A Phase 1, Dose-escalation, First-in-human Study of ARQ 087, an Oral Pan-FGFR Inhibitor, in Adult Subjects with Advanced Solid Tumors

K. P. Papadopoulos1, A. W. Tolcher2, M. Kittaneh3, A. Patniak4, D. W. Rasco5, G. Chambers3, G. Newth1, R. Savage3, T. Hall1, B. Schwartz2, J. Kazakian1, F. M. LoRusso1

1South Texas Accelerated Research Therapeutics, San Antonio, TX, USA; 2Karmanos Cancer Institute, Detroit, MI, USA; 3ArQule, Inc., Woburn, MA, USA

Abstract #389

BACKGROUND

 Dysregulation of Fibroblast Growth Factor Receptor (FGFR) signaling has been implicated in a number of developmental abnormalities and in several human cancers, e.g., lung, gastric, breast, and urothelial cancer and cholangiocarcinoma.1-3 ARQ 087 is a novel, ATP competitive multi-kinase inhibitor with pan-FGFR activity against FGFR1-3. ARQ 087’s clinical activity against FGFR1 and FGFR2 was observed in preclinical models in vitro and in vivo, displaying effects on a variety of human tumor cell lines and xenograft models.

METHODS

As of 15 October 2014, 14 subjects have been treated with ARQ 087. Enrollment in Dose-escalation cohorts is completed. Enrollment in the Food-effect cohorts is ongoing, and presented data are preliminary.

Study Design: Open Label, Dose Escalation

- Cohorts 1-6: 25 – 200 mg QD
- Cohorts 7-10: 250 – 425 mg QD

Expanded/Food-effect Cohorts

- Cohort 11-15: 25 mg QOD
- Cohort 16-20: 25 mg QOD

- Cohort 21-25: 50 mg QOD
- Cohort 26-30: 100 mg QOD
- Cohort 31-35: 150 mg QOD
- Cohort 36-40: 200 mg QOD
- Cohort 41-45: 250 mg QD
- Cohort 46-50: 325 mg QD
- Cohort 51-55: 425 mg QD
- Cohort 56-60: 400 mg QD

- Cohort 61-65: 400 mg QD

Cohort 1: 25 mg QOD
Cohort 2: 25 mg QD
Cohort 3: 50 mg QD
Cohort 4: 100 mg QD
Cohort 5: 150 mg QD
Cohort 6: 200 mg QD
Cohort 7: 250 mg QD
Cohort 8: 325 mg QD
Cohort 9: 425 mg QD
Cohort 10: 400 mg QD

Intra-subject dose escalation not to exceed 3+3* subjects per cohort (*if DLT; and clinical activity not met).

Efficacy

- Pretreatment levels of each FGF were compared to the levels observed during treatment with ARQ 087. On average, FGF protein levels increased in a dose proportional manner from 250 – 425 mg QD.

- The authors express their sincere appreciation and gratitude to patients, their families and investigators who participated in the study.

RESULTS

- ARQ 087 showed a manageable safety profile in subjects with advanced solid tumors.
- The BID has been identified as the MTD.
- Only two subjects (1%) experienced Grade 1 drug-related hypophosphatemia; however, increase in phosphates within normal ranges was noted in 57% (36%) treated subjects.
- 10 subjects (16%) enrolled in the Dose Escalation cohorts (N=54) had confirmed SD 3+6 weeks (adenocarcinotic [2], endometrial and ovarian adenocarcinoma, urothelial metastasis; carcinoid, metastases, chondrosarcoma, and lymphosarcoma).
- Increased FGF levels are a potential surrogate marker for FGFR receptor engagement. Evaluation of other potential biomarkers is ongoing.

- The Expanded cohort enrollment will include subjects with pre-defined tumor types and known FGFR1-3 status.

CONCLUSIONS

- Further development of ARQ 087 as monotherapy or in combination with other anti-cancer agents is deemed feasible considering its favorable safety profile and preliminary evidence of biological activity.

ACKNOWLEDGMENTS

The authors thank the patients, their families, and investigators who participated in this study. They also thank Mark Wang and SQ for providing statistical and editorial assistance. This work is supported by the National Cancer Institute (U54 CA 142994) and ArQule, Inc., Woburn, MA, USA.

REFERENCES

5. LoRusso PM et al. Park 8 of 2013, 2012-077684.