

## Market Overview: Anti-PDL1 in Bladder Cancer a \$4B Opportunity; Patient Selection and Prior Bacillus Calmette-Guérin Exposure Likely Drivers of Response for Roche's Anti-PDL1

Compelling data with anti-PDL1 among other solid and blood cancers expected at ASCO 2014. We anticipate that AstraZeneca (AZN) will showcase data from its growing portfolio of immune-therapeutics at ASCO. We anticipate that the company will present compelling data with their anti-PDL1 across several indications, most notably in previously undisclosed bladder cancer from their ongoing 344 patient phase I trial. Bladder cancer is sizeable and poorly treated indication with little treatment advances over the last 15 years. We calculate a peak revenue potential of \$4bn for this indication alone.

**We suspect anti-PDL1 has shown significant activity in bladder cancer.** We highlights that cancers with mutagenic causation are most likely responsive to anti-PD1/immunotherapy at baseline. These include lung cancer (smoking), mesothelioma (asbestos), and skin cancer (UV radiation). Like these aforementioned cancers, bladder cancer incidence is strongly associated with the important mutagens of smoking, chemicals and previous chemotherapy. Further evidence for the immune-responsiveness of bladder cancer is the strong benefit TCC (transitional cell carcinoma) derive from of intra-bladder administration of Bacillus Calmette-Guérin or BCG (a much older immunotherapy) which remains the standard of care.

In addition to seeing if our thesis relating to bladder cancer as PDL1 responsive is confirmed, we are also intrigued to see what percentage of responders received prior BCG therapy. We suspect that patients who experienced prior treatment with BCG vaccine have more profound response rates compared with those patients who were BCG naive. Data for a more profound response in BCG-treated patients lends significant support for the utility of therapeutic vaccines to enhanced antigen presentation prior to checkpoint blockade therapy. As we have highlighted, Roche has recently added two very attractive cancer vaccine platforms (Inovio and Immutics) to its portfolio.

Roche has suggested that other companies have thus far failed to elicit strong responses with their PD1 targeted agents in this undisclosed cancer type. While a mechanistic explanation is possible, **we suspect patient selection and prior BCG exposure is a more likely suggestion, assuming the undisclosed target is indeed bladder cancer.**

### Advanced Bladder cancer is a potential \$4bn sales opportunity

	US	EU-5
Incidence of bladder cancer	72,570	77,963
<b>% distribution by grading</b>		
% <i>in-situ</i>	50%	50%
% <i>localized</i>	30%	30%
% <i>regional / distant</i>	20%	20%
<b>Eligible patient population</b>		
<i>pts with localized disease with a relapse</i>	21,800	23,400
<i>pts with regional/distant disease</i>	7,300	7,800
	14,500	15,600
Per Patient Treatment Cost (\$)	120,000	72,000
<b>Annual Sales (\$m)</b>		
<i>pts with localized disease with a relapse</i>	2,616	1,685
<i>pts with regional/distant disease</i>	876	562
	1,740	1,123

Source: Citi Research, Cancer.gov, European Journal of Cancer 49 (2013) 1374–1403

Source: Citigroup/Baum, February 11, 2014

Oncology Indication: Bladder

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