

Tracon Pharmaceuticals (TCON)

First Patient Dosed in Tracon's Phase III Study with TRC105 in Angiosarcoma

Tracon Pharma (NasdaqGM: TCON) announced that it has dosed the first patient in its registration enabling [Phase III](#) TAPPAS study with lead asset TRC105 (carotuximab), an anti-endoglin antibody, in angiosarcoma. This study is being conducted under a Special Protocol Assessment (SPA) agreement with the FDA. 124 patients are planned to enroll in the US and Europe, and will be randomized 1:1 to receive Novartis's (NYSE: NVS) VEGFR inhibitor *Votrient* (pazopanib) alone or in combination with TRC105. The trial employs an adaptive design that could allow for up to 200 patients to enroll. Progression free survival is the primary endpoint. Interim data from the Phase III trial are expected in the first half of 2018.

- First Patient Dosed in Pivotal Phase III Study.** There is currently no drug approved specifically for angiosarcoma, which is a rare form of soft tissue sarcoma. Notably, Tracon's study is the first Phase III study focused solely on this indication. 124 patients will be randomized between the US and EU with advanced angiosarcoma to receive TRC105 plus *Votrient* or *Votrient* monotherapy. Patients are being stratified based on cutaneous and non-cutaneous subtype, and the number of prior chemotherapies. Cutaneous disease comprises roughly half of the angiosarcoma population. This study has an adaptive design, which will allow the Company to shift enrollment following an interim analysis if needed to only include patients with cutaneous or non-cutaneous disease. This would occur if activity is seen in only one of the subtypes. As a reference, 9 patients with angiosarcoma have been treated with the combination of TRC105 and *Votrient*, and responses were seen in 2 patients with cutaneous angiosarcoma.
- Durable Responses Seen with TRC105 plus *Votrient* in Angiosarcoma.** The Phase III study is supported by Phase Ib/II data using the combination of TRC105 plus *Votrient* in 9 angiosarcoma patients. The most recent [update](#) from this study was at the Connective Tissue Oncology Society (CTOS) meeting in November 2016. As shown in **Figure 1**, 2 out of 5 patients with cutaneous angiosarcoma had ongoing complete responses (CRs) after 19 and 26 months at the time of the presentation. 8 of 9 patients experienced tumor reduction or clinical improvement following treatment, and the median PFS for all patients was 5.6 months. Although early, this data is promising to us considering responses to *Votrient* monotherapy are typically not seen in patients with angiosarcoma. Treatment with the combination of TRC105 and *Votrient* was generally safe and well tolerated. Adverse events specific to each individual drug were not increased with combination treatment.

Expected Upcoming Milestones

- H1 2017 – Full Phase IIa results for TRC105 in NCI sponsored trial in hepatocellular carcinoma.
- H2 2017 – Topline Randomized Phase IIb results for TRC105 in renal cell carcinoma.
- H1 2017 – Begin Phase I/II proof-of-concept study with TRC253.
- Late 2017 – Data from Phase II trial using TRC105 plus *Nexavar* in hepatocellular carcinoma.
- H1 2018 – Interim analysis of Phase III trial with TRC105 in angiosarcoma.
- 2018 – File IND for TRC694.

Analysts

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Market Data

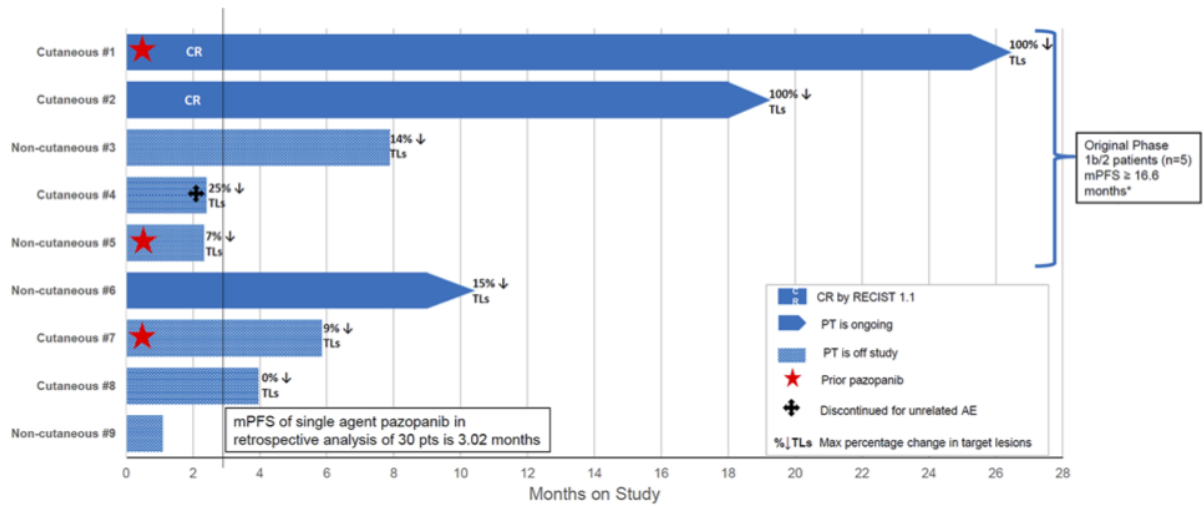
Price	\$4.00
Market Cap (M)	\$66
EV (M)	\$31
Shares Outstanding (M)	16.5
Fully Diluted Shares (M)	18.5
Avg Daily Vol	86,367
52-week Range:	\$3.60 - \$7.90
Cash (M)*	\$44.1
Net Cash/Share	\$2.13
Annualized Cash Burn (M)	\$29.1
Years of Cash Left	~1.5
Debt (M)	\$9.0
Short Interest (M)	0.16
Short Interest (% of Float)	1.9%

*Pro Forma

Financials

FY Dec	2014A	2015A	2016A
EPS	Q1 (0.88)A	(0.50)A	(0.54)A
	Q2 (0.65)A	(0.24)A	(0.68)A
	Q3 (1.23)A	(0.53)A	(0.48)A
	Q4 (1.64)A	(0.91)A	NA
FY	(4.40)A	(2.20)A	NA

Figure 1. Angiosarcoma Patient Responses to TRC105 Plus Votrient



Source: Company Presentation

- Mechanism of Angiosarcoma Development Correlated with Angiogenic Mutations.** The hypoxic environment in most solid tumors leads to neo-angiogenesis, providing the rationale for anti-VEGF therapy. The mechanism for angiogenesis in angiosarcoma differs in that it is often caused by mutations in angiogenic genes themselves. At a recent [KOL event](#), Dr. Mrinal Gounder, a sarcoma specialist at Memorial Sloan Kettering Cancer Center, mentioned that roughly [38%](#) of angiosarcomas have at least 1 driver mutation in an angiogenic signaling gene. *Votrient* is the only tyrosine kinase inhibitor (TKI) approved in sarcoma, and is approved in the second line setting. The overall response rate to *Votrient* in its [Phase III PALETTE](#) trial in sarcoma patients was 6%, and the median PFS was 4.6 months.

One of the main resistance mechanisms to VEGF inhibitors is the [upregulation of endoglin](#). On the other hand, inhibiting endoglin by itself can induce an upregulation of VEGF. By combining TRC105, an anti-endoglin antibody, with *Votrient*, a VEGFR inhibitor, Tracoon intends to better prevent cancer angiogenesis from occurring.

- There are approximately 1,700 New Angiosarcoma Patients per Year in the US and EU.** Soft tissue sarcoma (STS) accounts for approximately 1% of all adult cancers and 15% of pediatric cancers. According to the American Cancer Society, an estimated 12,390 Americans will be diagnosed with STS in 2017. This number is consistent with [data](#) from studies that include the SEER database of 26,758 cases of STS in the US collected between 1978 and 2001.

In the SEER data, 4% of STS cases were angiosarcoma, translating into roughly 500 new cases per year. The estimated incidence in Europe varies depending on the country or territory analyzed. Rates are as low as 1.8 per 100,000 from a small study in Sweden to 4.9/100,000 based on data from [RARECARE](#), a multi-country initiative to estimate the incidence and prevalence of rare cancers in Europe. Using the incidence from RARECARE, there are approximately 25,000 new cases of STS per year in the EU. A [study](#) from France and Italy estimated the angiosarcoma rate at 4.8% of all STS cases, which would translate into nearly 1,200 new cases of angiosarcoma per year in the EU.

- Phase III Angiosarcoma Trial Design.** This is an open-label, randomized [Phase III](#) trial evaluating the combination of TRC105 and *Votrient* in patients who have advanced angiosarcoma. An estimated 124 patients will be enrolled, although an adaptive design allows for up to 200 patients. Patients are being stratified based on cutaneous and non-cutaneous subtype, and number of prior chemotherapies. Enrollment of 124 patients will give 83% power to detect a hazard ratio (HR) of 0.55 for median PFS (7.3 months vs. 4.0 months), assuming an alpha of 0.05. Patients will be randomized 1:1 to receive TRC105 plus *Votrient* or *Votrient* alone.

One interesting aspect of this trial is that *Votrient* is only approved as a second line treatment for sarcoma, but US and European regulators have agreed to allow its use as a first line treatment in the trial. The primary endpoint is median PFS, and the secondary endpoints include overall response rate (ORR) and median overall survival (OS). An interim data readout from this trial is expected in the first half of 2018, with full data coming in late 2018 or early 2019.

Risk to Investment

We consider an investment in Tracon Pharmaceuticals to be a high-risk investment. Tracon Pharmaceuticals is a development stage company with no history of taking a treatment to market and currently has no FDA approved drugs in its portfolio. There are other companies attempting to develop anti-endoglin antibodies. Tracon's lead program has not yet enrolled patients in Phase III trials and has limited data to date. Furthermore, early indications of efficacy do not necessarily translate into positive late-stage results. Phase III clinical trials will result in significant additional expenses to the Company and may require additional rounds of dilutive financing. As with any company, Tracon Pharmaceuticals may be unable to obtain sufficient capital to fund planned development programs. There are regulatory risks associated with the development of any drug and Tracon Pharmaceuticals may not receive FDA approval for its candidates despite significant time and financial investments. Regulatory approval to market and sell a drug does not guarantee that the drug will penetrate the market, and sales may not meet expectations.

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