ImmunoGen Presents Full Data from Phase 3 FORWARD I Study of Mirvetuximab Soravtansine in Ovarian Cancer at ESMO

September 29, 2019

FORWARD I Did Not Meet Primary Endpoint of Progression-Free Survival; Promising Efficacy Results Seen in Folate Receptor Alpha (FRα) High Patients

Favorable Tolerability and Differentiated Safety Profile Observed with Mirvetuximab Monotherapy Compared to Chemotherapy

Exploratory Analyses Demonstrate Improved Efficacy Outcomes in FRα High Patients

Registration Study for Mirvetuximab in Ovarian Cancer on Track to Start by Year-End

Conference Call to be Held Monday, September 30 at 8:00 a.m. ET

WALTHAM, Mass.--(BUSINESS WIRE)--Sep. 29, 2019-- ImmunoGen, Inc. (Nasdaq: IMGN), a leader in the expanding field of antibody-drug conjugates (ADCs) for the treatment of cancer, today announced full data and additional exploratory analyses from the Phase 3 FORWARD I study evaluating mirvetuximab soravtansine compared to chemotherapy in women with folate receptor alpha (FRα)-positive, platinum-resistant ovarian cancer during an oral presentation at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona, Spain.

"While it is disappointing that FORWARD I did not meet the primary endpoint of progression-free survival, mirvetuximab demonstrated consistent and meaningful efficacy signals in patients with high levels of FRα expression and was well tolerated with a differentiated safety profile in both the ITT and FRα high populations," said Dr. Kathleen Moore, Associate Director of Clinical Research at the Stephenson Cancer Center at the University of Oklahoma. "Despite recently reported advances in frontline treatment with the addition of PARPi maintenance therapy, the majority of patients will unfortunately develop platinum-resistant disease with limited therapeutic options characterized by low response rates, short progression-free survival, and significant toxicities. The encouraging data from FORWARD I suggest the potential for a significant improvement over single-agent chemotherapy in the FRα high population and I look forward to the continued development of mirvetuximab for these patients in the upcoming Phase 3 study."

The FORWARD I Phase 3 trial randomized 366 patients 2:1 to receive either mirvetuximab or the physician's choice of single-agent chemotherapy (pegylated liposomal doxorubicin, topotecan, or weekly paclitaxel). Eligibility criteria included patients with platinum-resistant ovarian cancer that expressed medium or high levels of FRα, who had been treated with up to three prior regimens. The primary endpoint of this study was progression-free survival (PFS), which was assessed using the Hochberg procedure in the entire study population and in the subset of patients with high FRα expression. The Hochberg procedure enables the simultaneous testing of two overlapping populations. Under this statistical analysis plan, if the p-value of the primary endpoint in either population is greater than 0.05, the p-value in the other population needs to be less than or equal to 0.025 to achieve statistical significance.

Key Findings from the Phase 3 FORWARD I Study

- In the entire study population, the confirmed overall response rate (ORR) was higher for mirvetuximab than for chemotherapy (22% vs 12%, p-value 0.015), without a significant difference in the primary endpoint of PFS (HR 0.981, p-value 0.897) or overall survival (OS) (HR 0.815, p-value 0.248).
- In the pre-specified FRα high subgroup (218/366, 60%):
    - Median PFS (mPFS) was longer in patients who received mirvetuximab compared with chemotherapy (4.8 months vs 3.3 months, HR 0.693, p-value 0.049). Given that the p-value in the entire study population exceeded 0.05, the statistical analysis plan for the study required the p-value in the high subset to be less than or equal to 0.025 to achieve statistical significance.
    - Confirmed ORR was higher for mirvetuximab than for chemotherapy (24% vs 10%, p-value 0.014).
    - OS was longer in patients who received mirvetuximab compared with chemotherapy (HR 0.618, p-value 0.033).
    - The trend in improved OS in patients who received mirvetuximab compared with chemotherapy persisted with an additional 6 months of follow-up (updated through August 2019: HR 0.678, with median OS [mOS] 16.4 months vs 12.0 months, p-value 0.048).
- Mirvetuximab was well-tolerated, with fewer patients experiencing grade 3 or greater treatment emergent adverse events (TEAEs) (46% vs 61%), fewer dose reductions (20% vs 31%), and fewer discontinuations due to drug-related TEAEs (5% vs 8%) compared with chemotherapy.
- The safety profile of mirvetuximab was confirmed, with the most common drug-related adverse events including nausea (46% all grades; 1% grade 3 or greater), blurred vision (42% all grades; 2% grade 3 or greater), and keratopathy (33% all grades; 1% grade 3 or greater).
- Over twice the percentage of patients who received mirvetuximab compared with chemotherapy reported improved quality of life, as measured by at least a 15-point improvement in the abdominal/GI symptom subscale of the EORTC-QLQ OV28 (32% vs 14%).

Exploratory Analyses
"While FORWARD I generated promising outcomes in the FRα high subgroup, the anti-tumor activity did not reach the levels we have observed in our previous studies with mirvetuximab. Accordingly, we have undertaken a comprehensive assessment of the factors that may have contributed to the outcomes in FORWARD I. These exploratory analyses demonstrate that the use of a simplified scoring method to assess tumor samples for FRα expression inadvertently introduced a population of patients into FORWARD I with lower levels of FRα than intended," said Anna Berkenblit, M.D., Senior Vice President and Chief Medical Officer of ImmunoGen. "When we reassessed the FORWARD I tumor samples using the scoring method from our previous studies, we determined that a significant percentage of patients included in FORWARD I had low levels of FRα expression that should have precluded enrollment. For those patients with medium or high levels of FRα expression upon rescoring, we observed efficacy outcomes for mirvetuximab much more in line with our previous experience, with improved activity correlating with FRα expression and the strongest treatment effect for all efficacy endpoints in the intended FRα high patient population. These findings have informed the design of our planned Phase 3 registration trial in FRα high patients."

Previous studies with mirvetuximab have used a PS2+ scoring method to assess tumor samples for FRα expression to determine eligibility. The PS2+ scoring method assesses both intensity of staining (0, 1+, 2+, or 3+) and percentage of tumor cells staining at each intensity, with at least 50% of cells with at least 2+ staining considered FRα medium and at least 75% of cells with at least 2+ staining considered FRα high.

In preparation for launch of a companion diagnostic for commercial use, a simplified scoring method to assess FRα expression, known as 10X, was implemented prior to the start of FORWARD I. Eligibility was determined by scoring the percentage of tumor cells with positive membrane staining by ≤10X magnification without the need to separately assess level of intensity. A bridging study indicated that the 10X scoring method was sufficient for patient selection: staining visible at ≤10X magnification correlated with higher intensity staining (2+ and 3+), with lower intensity staining visible only at higher magnification.

Comparison to the much larger dataset from patients enrolled in FORWARD I, however, suggested a significant population shift towards increased prevalence of FRα expression under the 10X scoring method as compared to the PS2+ scoring method. Rescoring of the FORWARD I tumor samples by an independent pathologist, blinded to treatment assignment, using the PS2+ method demonstrated that 34% of patients enrolled in FORWARD I had FRα expression below the intended level. In addition, the FRα high subset enrolled in the study also contained a mixture of FRα expression when scored using the PS2+ method.

Key Findings from Exploratory PS2+ Scoring for FRα Determination in Phase 3 FORWARD Study
Exploratory efficacy analyses of the FORWARD I patients scored using the PS2+ method demonstrate improved outcomes correlated with FRα expression, with the strongest treatment effects for all efficacy endpoints in the PS2+ FRα high population (n=116). Compared with chemotherapy, mirvetuximab was associated with:

- Longer PFS (mPFS 5.6 months vs 3.2 months, HR 0.549 [95% CI 0.336, 0.897]);
- Higher confirmed ORR (29% vs 6%); and
- Longer OS (updated through August 2019: mOS 16.4 months vs 11.4 months, HR 0.678 [95% CI 0.410, 1.119]).

"With the results of these exploratory analyses, we have developed a clear view of which patients benefit most from mirvetuximab and how to best identify those patients," said Mark Enyedy, ImmunoGen's President and Chief Executive Officer. "We are working closely with FDA to finalize the design of a Phase 3 registration trial for mirvetuximab, which we call MIRASOL, and believe that the robust data generated from the FORWARD I analyses increase the likelihood of a positive outcome with this next study. We anticipate enrolling the first patient by the end of the year with topline readout in the first half of 2022."

ESMO Oral Presentation Details

- **Title:** "FORWARD I (GOG 3011): A Phase III study of mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), versus chemotherapy in patients (pts) with platinum-resistant ovarian cancer (PROC)" (Abstract #992O)
- **Date:** Sunday, September 29, 2019
- **Time:** 8:30 a.m. CEST/2:30 a.m. ET
- **Lead Author:** Kathleen Moore M.D., University of Oklahoma Health Sciences Center, Oklahoma City, OK

Additional information can be found at www.esmo.org.

CONFERENCE CALL INFORMATION
ImmunoGen will host a conference call on Monday, September 30, 2019 at 8:00 a.m. ET to discuss the complete findings from FORWARD I. Access the call using the information below.

PHONE
US Toll-Free: (877) 621-5803
Spain Toll-Free: 900971520
Barcelona Local: 0934923253
International: (470) 495-9491
Conference ID: 8295336

SLIDES/WEBCAST
Link: https://edge.media-server.com/mmc/p/jwvdobji

ABOUT MIRVETUXIMAB SORAVTANSINE
Mirvetuximab soravtansine (IMGN853) is the first folate receptor alpha (FRα)-targeting ADC. It uses a humanized FRα-binding antibody to target the ADC specifically to FRα-expressing cancer cells and a potent anti-tumor agent, DM4, to kill the targeted cancer cells.

ABOUT FORWARD I
FORWARD I is a Phase 3 trial in which 366 patients were randomized 2:1 to receive either mirvetuximab soravtansine or the physician's choice of single-agent chemotherapy (pegylated liposomal doxorubicin, topotecan, or weekly paclitaxel). Eligible patients were diagnosed with platinum-resistant ovarian cancer that expresses medium or high levels of folate receptor alpha (FRα) and were treated with up to three prior regimens. The primary endpoint of this study was progression free survival (PFS), which was assessed in the entire study population and in the subset of patients with high FRα expression. ImmunoGen estimates that 12,000-14,000 patients per year in the U.S. meet these criteria, with a comparable number in the major markets in Europe.

ImmunoGen partnered with the GOG Foundation Inc., a leader in clinical research in gynecologic malignancies, on FORWARD I, which was conducted in North America and Europe.

ABOUT IMMUNOGEN
ImmunoGen is developing the next generation of antibody-drug conjugates (ADCs) to improve outcomes for cancer patients. By generating targeted therapies with enhanced anti-tumor activity and favorable tolerability profiles, we aim to disrupt the progression of cancer and offer our patients more good days. We call this our commitment to “target a better now.”

Learn more about who we are, what we do, and how we do it at www.immunogen.com.

This press release includes forward-looking statements regarding ImmunoGen’s expectations related to: the design and potential success of ImmunoGen’s future mirvetuximab soravtansine studies and regulatory pathway, including the timing of initiating and receiving data from, as well as the likelihood of success of, the planned registration study of mirvetuximab. For these statements, ImmunoGen claims the protection of the safe harbor for forward-looking statements provided by the Private Securities Litigation Reform Act of 1995. Various factors could cause ImmunoGen’s actual results to differ materially from those discussed or implied in the forward-looking statements, and you are cautioned not to place undue reliance on these forward-looking statements, which are current only as of the date of this release. Factors that could cause future results to differ materially from such expectations include, but are not limited to: the timing and results of communications with FDA, risks and uncertainties related to the execution of the restructuring of the Company’s operations, the Company’s ability to control future spending and obtain additional funds to enable it to fund its continuing operations through the release of top-line results from the planned mirvetuximab pivotal study, the possibility that future studies fail to replicate the data indicated in the exploratory analyses of the FORWARD 1 data, and the risks and uncertainties inherent in the Company’s development programs, including clinical studies and regulatory processes, their timings and results. A review of these risks can be found under the heading “Risk Factors” in ImmunoGen’s Annual Report on Form 10-K for the year ended December 31, 2018 and subsequent documents filed with the Securities and Exchange Commission.

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