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Threshold Pharmaceuticals

Pharma & biotech

3 July 2013

Investment summary: A new threshold

The TH-302 Phase III study in soft tissue sarcoma (STS) has been expanded to include another 170 patients. This reflects new assumptions about survival in the doxorubicin control arm and faster-than-expected enrolment, and maintains the trial power to detect a four-month survival benefit. Importantly, we expect a modest impact on trial timelines (three to six months) and expenditure (Merck KGaA contributes 70% of trial costs).

Expanded TH-302 Phase III trial in STS…

Threshold has amended the protocol of its ongoing TH-302 Phase III study in front-line STS, with the FDA agreeing to changes under the existing SPA agreement. The trial is evaluating TH-302 + doxorubicin vs doxorubicin alone in subjects with metastatic or locally advanced unresectable STS. The trial expansion to 620 patients (from 450) and elimination of an interim PFS analysis (mid-2013) relates to the higher overall survival (OS) benefit seen with doxorubicin in recent studies (12.8 months in EORTC 62012) and faster-than-expected recruitment.

…remains powered to show four-month OS benefit

The addition of 170 patients maintains the study's 85% power to detect a four-month increase in median OS for TH-302+dox (16 months) vs dox alone (12 months). With the OS analysis based on 434 events (previously 323), the enlarged sample size strengthens the trial's ability to detect a clinically meaningful (four-month) and statistically significant ($p<0.05$) benefit for TH-302. Eliminating the interim PFS futility analysis makes sense in our view, given that the trial will be largely enrolled (around year-end 2013) by the time the analysis would be conducted and, moreover, an OS benefit is required for FDA approval.

Modest impact on trial timelines and cost

Importantly, we expect the STS trial expansion to have little impact on trial timelines (around a three- to six-month delay) and cost. On current projections, Threshold expects to undertake an interim OS analysis after 235 deaths in H114 (previously end-2013/early-2014) and final OS data in H115 (previously early-2015). Given that the interim analysis has a high statistical bar ($p<0.0023$) for early termination, we believe the most likely outcome is trial continuation to final OS data.

Valuation: EV of $212m

Despite the uptick in share price (c 11%) post the Phase III amendment, Threshold's EV of only $212m suggests the market still underestimates the potential of TH-302 in STS and pancreatic cancer (also Phase III), and the Merck partnership ($525m milestones, double-digit royalties and US co-promotion option).

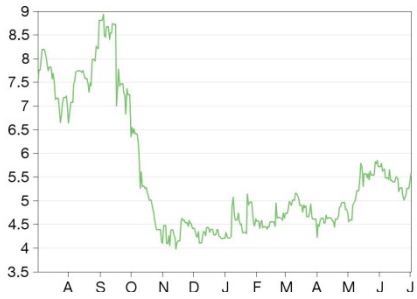
Consensus estimates

Year End	Revenue ($m)	PBT ($m)	EPS (c)	DPS (c)	P/E (x)	Yield (%)
12/11	-	(25.7)	(0.6)	0.0	N/A	N/A
12/12	5.9	(71.1)	(1.3)	0.0	N/A	N/A
12/13e	12.6	(24.7)	(0.6)	0.0	N/A	N/A
12/14e	13.7	(29.7)	(0.5)	0.0	N/A	N/A

Source: Bloomberg

Price	$5.58
Market cap	$316m

Share price graph



Share details

Code	THLD
Listing	NASDAQ
Sector	Pharma & biotech
Shares in issue	56.6m

Business description

Threshold Pharmaceuticals is a US biotech company focused on oncology drugs targeting tumour hypoxia, the low-oxygen condition found in most solid tumours and some blood cancers. TH-302 is in Phase III trials for soft tissue sarcoma (STS) and pancreatic trials in multiple other cancers. TH-302 is partnered with Merck KGaA.

Bull

- TH-302 has blockbuster potential.
- Merck funds 70% of TH-302 development costs.
- Net cash of $104m at end-Q113.

Bear

- Pancreatic cancer treatment landscape could change before 2015.
- TH-302 could fail to show survival benefit in STS Phase III study
- Single product risk.

Analysts

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