 259 | *58.73%* | Buy | 259 | *58.73%* | 99 | *38.22%* |
| MARKET PERFORM | Hold | 134 | *30.39%* | Hold | 134 | *30.39%* | 17 | *12.69%* |
| MARKET UNDERPERFORM | Sell | 5 | *1.13%* | Sell | 5 | *1.13%* | 0 | *0%* |
| COVERAGE IN TRANSITION | | 43 | *9.75%* | | 43 | *9.75%* | 0 | *0%* |
| TOTAL: | | 441 | *100%* | | 441 | *100%* | 116 | *26.30%* |

**Stock Price Chart of Rating and Target Price Changes:**

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.



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**Jeffrey H. Spurr**
**Director of Research**
(415) 835-3903

## RESEARCH PROFESSIONALS

### FINANCIAL SERVICES

**Alternative Asset Managers**
Devin Ryan (212) 906-3578
Brian McKenna (212) 906-3545

**Commercial & Specialty Finance**
Christopher York (415) 835-8965
Hannah Kim, CFA (415) 835-8962

**Consumer Finance**
David M. Scharf (415) 835-8942
Jeremy Frazer (312) 768-1796

**Financial Processing & Outsourcing**
David M. Scharf (415) 835-8942
Jeremy Frazer (312) 768-1796

**Insurance**
Matthew J. Carletti (312) 768-1784
Christine Worley (312) 768-1786

**Investment Banks & Brokers**
Devin Ryan (212) 906-3578
Brian McKenna (212) 906-3545

**Mortgage Operating Companies**
**REITs: Agency, Hybrid, & Commercial Mortgage**
Steven C. DeLaney (404) 848-7773
Trevor Cranston, CFA (415) 869-4431
Charter Robinson (757) 613-8955
Benjamin Zucker (212) 906-3529

### HEALTHCARE

**Biotechnology**
Liisa A. Bayko (312) 768-1785
Heather Behanna, PhD (312) 768-1795
Andrew Prigodich (312) 768-1788
Jason N. Butler, PhD (212) 906-3505
Caroline Palomeque (212) 906-3509
Michael G. King, Jr. (212) 906-3520
Eric Joseph, PhD (212) 906-3514

**Healthcare Services & Facilities**
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Arthur Kwok (415) 835-8908

**Life Science Tools & Diagnostics**
J. T. Haresco, III, PhD (415) 869-4477
Marie T. Casey, PhD (415) 835-3955

**Medical Devices**
J. T. Haresco, III, PhD (415) 869-4477
Marie T. Casey, PhD (415) 835-3955

**Medical Devices & Supplies**
David Turkaly (212) 906-3563
John Gillings (212) 906-3564

### REAL ESTATE

**Housing & Land Development**
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Bharathwajan Iyengar (415) 835-3902

**Lodging & Leisure**
Robert A. LaFleur (212) 906-3510
Whitney Stevenson (212) 906-3538

**Property Services**
Mitch Germain (212) 906-3546
Peter Lunenburg (212) 906-3537

**REITs: Healthcare, Residential, & Specialty**
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Arthur Kwok (415) 835-8908

**REITs: Office, Industrial, & Diversified**
Mitch Germain (212) 906-3546
Peter Lunenburg (212) 906-3537

**Residential Services**
Peter L. Martin, CFA (415) 835-8904
Aaron Hecht (415) 835-3963
Bharathwajan Iyengar (415) 835-3902

### TECHNOLOGY

**Communications Equipment & Internet Security**
Erik Suppiger (415) 835-3918
John Lucia (415) 835-3920

**Internet & Digital Media**
Ronald V. Josey III (212) 906-3528
Andrew Boone, CFA (415) 835-3957
Michael Wu (415) 835-8996

**Software**
Patrick Walravens (415) 835-8943
Peter Lowry (415) 869-4418
Caitlin Schields (415) 835-8960
Greg McDowell (415) 835-3934

**Wireless & Cloud Computing Technologies**
Alex Gauna (415) 835-8998

## ADDITIONAL CONTACTS

**Thomas R. Wright**
**Director of Equities**
(212) 906-3599

**Dan Wychulis**
**Director of Institutional Sales**
(617) 235-8530

**600 Montgomery Street, Suite 1100**
San Francisco, CA 94111
www.jmpsecurities.com