



# **Threshold Pharmaceuticals**

## Rich pipeline of opportunities

TH-302 is being investigated in a number of indications outside of the key soft tissue sarcoma (STS) and pancreatic cancer Phase III programmes. These include other solid tumors and blood cancers in combination with chemotherapy and antiangiogenics, and as monotherapy in certain cancers. Data from an ongoing Phase I/II glioblastoma and a Phase I/II multiple myeloma trial will be presented at ASCO on 30 May. These could be eligible for accelerated development, given the unmet medical need.

## Phase I/II data suggest activity in recurrent GBM...

There are some early stage data suggesting antiangiogenics, which inhibit new blood vessel growth, can induce tumour hypoxia (low oxygen), under which TH-302 is activated. An investigator-led Phase I/II dose escalation trial is ongoing examining TH-302 in combination with Avastin (bevacizumab) as third-line treatment in up to 34 recurrent glioblastoma (GBM) patients following failure of second-line treatment with Avastin. Tumour responses from 16 evaluable patients include one complete and two partial responses (PR), with nine stable disease (SD). Median PFS is 3.1 months, which compares to reference data of 37.5 days; three-month PFS is 52%. There were no grade 4 adverse events (AEs), and two grade 3 AEs. Updated and detailed data will be presented at ASCO. Recruitment at the highest 670mg/m<sup>2</sup> dose is ongoing.

## ...and also in multiple myeloma

Given the low oxygen environment within the bone marrow, a hypoxia-activated therapy could have a potential role in treating multiple myeloma (MM). Threshold has already conducted preclinical studies and a Phase I/II MM trial is ongoing, with data at ASCO. In this dose escalation trial TH-302 is being investigated in combination with dexamethasone (steroid used in MM treatment) for treating RR (relapsed/refractory) MM. Responses from nine patients at the maximum tolerated dose (MTD) include one PR, two minimal (MR) and four SD. Recruitment at the MTD continues (15 of 24 have been enrolled) and updated data will be at ASCO.

## Valuation: Undemanding EV of c \$129m

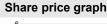
End-March net cash of \$86.4m implies an EV of only c \$129m, which seems undemanding given TH-302 has potential across a broad range of tumours, with Phase III trials in STS and pancreatic cancer ongoing. As part of the 2012 \$525m deal with Merck KGaA, Threshold could be entitled to a further \$170m development and \$245m sales related milestones, in addition to double-digit royalties.

Consensus estimates							
Year end	Revenue (\$m)	PBT (\$m)	EPS (\$)	DPS (\$)	P/E (x)	Yield (%)	
12/12	5.9	(71.1)	(1.31)	0.0	N/A	N/A	
12/13	12.5	(28.2)	(0.49)	0.0	N/A	N/A	
12/14e	15.8	(30.2)	(0.51)	0.0	N/A	N/A	
12/15e	21.2	(32.4)	(0.54)	0.0	N/A	N/A	
Source: Blo	oomberg						

#### Pharma & biotech

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#### **Share details**

Code	THLD
Listing	NASDAQ
Shares in issue	59.2m

#### **Business description**

Threshold Pharmaceuticals is a US oncology company focused on tumour hypoxia, a low-oxygen condition found in most solid tumours and some blood cancers. TH-302 is in Phase III for STS and pancreatic cancer, in addition to trials in several other cancers, and is partnered with Merck KGaA.

#### Bull

- TH-302 has potential in a number of cancer indications, as both monotherapy in some cancers, and in combination with chemotherapy and antiangiogenics.
- Merck KGaA funds 70% of TH-302 development.
- Solid cash position of \$86.4m.

#### Bear

- TH-302 could fail to show survival benefit in STS.
- Oncology is a highly competitive space.
- Single-product risk.

### **Analysts**

Dr Philippa Gardner +44 (0)20 3681 2521 Emma Ulker +44 (0)20 3077 5738

healthcare@edisongroup.com

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