REPORT SYNOPSIS

<table>
<tr><td>Name of Sponsor/Company:
ArQule, Inc.</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier
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<tr><td>Name of Test Product:
ARQ 197</td></tr>
<tr><td>Name of Active Ingredient:
ARQ 197</td></tr>
<tr><td>Title of Study:</td><td colspan="2">A Randomized Phase 2 Study of ARQ 197 versus Gemcitabine in Treatment-Naïve Patients with Unresectable Locally Advanced or Metastatic Pancreatic Adenocarcinoma</td></tr>
<tr><td>Phase of Development:</td><td colspan="2">Phase 2</td></tr>
<tr><td>Study Period:</td><td colspan="2">First Patient first visit date: 20 November 2007
Date of last patient visit: 28 February 2009</td></tr>
<tr><td>Investigator(s):</td><td colspan="2">See Appendix 16.1.4 for complete list of Investigators</td></tr>
<tr><td>Study Center(s):</td><td colspan="2">Poland: 402, 406, 410, 411, 412, 413, and 414
Latvia: 600, 601</td></tr>
<tr><td>Publication (reference):</td><td colspan="2">Not applicable</td></tr>
<tr><td>Study Objectives/Hypothesis:</td><td colspan="2">The primary objective of the study was to evaluate progression-free survival (PFS) in patients receiving ARQ 197 versus gemcitabine.
The secondary objectives of the study were to:
evaluate overall response rate (ORR) in patients receiving ARQ 197 versus gemcitabine,
evaluate 6-month and 1-year overall survival (OS) rates in patients treated with ARQ 197 versus gemcitabine, and
further characterize the safety profile of ARQ 197.
The exploratory objective of the study was to:
evaluate the circulating tumor cells (CTC) following treatment with ARQ 197 or gemcitabine.</td></tr>
<tr><td>Study Design/Methodology:</td><td colspan="2">This was a multi-center, open-label, randomized, Phase 2 study designed to evaluate the PFS of treatment-naïve patients with unresectable (locally advanced or metastatic) pancreatic adenocarcinoma following treatment with either ARQ 197 (ARQ arm) or gemcitabine (GEM arm). The study also evaluated other efficacy and safety parameters including ORR, OS and adverse events in the two treatment arms.
Patients randomly assigned to the GEM arm received an intravenous infusion of gemcitabine over 30 minutes at a dose of 1000 mg/m^2. The dosing schedule of gemcitabine was once weekly for the first cycle (four weeks), then once weekly for three consecutive weeks followed by a week of rest for each subsequent cycle.
Patients randomly assigned to the ARQ arm received 120 mg of ARQ 197 twice daily (240 mg/day) throughout the treatment period.
Treatment with study medication continued until unacceptable toxicity, documented progression of disease, or another discontinuation criterion was met. A cycle was defined as 28 days for both treatment arms. Cycles were repeated every four weeks (28 days) based on toxicity and response.</td></tr>
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Duration of Treatment for Individual Patient:	The assigned treatment continued until unacceptable toxicity, disease progression (clinical or radiological) or another discontinuation criterion was met. It was expected that most patients would receive between three and six cycles of gemcitabine or ARQ 197 for a treatment period of 12 to 24 weeks.
Number of Patients:	Planned: 72 patients Enrolled/Randomized: 43 patients enrolled Discontinued: 43 patients
Diagnosis and Main Criteria for Study Entry:	The study enrolled adult treatment-naïve patients with a histologically or cytologically confirmed locally advanced or metastatic pancreatic adenocarcinoma.
Investigational Product:	ARQ 197 Dosage Form: capsule Route of Administration: oral Packaging Information: The 120 mg capsules were packaged in bottles.
Comparator Product Information:	Gemcitabine Dosage Form: Powder for solution Route of Administration: Intravenous infusion Packaging Information: 200 mg vial for injection and 1000 mg vial for injection

Lot Numbers for ARQ 197 and Gemcitabine per Site

Site Number	ARQ 197 120 mg	GEM 200 mg	GEM 1000 mg
402	0708039A 0710043A	A 394131 A 330422 A 423633 A 425642F A 062010	A393527 A410638 7807A 7836A A260441
406	0708039A	NA	NA
410	0708039A	A394131	A410638 A393527 A413932 A330093
411	0708039A	A394131 A330422 A423633 A425642F A451131F A463770D	A410638 A410636 A330093 7807A 7836A 7846C 7844E A393527
412	0708039A	A 423633 425642F	7836A 7846C

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			A451131S A 463770D	7844E
	413	0708039A 0710043A	NA	NA
	414	0708039A 0710043A	A 330422 A 394131 A 423633 A 425642F A 463770D	A 330093 A 330087 A 410638 A 353527 A 7846C A 7836A A 393527 A 469842A
	601	0708039A	A418338	A428265

Criteria for Evaluation:

Efficacy:

UUProgression-free survival: The time of disease progression-free survival was calculated from randomization until disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) or death due to any cause. Patients who were alive and progression free were censored at the date of their last tumor evaluation.

Tumor evaluations: Tumor evaluations were performed in 8-week intervals. Tumor response (complete response [CR], partial response [PR], stable disease [SD], progressive disease [PD] and ORR) was evaluated using RECIST.

Overall survival: Overall survival time was calculated from the date of randomization until death due to any cause.

Pharmacokinetics/Pharmacodynamics: Not applicable

Safety: Data on vital signs, physical examination, adverse events, serum chemistry, hematological laboratory tests, and electrocardiograms were collected.

Statistical Methods:

This study was not powered to show statistically significant differences between the treatment arms. Therefore, the analyses are primarily descriptive in nature. There was no formal interim analysis and no specified stopping rule.

A total of 43 patients were enrolled in this study, however, 40 patients received study drug and constituted the Safety Population. The Safety Population was defined as all patients who received any amount of ARQ 197 or gemcitabine.

Summary:

Efficacy Results:

There were 40/43 patients (93.0%), 19/22 patients (86.4%) in the ARQ 197 treatment arm and 21/21 patients (100.0%) in the gemcitabine treatment arm, who were included in the Intent-to-Treat (ITT) patient population.

Progression-free survival: For the ITT population, the median PFS was 58 days for the patients receiving ARQ 197 and 148 days for those patients receiving gemcitabine. For the Evaluable population, the median PFS was 60 days for the patients receiving ARQ 197 and 153 days for those patients receiving gemcitabine.

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Tumor evaluations: No patient in the ITT population who was treated with either ARQ 197 or gemcitabine achieved a CR. Four out of 21 patients (19.0%) who received gemcitabine had a PR (patients 05, 17, 26, and 36). Three out of 19 patients (15.8%) in the ARQ 197 treatment arm and 10 out of 21 patients (47.6%) in the gemcitabine treatment arm achieved a best response of stable disease (SD). Six out of 19 patients (31.6%) who received ARQ 197 and three out of 21 patients (14.3%) who received gemcitabine demonstrated progression of disease.

Overall survival: The estimated 6-month and 1-year survival rates were 36.9% and 30.8% for the ARQ 197 treatment arm and 65.0% and 28.6% for the gemcitabine treatment arm for the ITT population. The estimated 6-month and 1-year survival rates were 66.7% and 55.6% for the ARQ 197 treatment arm and 71.4% and 33.3% for the gemcitabine treatment arm for the Evaluable population.

Circulating Tumor Cells (CTC): c-MET expression was positive in eight of the 13 samples (62%). CTCs were obtained from eight of 13 patients tested at the end of treatment and three were positive for c-MET (38%). No FISH data were obtained due to the poor quality of the CTCs obtained.

No overall conclusions can be deduced since the study was stopped early for futility.

Safety Results:

Extent of Exposure: In the ARQ 197 treatment arm, 19 patients received a mean cumulative dose over the whole study of 15246.3 mg (range: 240 – 72720 mg) and had a mean duration of exposure of 63.5 days (range: 1 – 303 days). In the gemcitabine treatment arm, 21 patients received a mean cumulative dose over the whole study of 12070.0 mg/m^2 (range: 2000 – 25000 mg/m^2) and had a mean duration of exposure of 72.8 days (range: 16 – 140 days).

Adverse Events:

There were a total of 40 patients evaluable for safety (19 patients in the ARQ 197 treatment arm and 21 patients in the gemcitabine treatment arm).

The following table summarizes the number of patients with treatment-emergent adverse events (TEAEs).

	ARQ-197 (N=19)	**Gemcitabine (N=21)**	**All Patients (N=40)**
At Least One TEAE	17 (89.5%)	21 (100.0%)	38 (95.0%)
At Least One TEAE Related to Study Drug	8 (42.1%)	18 (85.7%)	26 (65.0%)
At Least One Severe (Grade 3 or Worse) TEAE	13 (68.4%)	16 (76.2%)	29 (72.5%)
At Least One Serious TEAE	12 (63.2%)	9 (42.9%)	21 (52.5%)
At Least One Serious TEAE Related to Study Drug	0 (0.0%)	3 (14.3%)	3 (7.5%)
TEAEs Leading to Treatment Discontinuations	5 (26.3%)	8 (38.1%)	13 (32.5%)
TEAEs Leading to Deaths	9 (47.4%)	4 (19.0%)	13 (32.5%)

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The five most common TEAEs for those patients receiving ARQ 197 were malignant neoplasm progression (9/19 patients, 47.4%), fatigue (8/19 patients, 42.1%), peripheral edema (5/19 patients, 26.3%), anorexia (5/19 patients, 26.3%), and ascites (5/19 patients, 26.3%). The five most common TEAEs for those patients receiving gemcitabine were decreased platelet count (8/21 patients, 38.1%), fatigue (7/21 patients, 33.3%), peripheral edema (7/21 patients, 33.3%), pyrexia (7/21 patients, 33.3%), and anemia (7/21 patients, 33.3%).

There were 29/40 patients (72.5%) with at least one severe TEAE: 13/19 patients (68.4%) in the ARQ 197 treatment arm and 16/21 patients (76.2%) in the gemcitabine treatment arm. The severe TEAEs occurring in more than 5% patients included malignant neoplasm progression (13/40, 32.5%) (9/19 [47.4%] in ARQ 197 treatment arm and 4/21 [19.0%] in gemcitabine treatment arm), increased blood alkaline phosphatase (5/40, 12.5%), (3/19 [15.8%] in the ARQ 197 treatment arm and 2/21, [9.5%] in the gemcitabine treatment arm), fatigue (8/40, 20.0%) (4/19 [21.1%] in the ARQ 197 treatment arm and 4/21 [19.0%] in the gemcitabine treatment arm), hyperbilirubinemia (3/40, 7.5%), (3/19 [15.8%] in the ARQ 197 treatment arm and none in the gemcitabine treatment arm), and increased gamma-glutamyl transferase (5/40, 12.5%), (2/19 [10.5%] in the ARQ 197 treatment arm and (3/21 [14.3%] in the gemcitabine treatment arm).

The maximum severity of TEAEs by patients was classified as mild in 1/40 (2.5%) of all patients (1/19, 5.3% of patients in the ARQ 197 treatment arm and no patients in the gemcitabine treatment arm), as moderate in 8/40 (20.0%) of all patients (3/19, 15.8% of patients in the ARQ 197 treatment arm and 5/21, 23.8% of patients in the gemcitabine treatment arm), as severe in 13/40 (32.5%) of all patients (3/19, 15.8% of patients in the ARQ 197 treatment arm and 10/21, 47.6% in the gemcitabine treatment arm), and as life-threatening in 3/40 (7.5%) of all patients (1/19, 5.3% of patients in the ARQ 197 treatment arm and 2/21, 9.5% in the gemcitabine treatment arm).

There were 13 patients (32.5%), nine patients (47.4%) in the ARQ 197 treatment arm and four patients (19.0%) in the gemcitabine treatment arm, who experienced a TEAE which lead to the patient's death, none of which were considered related to treatment. Malignant neoplasm progression was the reason for death for all nine patients in the ARQ 197 and two patients in the gemcitabine treatment arm. The other two gemcitabine patients died from cardiac arrest and fatigue/malignant neoplasm progression. There were 14 patients who died more than 30 days after the last dose of study medication.

There were 21 patients (52.5%) with at least one serious adverse event (SAE): 12 patients (63.2%) in the ARQ 197 treatment arm and nine patients (42.9%) in the gemcitabine treatment arm. The most common SAE was malignant neoplasm progression with a total of 13 patients (32.5%), nine patients (47.4%) in the ARQ 197 treatment arm and four patients (19.0%) in the gemcitabine treatment arm.

There were a total of 13 patients (32.5%), five patients (26.3%) in the ARQ 197 treatment arm and eight patients (38.1%) in the gemcitabine treatment arm, who discontinued treatment due to an AE. The most common TEAEs were fatigue, with a total of three patients (7.5%), all in the gemcitabine treatment arm, and malignant neoplasm progression, with a total of three patients (7.5%), one patient (5.3%) in the ARQ 197 treatment arm and two patients (9.5%) in the gemcitabine treatment arm.

One patient had a clinically significant electrocardiogram result. Patient 15, in the gemcitabine treatment arm, had a normal pre-study electrocardiogram but had atrial fibrillation at the end of treatment evaluation that was considered clinically significant by the Investigator but not related to gemcitabine. No action was taken and the patient recovered with sequelae.

Twenty-nine of the 40 patients (72.5%), 13/19 patients (68.4%) in the ARQ 197 treatment arm and 16/21 patients (76.2%) in the gemcitabine treatment arm, had an abnormal physical examination at some time in the study.

Pharmacokinetic/Pharmacodynamic Results: Not applicable

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Conclusions:

There were a total of 43 patients with pancreatic adenocarcinoma enrolled in this multi-center, open-label, randomized, Phase 2 study designed to evaluate the PFS, ORR, and OS following treatment with either ARQ 197 (ARQ arm) or gemcitabine (GEM arm).

There were 40/43 patients (93.0%), 19/22 patients (86.4%) in the ARQ 197 treatment arm and 21/21 patients (100.0%) in the gemcitabine treatment arm, who were included in the ITT patient population. The median PFS was 58 days for the patients receiving ARQ 197 and 148 days for those patients receiving gemcitabine.

No patient in the ITT population who was treated with either ARQ 197 or gemcitabine achieved a CR. Four out of 21 patients (19.0%) who received gemcitabine had a PR. Three out of 19 patients (15.8%) in the ARQ 197 treatment arm and 10 out of 21 patients (47.6%) in the gemcitabine treatment arm achieved a best response of stable disease (SD). Six out of 19 patients (31.6%) who received ARQ 197 and three out of 21 patients (14.3%) who received gemcitabine demonstrated progression of disease.

The estimated 6-month survival rate was 66.7% for the ARQ 197 treatment arm and 71.4% for the gemcitabine treatment arm for the Evaluable population.

There were a total of 40 patients evaluable for safety (19 patients in the ARQ 197 treatment arm and 21 patients in the gemcitabine treatment arm). The five most common TEAEs for those patients receiving ARQ 197 were malignant neoplasm progression (9/19 patients, 47.4%), fatigue (8/19 patients, 42.1%), peripheral edema (5/19 patients, 26.3%), anorexia (5/19 patients, 26.3%), and ascites (5/19 patients, 26.3%). The five most common TEAEs for those patients receiving gemcitabine were decreased platelet count (8/21 patients, 38.1%), fatigue (7/21 patients, 33.3%), peripheral edema (7/21 patients, 33.3%), pyrexia (7/21 patients, 33.3%), and anemia (7/21 patients, 33.3%).

Date of the Report: 14 July 2011