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MORGAN STANLEY RESEARCH
NORTH AMERICA

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Stock Rating
Overweight

Industry View
In-Line

Tesaro Inc.

Takeaways from Post-ASCO PARP Inhibitor Call

Impact on our views: Our expert call with a clinical trialist specializing in PARP inhibitor development in ovarian cancer supports our view that conclusions on relative efficacy among PARP inhibitors could remain challenging ahead of survival data from approaching Phase III trials.

Differentiation still the question. Our expert views the PARP inhibitor class as broadly active, yet with insufficient evidence so far to distinguish among agents on efficacy or safety. While potency differences exist, he notes that a reliable translation of potency to clinical efficacy has not emerged as a clear theme.

PARP inhibitor potential beyond germline BRCA+ ovarian emphasized. Our expert highlighted ~50% of high-grade serous ovarian cancers (HGSOC) having sporadic (i.e., non-germline) defects in DNA repair that could be susceptible to PARP inhibition. Recall, Tesaro is exploring the non-gBRCA+ population broadly in a defined Phase III cohort, in addition to the gBRCA+ cohort. We understand Clovis' planned Phase III is also exploring HGSOC beyond gBRCA+, where analyses in non-gBRCA+ call for an upcoming biomarker study to define homologous repair defects in DNA repair. This approach could imply narrower addressable populations in HGSOC depending on the breadth of the biomarker evidence, though efficacy enrichment by biomarker status is also possible. Astra's Phase III ovarian trials are restricted to gBRCA+ patients, a lower-risk, lower-reward tack. We see Tesaro's strategy as addressing the largest potential market opportunity.

Expert highlighted niraparib's activity in platinum resistant disease, an intriguing hallmark of activity. Whether this observation suggests higher activity vs. other PARP inhibitors is unknown, but worth pursuing.

Replay: (800) 585-8367. Passcode: 93251631.

See page 2 for additional takeaways from our call.

Key Ratios and Statistics

Reuters: TSRO.O Bloomberg: TSRO US
Biotechnology / United States of America

Shr price, close (Jun 11, 2013)	$40.93
Mkt cap, curr (mm)	$1,094
52-Week Range	$51.95-11.05

Additional takeaways from our expert call

Safety and tolerability across PARP inhibitors broadly similar. Remarks from our expert as well as physician commentary at ASCO with direct experience deploying all four agents (niraparib, rucaparib, olaparib, BMN-673) in the clinic support good safety and tolerability across the class. Whether safety/tolerability could emerge as a point of differentiation among PARP inhibitors remains an open question for Phase III.

Highlighted opportunity for PARP inhibitors in pancreatic cancer. This is an area which has not received much attention with the focus (beyond ovarian and breast) instead on Ewing's sarcoma and small cell lung cancer, as well as prostate and gastric.

Novel endpoint of PFS2 looks interesting. Given the known challenges in demonstrating an OS benefit in ovarian cancer with PARP inhibitors, the novel supplementary endpoint of PFS2 (time to progression on second subsequent therapy) could serve as a potential intermediate readout between PFS and OS. Tesaro has selected PFS2 as a secondary endpoint in their Phase III ovarian trial.

Anticipates broader screening for gBRCA+ mutations. According to our expert, the medical community may be under-diagnosing patients for gBRCA+ mutations. In an Australian study, among 22% of HGSOC with a gBRCA+ mutation in a large data set, ~40% had no familial history that would be predictive of gBRCA+ status. He sees this trend of under-diagnosing gBRCA mutations as driving more routine and broader BRCA testing, such as in Canada (British Columbia, Ontario, among others) as well in the UK.

According to our expert, dose response for PARP inhibitors may not follow traditional logic. Our expert noted that pushing the PARP inhibitor dose might not be required to achieve desired efficacy. There is contrasting evidence regarding this hypothesis from examining ASCO data in ovarian cancer. For niraparib, while numbers are low (13 platinum sensitive patients in ASCO poster), the response rate at the recommended dose of 300 mg was 75% (3/4) vs a lower 33% (3/9) response rate below 300 mg. On the other hand, for BMN-673 the response rate at the 1g MTD was 33% (4/12) vs a higher 58% (7/12) across lower doses (100-900 µg). Given small numbers, interpreting these divergent trends across PARP inhibitors will require more data.

Countering the "re-treat with platinum" argument for platinum sensitive relapsers. Retreatment with platinum in relapsing platinum-sensitive ovarian patients has its logic, but data suggest treatment with a PARP inhibitor could be preferable. According to our expert, relapsing platinum sensitive patients re-treated with platinum achieve 4-5 months PFS, whereas PFS for olaparib was ~11 months. Moreover, 24% of olaparib patients in Study 19 have been on study for 3+ years, a key differentiator of efficacy.

Skeptical on chemo combinations with PARP inhibitors. Our expert is unconvinced on prospects for combination chemotherapy strategies for PARP inhibitors in ovarian cancer. He notes no differences in PFS when adding chemotherapy to PARP inhibition given required dose compromises when combining agents. This commentary supports the maintenance approach as the primary late-stage development route.

Longer-term questions for the evolving PARP inhibitor field: 1) Can patients be re-challenged with another PARP inhibitor after failure on one PARP inhibitor? 2) Are PARP inhibitors effective post chemotherapy? and, 3) What is the potential for PARP inhibitors in platinum resistant patients?

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(as of May 31, 2013)

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Underweight/Sell	**469**	**17%**	**117**	**11%**	**25%**
Total	**2,834**		**1019**		

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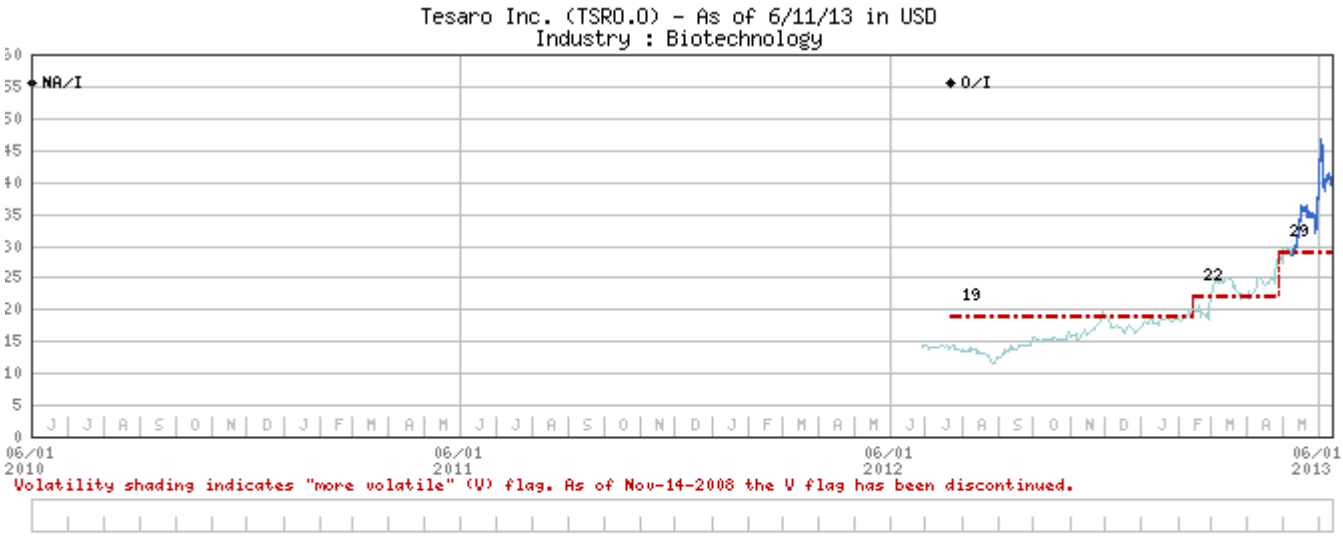
Stock Price, Price Target and Rating History (See Rating Definitions)



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Industry Coverage:Biotechnology

Company (Ticker)	Rating (as of)	Price* (06/11/2013)
David Friedman, M.D.		
AMAG Pharmaceuticals, Inc. (AMAG.O)	E (11/21/2011)	$20.57
Alexion Pharmaceuticals (ALXN.O)	O (09/07/2010)	$93.03
Alnylam Pharmaceuticals (ALNY.O)	O (06/11/2013)	$30.59
Auxilium Pharmaceuticals (AUXL.O)	E (05/03/2013)	$16.98
Chimerix Inc (CMRX.O)	O (05/06/2013)	$23.72
Cubist Pharmaceuticals Inc. (CBST.O)	O (10/03/2012)	$51.32
Elan Corporation PLC (ELN.N)	++	$13.56
Idenix Pharmaceuticals, Inc. (IDIX.O)	E (03/18/2011)	$5.26
Incyte Corporation (INCY.O)	U (01/23/2013)	$20.44
InterMune (ITMN.O)	E (09/07/2010)	$9.74
Ironwood Pharmaceuticals, Inc. (IRWD.O)	E (04/24/2013)	$12.81
Lexicon Pharmaceuticals, Inc. (LXRX.O)	U (06/11/2013)	$2.35
NPS Pharmaceuticals (NPSP.O)	O (10/03/2012)	$15.68
Synageva Biopharma Corp (GEVA.O)	O (04/20/2012)	$40.86
Theravance Inc (THRX.O)	++	$36.35
Vertex Pharmaceuticals (VRTX.O)	E (05/08/2012)	$81.4
XenoPort Inc (XNPT.O)	U (06/11/2013)	$5.23
Yigal Nochomovitz, Ph.D.		
ImmunoGen Inc. (IMGN.O)	E (11/13/2012)	$16.35
Infinity Pharmaceuticals Inc (INFI.O)	O (02/19/2013)	$17.34
Pharmacyclics Inc. (PCYC.O)	E (03/19/2013)	$88.89
Tesaro Inc. (TSRO.O)	O (07/23/2012)	$39.5
Sara Slifka		
Neurocrine Biosciences Inc (NBIX.O)	O (10/03/2012)	$12.87
Optimer Pharmaceuticals (OPTR.O)	U (10/03/2012)	$14.71

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