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Global Pharmaceuticals
Tortoise and the Hare

Will the rapid adoption of BMY's Opdivo and MRK's Keytruda in melanoma and refractory lung cancer be enough to meet revenue expectations?: Proprietary prescribing data from AlphaImpactRx highlights that the adoption of Opdivo and Keytruda has been very rapid, with the two drugs combined capturing 75% and 63% of the on-label indications in refractory melanoma and squamous NSCLC, respectively. Triangulating these data with Q2 results commentary and a relatively short 3 months duration of treatment implies that Opdivo and Keytruda are on track to achieve combined US revenues of $1.7bn in melanoma and refractory lung cancer. While enough to meet near-term expectations, medium-term expectations remain geared to the front-line lung cancer opportunity, with incremental data released at the World Lung Cancer meeting 6-9 September providing insight into competitive positioning.

Opdivo/Keytruda trends supportive of near-term estimates, but medium-term expectations remain dependent on ex-US execution and first-line NSCLC outcomes: We project Opdivo revenues of $762m and Keytruda revenues of $502m in 2015E, slightly above consensus expectations. Achieving Opdivo revenues expectations of circa $7bn or greater in 2020E remains dependent on execution in the tougher ex-US payor environment and successful execution in the increasingly competitive first-line NSCLC setting. Data presented at the World Lung Cancer meeting in Denver 6-9 September are set to provide incremental insight into what the best strategy is in first-line NSCLC data – anti-PD(L)-1 monotherapy in PDL-1 over-expressors versus anti-PD(L)-1 plus chemo versus anti-PD(L)-1 plus Yervoy in all comers. Competitive data to the immuno-oncology class presented at the World Lung Cancer and ESMO cancer meetings might also raise the competitive stakes.

Top-down assumptions support our $21bn immuno-oncology company sales forecasts, but a number of key variables remain unanswered: Combining our individual US and EU Pharma company models together we currently forecast immuno-oncology revenues of $21bn in 2023E, with BMY capturing just over half the revenue opportunity. However key unanswered questions remain such as the average duration of treatment, patient eligibility rates and patient triaging. Flexing the average duration of treatment in NSCLC from 3 months (observed in clinical trials) to 6 months drives an illustrative $13bn in additional revenues in 2023E. From a downside risk perspective, our 90% patient eligibility rate assumption across the majority of tumours types could be too aggressive based on the "flat" 60-65% Opdivo treatment rate observed in refractory squamous NSCLC to date. Assuming an eligibility rate of 65% would trim our immuno-oncology revenues by circa $5.5bn. Opdivo and Keytruda represent $22/share and $10/share of our BMY and MRK valuations, respectively. Every incremental $1bn in revenues would drive 5% and 3% upside to our BMY and MRK valuations, respectively.

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INDUSTRY UPDATE

European Pharmaceuticals
NEUTRAL
Unchanged

Japan Biopharmaceuticals
NEGATIVE
Unchanged

U.S. Major Pharmaceuticals
NEUTRAL
Unchanged

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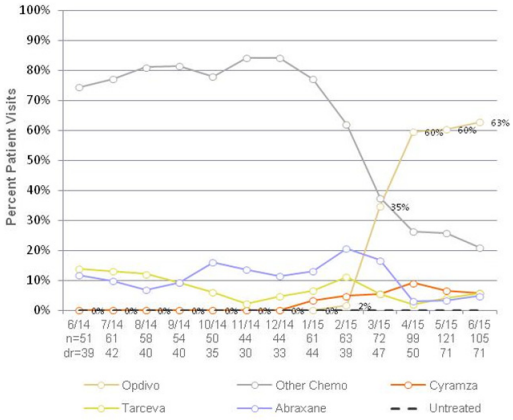
Executive summary

BMY's Opdivo and MRK's Keytruda on track for US revenues of $1.7bn in melanoma and refractory lung cancer, but is this enough to meet heightened expectations?: We have triangulated comments made on the Q2 earnings calls, reported and IMS estimated revenue data and proprietary AlphaImpactRx prescribing data in analyzing the US launches of Opdivo and Keytruda. The good news is that adoption has been very rapid, with the two drugs combined capturing 75% and 63% of the on-label indications in refractory melanoma and squamous NSCLC, respectively. However on the basis that the duration of treatment remains relatively short at just 3 months, we estimate that the melanoma indication will likely generate $715m in US revenues and the refractory NSCLC indication (squamous plus non-squamous) $1.0bn in US revenues.

FIGURE 1

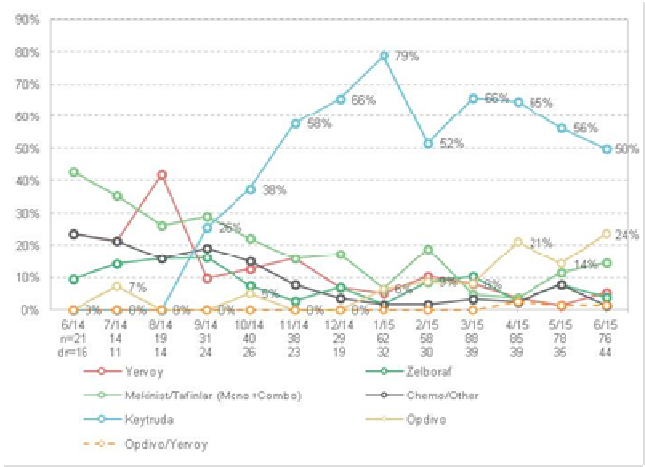
Opdivo has captured a 63% patient share of the refractory squamous NSCLC opportunity



Source: Barclays Research, AlphaImpactRx

FIGURE 2

Keytruda and Opdivo have captured a 74% patient share of the refractory metastatic melanoma opportunity



Source: Barclays Research, AlphaImpactRx

While supportive of near-term consensus estimates, our projections imply that BMY/MRK remain dependent on ex-US execution and US revenues in the increasingly competitive first-line NSCLC setting to meet consensus estimates over the medium-term. Data presented at the World Lung cancer meeting in Denver 6-9 September are set to provide incremental insight into what the best strategy is in first-line NSCLC data: a PD-1 blocker in PDL-1 higher expressers (MRK; BMY) versus a PD(L)-1 inhibitor plus an anti-CTLA4 in all comers (BMY; AZN) versus a PDL-1 blocker plus chemotherapy in all comers (ROG; AZN). Competitive data to the immuno-oncology class presented at the World Lung Cancer and ESMO meetings might also raise the competitive stakes.

FIGURE 3

Key presentations at the World Lung Cancer meeting 7-9 September

Opdivo	10.45-12.15 7 Sept	Safety and Efficacy of First-Line Nivolumab (NIVO; Anti-Programmed Death-1 [PD-1]) and Ipilimumab in Non-Small Cell Lung Cancer (NSCLC)
Atezolizumab	10.45-12.15 7 Sept	Atezolizumab (MPDL3280A) Combined with Platinum-Based Chemotherapy in Non-Small Cell Lung Cancer (NSCLC): A Phase Ib Safety and Efficacy Update
Other approaches	10.45-12.15 7 Sept	A DLL3-Targeted ADC, Rovalpituzumab Tesirine, Demonstrates Substantial Activity in a Phase I Study in Relapsed and Refractory SCLC
	10.45-12.15 8 Sept	TG4010 Immunotherapy plus Chemotherapy as First Line Treatment of Advanced NSCLC: Phase 2b Results

Source: Barclays Research; World Lung Cancer meeting

Top-down assumptions support our $21bn immuno-oncology company sales forecasts, but a number of key variables remain unanswered. Combining our individual company models together we currently forecast immuno-oncology revenues of $21bn in 2023E, with BMY capturing just over half the revenue opportunity. However key unanswered questions remain such as the average duration of treatment, patient eligibility rates and patient triaging. Flexing the average duration of treatment in NSCLC from 3 months (observed in clinical trials) to 6 months drives an illustrative $13bn in additional revenues in 2023E. Assuming our market share assumptions are correct, this would add an incremental $4.8bn in Opdivo revenues in 2023E, an incremental $3.6bn to Keytruda sales and an additional $3.1bn to Roche's atezolizumab revenues. From a downside risk perspective, our 90% patient eligibility rate assumption across the majority of tumours types could be too aggressive based on the "flat" 60-65% Opdivo treatment rate observed in refractory squamous NSCLC to date. Assuming an eligibility rate of 65% would trim our immuno-oncology revenues by circa $5.5bn.

FIGURE 4
Immuno-Oncology New Calendar

Est. Timing	Events	Importance
7-9 Sept	High	Opdivo+Yervoy phase 2 data in 1L NSCLC (CheckMate-026); presented at World Lung Cancer meeting
7-9 Sept	Medium	Roche atezolimzumab+chemo phase 1b data in 1L NSCLC; presented at World Lung Cancer meeting
25-29 Sept	High	Roche atezolizumab phase 3 data in PDL-1 selected NSCLC; BIRCH trial presented at ESMO
25-29 Sept	Medium	Pfizer avelumab update as ESMO in lung, ovarian, bladder, gastric cancer
30 Sept	Medium	FDA approval decision Opdivo+Yervoy 1L melanoma (CM-069 trial)
2 Oct	High	FDA approval decision Keytruda in 2L NSCLC
Nov	Medium	FDA approval decision Tefinlar+Mekinist 1L melanoma (COMBI-D trial)
27 Nov	Medium	FDA approval decision Opdivo vs. dacarbazine 1L melanoma (CM-066 trial)
H2'15/Q1'16	High	Roche potential filing of atezolimzumab in NSCLC and bladder cancer
H2'15	High	Phase 3 Keytruda 2L NSCLC data in PDL-1 +ve patients (PS>1%); KEYNOTE-010
End 2015	Medium	Phase 3 AZN durvalumab 3L NSCLC in PDL-1 +ve patients; ATLANTIC trial
Q4'15/Q1'16	High	Yervoy/chemo combo Phase 3 trial in squamous NSCLC data readout
H2'15 / H1'16	High	Opdivo I/O combo trials (anti-KIR, anti-LAG3, CD137) data
H1'16	High	Potential approval decision for Roche's atezolimzumab in NSCLC and bladder cancer
Mid 2016	High	Phase 3 Keytruda 1L NSCLC data in PDL-1 +ve patients (PS>50%); KEYNOTE-024
Mid 2016	High	Phase 3 Opdivo1L NSCLC data in PDL-1 +ve patients (>1%); CHECKMATE-026 recruiting ahead of schedule
2016	High	Opdivo+LAG3 phase 1 combo data; additional Opdivo data in HL, NHL, bladder
End 2015/2016	High	Pfizer claiming 6 phase 3 trials initiated with avelumab by end 2015 across lung cancer, ovarian, bladder, gastric, renal (up to 20 studies in total); 2L NSCLC avelumab vs Taxotere started, Inlyta+avelumab RCC ph3 will start 2015, 1L NSCLC will start soon

Source: Barclays Research, Company data

BMY's valuation is more levered to Opdivo than MRK is to Keytruda. Based on Bloomberg estimates, our 2020E forecast $6.9bn for Opdivo is approximately 10% higher than the consensus mean. However, we believe that consensus sell-side models carry higher estimates than those reported by Bloomberg, with the BMY compiled consensus projecting >$7bn in Opdivo revenues in 2020E *before* the early termination of the CheckMate-057 trial because of a significant survival benefit. Opdivo is projected to be just 5% of BMY's total sales in 2015E but it will be the largest portion of total sales by 2023E when we estimate it will make up 44% of revenue. Opdivo is estimated to represent just 5% of BMY's earnings this year but is anticipated to generate nearly half of BMY's EPS in 2023E. Given the high sales and earnings contribution from Opdivo, we estimate that each incremental $1 billion in 2023E Opdivo sales drives a $2.50-$3.00/share impact on BMY's intrinsic value.

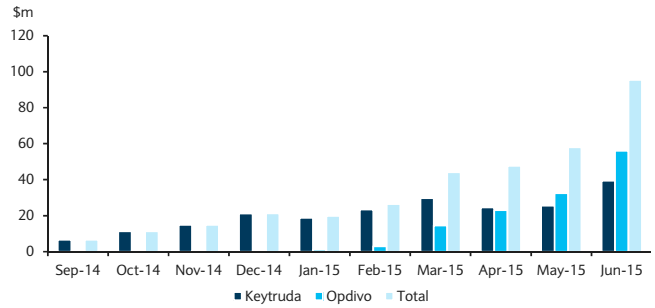
Our 2020E Keytruda estimate of $5.3bn is +51% relative to the Bloomberg mean, but closer to +15% above the company compiled consensus of approximately $4.6bn in 2020E. Keytruda is an important element of MRK's investment case, growing from 1% of group sales in 2015 to 14% of sales in 2023E. Whilst MRK is less levered to immuno-oncology relative to BMY, it is still central to the investment case alongside high risk high reward assets in cholesterol and Alzheimer's. Indeed, Keytruda is expected to contribute nearly a fifth (18%) of MRK's earning by 2023E. We estimate that an incremental $1 billion in Keytruda sales by 2023E would increase MRK's valuation by $1.50-$2.00/share depending on the speed of the sales ramp.

Lung cancer has driven an acceleration in I/O revenues

BMY reported Opdivo revenues of $122m in Q2, with the majority of sales from the US ($107m). The majority of Merck's Keytruda revenues were also generated in the US, $86m from a Q2 total of $122m. While there is a "catch-up" in the last month of each quarter for IMS estimated US sales, Opdivo/Keytruda revenues nonetheless appear to have accelerated in June following the presentation of positive lung cancer data at the AACR and ASCO meetings and the NCCN recommendation for Opdivo use in both refractory squamous and non-squamous patients. For the quarter overall, IMS estimated and company reported Opdivo/Keytruda revenues appear to correlate closely.

FIGURE 5

Lung cancer drives Opdivo/Keytruda revenue growth



Source: Barclays Research, IMS Health

FIGURE 6

Opdivo/Keytruda US Q2 sales closely correlate with IMS data

	Q3'14	Q4'14	Q1'15	Q2'15
Keytruda IMS estimated	7	47	72	89
Keytruda reported		44	66	86
Opdivo IMS estimated	-	0	19	112
Opdivo reported		1	38	107

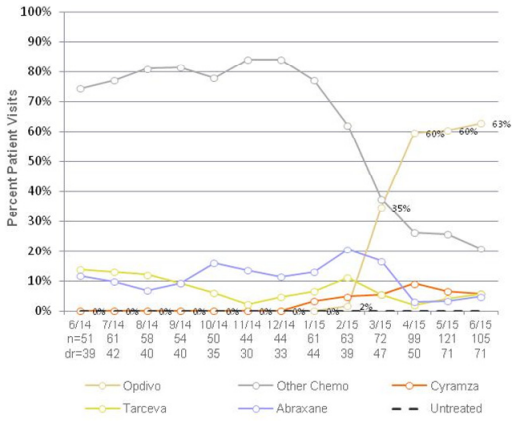
Source: Barclays Research, IMS Health, company data

AlphaImpactRx data demonstrate rapid uptake in squamous lung cancer…

BMY commented on its Q2 earnings call that US Opdivo revenues had benefited from a strong launch in lung cancer during Q2, with a 66% share achieved in refractory squamous NSCLC. This should be supported by the filing of the CheckMate-057 data in refractory non-squamous NSCLC in the coming months. In melanoma, BMY believes that Opdivo is at parity with Keytruda in the community setting and gaining share in the institutional setting. Outside the US, BMY stated that the launch of Opdivo in Germany was strong with a $8,163/month treatment cost.

FIGURE 7

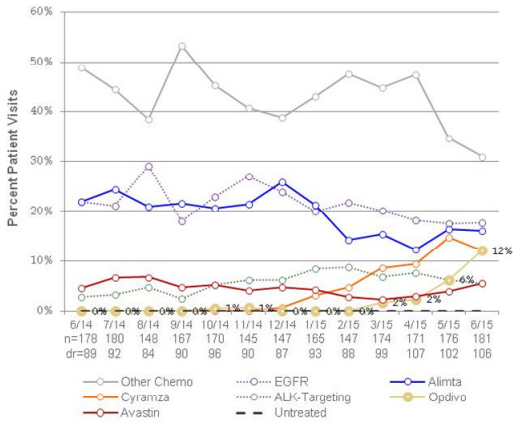
Refractory squamous mNSCLC patient share



Source: Barclays Research, AlphaImpactRx

FIGURE 8

Refractory non-squamous mNSCLC patient share



Source: Barclays Research, AlphaImpactRx

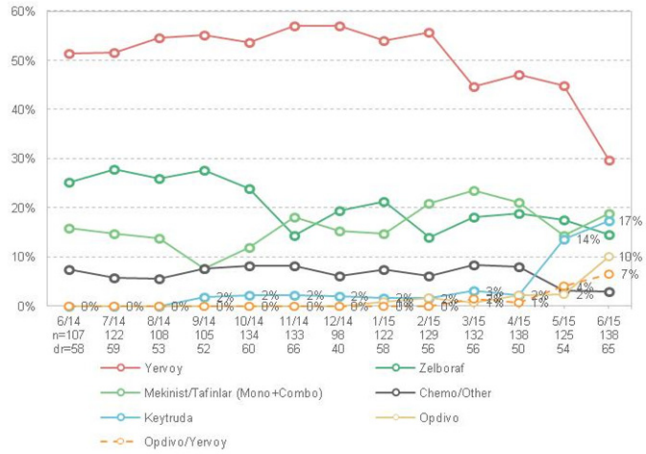
These comment fit with proprietary data from AlphaImpactRx, which provide a unique leading indicator insight into the US performance of Opdivo and Keytruda on an indication and line of therapy basis. AlphaImpactRx data suggest that Opdivo rapidly achieved a 60-65% share of refractory squamous NSCLC patients and that penetration rates have remained stable for 3 months. It is unclear whether this is a function of slower uptake in the community hospital setting and/or an indication of the proportion of refractory squamous NSCLC patients with autoimmune conditions who are contraindicated against Opdivo treatment. Opdivo off-label penetration in the refractory non-squamous NSCLC setting has risen to 12% following presentation of the CheckMate-057 data at ASCO and subsequent endorsement by the NCCN.

…and in the malignant melanoma setting

Merck commented on its Q2 earnings call that sales of Keytruda were split 85% / 15% between melanoma and lung cancer, respectively, with 70% of melanoma revenues on-label in the refractory setting. It was estimated that Keytruda has a 60% patient share in Yervoy-refractory melanoma and is the No.1 melanoma drug overall. These comments are supported by data from ImpactRx which show that the overall use of immune-oncology drugs (Yervoy, Opdivo, Keytruda) has increased from 40% in June 2015 to 64% in June 2015, with Keytruda overtaking Yervoy as the No.1 melanoma drug with a 27% overall market share. In the first-line setting BMY has the leading share, with a 30% penetration rate for Yervoy monotherapy and a 17% penetration rate for Opdivo as monotherapy and in combination with Yervoy. In the on label refractory setting, Keytruda supported by a more convenient dose regimen and earlier launch holds 50% market share compared to 24% share for Opdivo. In first line patients with BRAF mutations, Mekinist/Tafinlar and Zelboraf have continued to hold around two thirds of patient starts.

FIGURE 9

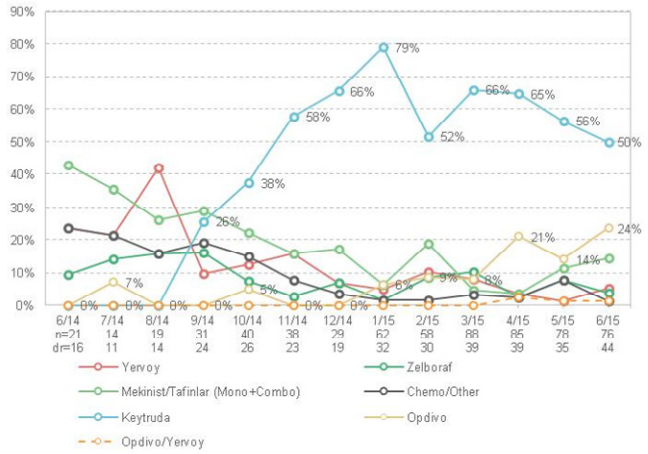
First line metastatic melanoma share



Source: Barclays Research, AlphaImpactRx

FIGURE 10

Refractory metastatic melanoma share



Source: Barclays Research, AlphaImpactRx

Triangulating I/O revenues & proprietary market share data

We have combined the US revenue estimates reported in Q2 with commentary from the companies and the AlphaImpactRx data in an attempt to understand underlying market dynamics. The key uncertainty remains the average duration of therapy with Opdivo and Keytruda, with durable responders putting upward pressure on the mean number of doses seen in clinical trials but real word compliance likely a downward pressure. In our calculations we have assumed that the average duration of therapy is 3 months compared to a median number of doses of six for Opdivo in the NSCLC trial (median duration 2.8 months). Using this approach we estimate that melanoma and refractory NSCLC will generate annual revenues of $1.7bn in the US.

Opdivo/Keytruda on course for $1.7bn in US revenues

Using this approach, we estimate that Opdivo US Q2 revenues were split 71% / 29% in favour of lung cancer, where we estimate the steady state penetration rates were 61% in refractory squamous patients and 7% in refractory non-squamous patients. Assuming a steady increase in penetration rates during the second half of 2015 driven by Opdivo+Yervoy combination use in front-line melanoma and FDA approval of Opdivo in refractory non-squamous NSCLC in Q4'15, we estimate FY'15 US revenues of Opdivo will reach $534m. We project annualized Opdivo US sales in these four indications of $1.05bn based on current dynamics.

FIGURE 11
Opdivo US revenue estimates

	Total	Melanoma	1L melanoma	2L+ melanoma	2L+ NSCLC	2L+ Sq NSCLC	2L+ Non-sq NSCLC
Opdivo Q1	38						
Opdivo Q2	107	31	15	16	76	56	19
Opdivo Q3E	171	66	45	21	106	59	47
Opdivo Q4E	218	85	63	23	133	60	73
FY 2015E	534						
Peak Opdivo quarterly	263	96	71	24	167	51	116
Peak Opdivo annual	1,051	383	286	97	668	203	465
Penetration rates							
Opdivo Q2E			9%	20%		61%	7%
Opdivo June (E)			17%	24%		63%	12%
Opdivo Q3E			25%	26%		64%	16%
Opdivo Q4E			35%	28%		65%	25%
Opdivo peak (E)			40%	30%		55%	40%

Source: Barclays Research; quarterly penetration rates calculated as steady state rates assuming 3 months average duration of therapy

For Keytruda, we have adopted the 85% / 15% split in favour of melanoma as communicated by the company on the Q2 earnings call despite AlphaImpactRx not picking up any use in NSCLC through June. Assuming modest market share erosion in refractory melanoma and FDA approval in refractory NSCLC 2 October 2015, we estimate FY'15 US revenues of Keytruda will reach $400m using a triangulation approach.

The FDA approval of Keytruda in lung cancer remains a key focal and debating point. Merck has filed for approval in NSCLC based on the KEYNOTE-001 trial which enrolled both 1L and 2L+patients with both squamous and non-squamous histologies, requesting approval at the 2mg/kg Q3W dose (despite Keytruda being studied at 10mg/kg in KEYNOTE-001) and across all PD-L1 expression levels. While only about 100 patients in the registration file are PD-L1 negative, MRK believes the responses observed in these patients cannot be

discounted. However, the potential NSCLC label remains a point of debate and an overhang for MRK shares, which we see as range-bound ahead of the FDA's decision and with the potential for significant volatility.

FIGURE 12
Keytruda US revenue estimates

	Total	Melanoma	1L melanoma	2L+ melanoma	NSCLC	2L+ Sq NSCLC	2L+ Non-sq NSCLC
Keytruda Q1	66						
Keytruda Q2	86	76	23	53	13	3	10
Keytruda Q3EE	98	82	37	45	16	5	12
Keytruda Q4EE	150	101	64	37	49	11	37
FY 2015E	400						
Peak Keytruda quarterly	170	83	41	42	87	14	73
Peak Keytruda annual	678	332	165	167	346	55	291
Penetration rates							
Keytruda Q2E			11%	57%		*4%*	*3%*
Keytruda June (E)			17%	50%		*na*	*na*
Keytruda Q3E			18%	48%		5%	4%
Keytruda Q4E			19%	47%		9%	11%
Keytruda peak (E)			20%	45%		15%	25%

Source: Barclays Research; quarterly penetration rates calculated as steady state rates assuming 3 months average duration of therapy

Shifting focus to first-line NSCLC

We project that the frontline use of Opdivo, Keytruda and competing I/O agents will represent circa 60% of NSCLC revenues *without* factoring in an increase in the average duration of therapy relative to the duration of treatment in the refractory setting. The battle for first-line patients is going to be fierce and at this stage the outcome is difficult to predict.

BMY is targeting PDL-1 positive patients with Opdivo versus chemotherapy in the CheckMate-026 trial (recruiting ahead of schedule) and then exploring the combination use of Opdivo plus Yervoy in all comers. MRK is targeting PDL-1 positive patients versus chemotherapy in the Keynote-024 and -042 trials. In contrast Roche is pursuing a chemotherapy combination strategy with atezolizumab in the Impower 130, 131 and 150 trials as outlined below. AstraZeneca is playing to its strengths and in part hedging its bets by exploring the combination of MEDI4736 with tremelimumab (BMY approach), Iressa and chemotherapy (Roche's approach).

The World Lung Cancer meeting with provide incremental data on the relative efficacy and tolerability of Opdivo in combination with Yervoy (CheckMate-012 trial), with circa 50 patients per dosing subgroup and survival data up to 6 months. CheckMate-012 informed the design of the phase 3 CheckMate-227 trial and BMY has intimated that the tolerability of Opdivo+Yervoy was comparable to Opdivo monotherapy. In the same session on Monday, 7 September, Roche will present additional follow-up from the frontline trial phase 1b trial combining aterozlizumab with chemotherapy where the focus will be on the durability of the 60-75% response rates presented at ASCO from data with relatively short follow-up. Roche appears confident that the responses observed in the phase 1b trial are durable I/O-type responses, whereas BMY maintains that the responses observed with Opdivo+chemo were relative short in duration and came at the expense of additive toxicity.

FIGURE 13

Key presentations at the World Lung Cancer meeting 7-9 September

Opdivo	10.45-12.15 Mon 7 Sept	Phase 3, Randomized Trial (CheckMate-017) of Nivolumab (NIVO) vs. Docetaxel in Advanced Squamous (SQ) Cell Non-Small Cell Lung Cancer (NSCLC)
	10.45-12.15 Mon 7 Sept	Safety and Efficacy of Nivolumab in an Ongoing Trial of a PD-L1+/- Patient Population with Metastatic Non-Small Cell Lung Cancer
	10.45-12.15 Mon 7 Sept	Longer-Term Follow-Up of a Phase 2 Study (CheckMate-063) of Nivolumab in Patients with Advanced, Refractory Squamous Non-Small Cell Lung Cancer
	10.45-12.15 Mon 7 Sept	**Safety and Efficacy of First-Line Nivolumab (NIVO; Anti-Programmed Death-1 [PD-1]) and Ipilimumab in Non-Small Cell Lung Cancer (NSCLC)**
Atezolizumab	10.45-12.15 Mon 7 Sept	**Atezolizumab (MPDL3280A) Combined with Platinum-Based Chemotherapy in Non-Small Cell Lung Cancer (NSCLC): A Phase Ib Safety and Efficacy Update**
Keytruda	10.45-12.15 Mon 7 Sept	Pembrolizumab for ED SCLC: Efficacy and Relationship with PD-L1 Expression
	16.45-18.15 Wed 9 Sept	A Phase II Trial of Pembrolizumab for Untreated Brain Metastases from Non-Small Cell Lung Cancer
Other approaches	10.45-12.15 Mon 7 Sept	**A DLL3-Targeted ADC, Rovalpituzumab Tesirine, Demonstrates Substantial Activity in a Phase I Study in Relapsed and Refractory SCLC**
	10.45-12.15 Tue 8 Sept	TG4010 Immunotherapy plus Chemotherapy as First Line Treatment of Advanced NSCLC: Phase 2b Results
	10.45-12.15 Tue 8 Sept	MUC1-Targeted Dendritic Cell-Based Vaccine Immunotherapy in Patients with Standard Treatments-Refractory Non-Small-Cell Lung Cancer
	16.45-18.15 Tue 8 Sept	Mesothelin-Targeted CAR T-Cell Therapy for the Treatment of Heterogeneous Antigen-Expressing Lung Adenocarcinoma

Source: Barclays Research; World Lung Cancer meeting

First-line NSCLC opportunity likely to fragment

The fragmentation of the frontline NSCLC opportunity appears even more likely, with a diverse set of treatment approaches. The 60-75% response rate seen with Roche's atezolimzumab in combination with chemotherapy in the first-line NSCLC patient setting with an encouraging safety profile supports the initiation of a 3,750 patient pivotal program across all comers and PD-L1+ve patients. Assuming the responses remain durable, these atezolimzumab data are exciting when considered against the circa 30% response rates seen with chemotherapy alone. BMY has chosen not to pursue PD-1+chemotherapy combinations, MRK has not started chemotherapy combination program and AZN has jumped straight into phase 3 with a MEDI4736+chemotherapy combination study.

Merck is pursuing a monotherapy approach with Keytruda in PDL-1 positive (PS>1) and highly positive (PS>50) first-line patients. Roche is partly hedged in also pursuing PDL-1 positive patients as a monotherapy. BMY is following a head-to-head strategy versus chemotherapy combination approach in PDL-1 positive patients which puts the success of its PDL-1 diagnostic approach in focus. From a combination standpoint, BMY is pursuing the combination of Yervoy with chemotherapy in first-line squamous NSCLC (CheckMate-104) and will study the combination of Opdivo+Yervoy versus Opdivo alone versus chemotherapy (CheckMate-227) with a presumably higher dose regimen in PD-L1 non-expressors informed by the CheckMate-067 data.

AstraZeneca is initiating a broad program in NSCLC enrolling more than 5,600 patients and is pursuing a wide variety of approaches. In front-line NSCLC, AstraZeneca is initiating two trials which explore the combination of MEDI4736 with tremelimumab and a trial in combining MEDI4736 with chemotherapy. We estimate that 26% of first-line non-squamous NSCLC patients are EGFR mutant positive where AstraZeneca is exploring the combination of MEDI4736 with Iressa. The PACIFIC and ADJUVANT trials explore the use of MEDI4736 in earlier stages of disease.

FIGURE 14

First-line NSCLC trials – an increasingly competitive environment

Trial ID	Patients /Indications	n	Treatment Arm	Primary endpoint	Start	Complete
Impower 110	1st line non-squamous, PDL-1+	400	atezolizumab (1200mg q21d) + carboplatin/cisplatin + pemetrexed v carboplatin/cisplatin + pemetrexed (PD-L1 selected (IC/TC2-3))	PFS	Apr-15	2017
Impower 111	1st line squamous, PD-L1+	400	atezolizumab (1200mg q21d) v gemcitabine/cisplatin or carboplatin (PD-L1 selected (IC/TC2-3))	PFS	Apr-15	2018
Impower 130	1st line non-squamous	550	atezolizumab (1200mg q21d) + nab-paclitaxel/carboplatin v nab-paclitaxel/carboplatin	PFS	Mar-15	2017
Impower 131	1st line squamous	1200	atezolizumab (1200mg q21d) + carboplatin/paclitaxel, v atezolizumab + nab-paclitaxel/carboplatin v nab-paclitaxel/carboplatin	PFS	Mar-15	2017
Impower 150	1st line non-squamous	1200	atezolizumab (1200mg q21d) + carboplatin/cisplatin + Avastin v atezolizumab + carboplatin/cisplatin v Avastin + carboplatin/cisplatin	PFS	Mar-15	2017
KEYNOTE 024	1st line, PDL-1+, all histologies	300	pembrolizumab 200mg q21d v paclitaxel/carboplatin or pemetrexed/carboplatin or pemetrexed/cisplatin or gemcitabine/cisplatin (PS>50%)	PFS	Aug-14	Jun-16
KEYNOTE 042	1st line, PDL-1+, all histologies	1240	pembrolizumab 200mg q21d v carboplatin/paclitaxel or carboplatin/pemetrexed (PS>1%)	OS	Oct-14	Jun-18
CHECKMATE 026	1st line, PDL-1+, all histologies	535	nivolumab (3mg/kg q2w) v investigator's choice chemotherapy (PDL-1 >1%)	PFS	Mar-14	Aug-16
CHECKMATE 227	1st line, all histologies	1980	PDL-1+: nivolumab + ipilimumab v nivolumab v chemo doublet; PDL-1-: nivolumab + ipilimumab dose A v dose B v chemo doublet	PFS/OS	Aug-15	Jan-18
MYSTIC	1st line	675	MEDI4736 v MEDI+tremelimumab v platin based chemo	PFS	Jul-15	Apr-18
	1st line	Planned	MEDI4736 + tremelimumab v SOC			
	1st line	planned	MEDI4736 + chemo			
	1st line	Planned	MEDI4736 + Iressa v SOC (EGFRm+)			

Source: Barclays Research, clinicaltrials.gov, company data

Key modelling questions

Duration of treatment

AlphaImpactRx data demonstrate that Opdivo captured a 60% treatment share of the refractory squamous NSCLC market within a matter of weeks, becoming the new standard of care. A key consideration when modelling revenue potential is the average duration of therapy with Opdivo appears to remain surprisingly short. The average duration of treatment with Roche's atezolizumab in the POPLAR trial was 3.6 months, equivalent to a six doses. The median number of Opdivo doses in the CheckMate-057 trial was also 6 doses, although up to 8 doses in the CheckMate-017 trial. While the mean number of doses should be greater in diagnostically-enriched patients and should improve as the subgroup of patients gaining most benefit remain on PD(L)-1 treatment, compliance outside a clinical trial setting would likely be lower especially with the immunogenic "flare responses" observed to date. Furthermore the overall survival curves in CheckMate-057, whilst yet to mature, do not demonstrate an overall survival "plateau" which could drive a significant uplift in mean treatment duration. Treatment practice might evolve to use PD(L)-1 agents as acute as opposed to maintenance treatments, improving the chances of delivering a more immunogenic tumour state and enhancing outcomes for subsequent therapies where direct tumour shrinkage is not achieved.

Patient eligibility rates

Opdivo captured a 60% treatment share of the refractory squamous NSCLC market within a matter of weeks, becoming the new standard of care. The treatment share has remained relatively stable increasing to just 63% in June. 26% of patients continue to receive chemotherapy in this setting, with 6% of patients treated with Cyramza and 6% of patients receiving Tarceva-based therapy. It is not clear why the Opdivo penetration rate has plateaued. It could be a function of physician education and more progressive adoption in the community hospital setting. In contrast, it could reflect the prevalence of contraindications against the use of Opdivo such as pre-existing autoimmune disease, symptomatic interstitial lung disease and systemic immune-suppression. We have assumed that 10% of patients are excluded from treatment with Opdivo and alternative I/O agents, but there is a possible that the proportion is significantly higher and is gating the penetration rate in refractory squamous NSCLC.

Patient triaging

The key debate emerging at the ASCO 2015 meeting and about to heat up with the anticipated US approval of Keytruda 2 October is whether effort should be spent on diagnostically triaging treatment of lung cancer patients who have failed on prior therapy. The incremental data presented (BMY's CheckMate-057) supports Roche's and Merck & Co's diagnostic approach that suggests that: (1) a subgroup of patients achieve significant and rapid clinical benefit with anti-PD(L)-1 therapy; (2) a large proportion of patients achieve improved survival with anti-PD(L)-1 therapy compared to chemotherapy, with outcomes seemingly enhanced for subsequent therapies; (3) a significant percentage of patients fare no better than with chemotherapy, but treatment with anti-PD(L)-1 therapies could be justified on the basis of better tolerability.

FIGURE 15

Triaging NSCLC patient treatment by PD-L1 expression

POPLAR	% pts	HR	CM-057	% pts	HR	KEYNOTE-01	% pts	12mOS
IC0/TC0	32%	1.22	<1%	46%	0.9	PS<1%	34%	c.40%
IC1/TC1	**31%**	**0.63**	1-5%	14%	>1.0	PS 1-49%	43%	c.40%
IC2/TC2	**20%**	**0.56**	5-10%	4%	>1.0	**PS>50%**	**23%**	**c.58%**
IC3/TC3	**16%**	**0.47**	**>10%**	**36%**	**0.4**			

Source: Barclays Research; company data

PDL-1 expression is a continuous and inducible variable, impacting its value as predictable and prognostic biomarker. However imperfect enrichment for treatment benefit can still move the field forward, altering the health economics and informing treatment prioritisation for patient subgroups compared to established standard of care. Has Roche perfected an imperfect panacea in the POPLAR study? Will payors triage patient treatment using the Roche diagnostic approach, treating second-line NSCLC IC1-3 patients (circa 65% of patients) with atezolizumab and considering anti-PD(L)-1 treatment instead of Taxotere (on the basis of improved tolerability) if higher treatment costs can be supported? Roche has focused on the IC/TC2-3 population in the 635 patient BIRCH trial which, together with POPLAR, will form the basis of regulatory filing for atezolizumab in the FDA breakthrough designation setting of PDL-1 positive NSCLC. This begs the question which patient subgroup will Roche seeking approval for atezolizumab in? Whilst Roche has been able to show a relative survival benefit versus chemotherapy in circa 65% of patients using a dual IC/TC immunohistological approach, BMY and MRK have shown a relative benefit in just 36% and 23% of patients, respectively.

PDL-1 negative patients do not seem to suffer lower efficacy compared to chemotherapy and possibly benefit from better tolerability. Hence the answer as to whether negative

patients should receive anti-PD(L)-1 treatment or chemotherapy remains unclear. This important question will be addressed by results from the atezolizumab OAK trial around mid-2016, which is assessing this prospectively. Ahead of these data, it seems fair to conclude that the lung cancer opportunity is likely to fragment and not be dominated by one player, with different approaches having arguments for and against. Clearly the question of treatment prioritisation and triaging of patients is more a question for payors both in the US and more price sensitive regions such as Europe, as opposed to physicians.

Modelling and sensitivity analysis

Combining our individual company models together we currently forecast immuno-oncology revenues of $21bn in 2023E, with BMY capturing just over half the revenue opportunity. The discussion above highlights how competitive the lung cancer opportunity is set to become and our forecasts are likely to change as different combination approaches are validated (or otherwise), as pivotal trials read-out and as additional tumour types potentially move forward through clinical development. At this stage, building a top-down model based on the assumptions outlined in Figure 17 below support our company model forecasts with the main outlier being the revenue potential of Roche's atezolizumab beyond 2020E where we see significant upside to our estimates.

FIGURE 16

Immuno-oncology revenue outlook – company forecasts

$m	2014A	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Yervoy (BMY)	1,308	1,298	1,454	1,606	1,847	2,032	2,163	2,304	2,455	2,616
Opdivo (BMY)	6	762	2,527	3,878	5,257	6,308	6,939	7,633	8,205	8,615
Keytruda (MRK)	50	502	1,650	3,235	4,520	5,102	5,357	5,625	5,906	6,201
atezolizumab (ROG)				314	748	2,124	2,602	2,602	2,602	2,602
durvalumab (AZN)				105	280	455	613	753	866	954
avelumab (PFE/MRG)	0	0	0	0	78	127	199	279	391	547
Total	1,364	2,562	5,631	9,138	12,730	16,148	17,872	19,195	20,424	21,535

Source: Barclays Research; company data

FIGURE 17

Immuno-oncology revenue outlook – assumptions per indication

	NSCLC	SCLC	Bladder	TNBC	mRCC	H&N	Gastric	Melanoma	GBM
% Eligible patients	90%	40%	90%	90%	90%	90%	90%	68%	90%
Duration of therapy (m)	3.0	2.0	3.0	3.0	3.0	6.0	3.0	6.0	3.0
% Treated patients	75-100%	100%	99%	100%	100%	50%	99%	100%	100%
US revenues ($m)	5,786	185	626	358	557	962	420	590	424
Opdivo (BMY)	37%	50%	33%	0%	40%	33%	33%	50%	100%
Keytruda (MRK)	28%	50%	33%	50%	20%	33%	33%	50%	0%
atezolizumab (ROG)	24%	0%	33%	50%	40%	33%	0%	0%	0%
durvalumab (AZN)	6%	0%	0%	0%	0%	0%	33%	0%	0%
avelumab (PFE/MRG)	6%	0%	0%	0%	0%	0%	0%	0%	0%

Source: Barclays Research; company data; assumed treatment rates in NSCLC: 75% 1L non-squamous, 92% 2L non-squamous, 100% squamous

FIGURE 18

Overview of anti-PD(L)-1 programs from BMY, MRK, ROG and AZN

	BMY	MRK	ROG	AZN
Take-away from analyst meeting	"Positive results from 8 registrational trials, >50 trials ongoing"	">14,000 patients, 85 trials, 30 tumour types"	" 15 phase 2/3 studies – going deep where strong scientific rationale"	">8,300 patients including >5,600 patients in NSCLC"
Lung	3 reg (4 reg planned)	3 ph3	6 ph3, 3 ph2	8 phase 3, 1 ph2
Melanoma	1 reg	3 ph3		
Bladder	1 reg (1 reg planned)	1 ph3	2 ph3, 2 ph2	1 ph3
SCCHN	1 reg (1 reg planned)	2 ph3		1 ph3, 2 ph2
Gastric	1 reg (1 reg planned)	1 ph3		1 ph2
Renal	2 reg(1 reg planned)		1 ph3, 1 ph2	
GBM	1 reg (1 reg planned)			
HCC	1 reg planned			
HL	1 reg (1 reg planned)			
NHL	1 reg (1 reg planned)			
Breast (TNBC)			1 ph3	
Pancreas				1 ph2
Mesothelioma				1 ph2

Source: Barclays Research, Company data (based on ASCO 2015 analyst meeting statements)

FIGURE 19

Immuno-oncology revenue outlook – top-down projections

($m)	2014A	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Opdivo	6	714	2,838	3,552	4,890	5,918	6,819	7,577	8,181	8,593
Keytruda	50	528	1,460	2,662	3,296	4,024	4,694	5,425	6,073	6,628
atezolizumab		0	0	759	1,465	2,322	3,668	4,274	4,884	5,241
durvalumab		0	0	0	0	157	420	779	969	1,087
avelumab		0	0	0	0	131	297	397	640	743
Total	56	1,242	4,298	6,973	9,651	12,552	15,897	18,452	20,747	22,292

Source: Barclays Research; company data; assumed treatment rates in NSCLC: 75% 1L non-squamous, 92% 2L non-squamous, 100% squamous

A key variable as discussed above remains the average duration of therapy. Simply flexing the average duration of treatment in NSCLC (all lines, all histologies) from 3 months to 6 months on the back of physician education/experience, combination use and longer survival rates in the front line setting drives an illustrative $13bn in additional revenues in 2023E. Assuming our market share assumptions are correct, this would add an incremental $4.8bn in Opdivo revenues in 2023E, an incremental $3.6bn to Keytruda sales and an additional $3.1bn to Roche's atezolizumab revenues. From a downside risk perspective, our 90% patient eligibility rate assumption across the majority of tumours types could be too aggressive based on the "flat" 60-65% Opdivo treatment rate observed in refractory squamous NSCLC to date. Assuming an eligibility rate of 65% would trim our immuno-oncology revenues by circa $5.5bn.

Opdivo and Keytruda sensitivity analysis and valuation

Our base case currently projects 2015E Opdivo sales at $762m with sales expected to ramp sharply over the coming years to $6.9bn by 2020E and to $8.6bn by 2023E. The more than doubling of sales next year in 2016 should be driven by lung cancer with increased adoption driven by approval in refractory non-squamous NSCLC. Sales growth in subsequent years will likely be driven by a mix of penetration into front line NSCLC and additional indications including renal cell carcinoma, head & neck, bladder, and potentially certain haematological indications. Combination use with other checkpoint inhibitors such as Yervoy and experimental agents including lirulumab, urelumab, IDO(s), and CD-137 carries the potential to drive incremental revenues and longer duration of treatment.

Under our current assumptions, our estimates are modestly ahead of the consensus mean, with the difference likely attributable to assumptions in melanoma and lung penetration in the near term and different risk assumptions for other indications over the longer term.

FIGURE 20
Opdivo Estimates

$ millions	2015E	2016E	2017E	2018E	2019E	2020E
Consensus	687	2,013	3,337	4,668	5,525	6,282
Barclays	762	2,527	3,878	5,257	6,308	6,939
Delta	11%	26%	16%	13%	14%	10%

Source: Barclays Research, Bloomberg.

Opdivo is forecasted to become an increasingly important component of BMY's sales and earnings mix over time. While Opdivo will likely be just 5% of sales this year, we project that it will become 44% of total revenue by 2023E. Similarly, while Opdivo will be small contributor to earnings in 2015, we estimate that it will make up nearly half BMY's earnings in 2023E, which raises the issue of concentration risk should a disruptive, next generation technology emerge as a viable therapeutic option.

FIGURE 21
Estimated Opdivo Sales and Earnings Contribution

$ millions	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Total Revenue	15,781	17,210	19,080	20,283	21,525	21,852	22,058	22,060	19,490
Opdivo	762	2,527	3,878	5,257	6,308	6,939	7,633	8,205	8,615
% of Total Revenue	5%	15%	20%	26%	29%	32%	35%	37%	44%
EPS	1.79	2.37	2.99	3.31	3.75	3.81	3.91	4.03	3.60
Opdivo Contribution	0.10	0.38	0.66	0.96	1.23	1.36	1.51	1.66	1.75
% of EPS	5%	16%	22%	29%	33%	36%	39%	41%	49%

Source: Barclays Research, company reports.

Given the difference between our and consensus estimates, we have conducted a sensitivity analysis of the Opdivo sales ramp to BMY's intrinsic value. Our model estimates 2023E Opdivo sales at $8.6bn, which equates to a +29% CAGR from 2015-2023E. Based on this, we have stress tested the impact of up to an incremental (or decremental) $1 billion in sales. Over the same 2015-2023 time period, BMY's selling and marketing expense is expected to increase at a 0.5% CAGR in our model. However, given that the incremental sales would not requirement the same MS&A expense as a percentage of sales since BMY's oncology sales force could be leveraged, we have also tested changes operating expense in 50 bps increments in our sensitivity analysis. We estimate that each incremental $1 billion in 2023E Opdivo sales has approximately a $3.0/share impact on BMY's intrinsic value.

FIGURE 22
BMY DCF Valuation Sensitivity Analysis

2023E SG&A as % of Sales	2023E Opdivo Sales										
	$7.6B	$7.8B	$8.0B	$8.2B	$8.4B	$8.6B	$8.8B	$9.0B	$9.2B	$9.4B	$9.6B
21.6%	53.81	54.26	554.73	55.23	55.74	56.26	56.72	57.19	57.67	58.17	58.68
22.1%	53.47	53.93	54.40	54.89	55.40	55.93	56.39	56.86	57.34	57.84	58.36
22.6%	53.12	53.58	54.06	54.55	55.06	55.59	56.05	56.52	57.01	57.51	58.02
23.1%	52.77	53.23	53.71	54.20	54.72	55.25	55.71	56.18	56.66	57.17	57.68
23.6%	52.41	52.88	53.35	53.85	54.36	54.89	55.35	55.83	56.31	56.82	57.33
24.1%	52.05	52.51	52.99	53.49	54.00	54.53	54.99	55.47	55.96	56.46	56.98
24.6%	51.67	52.14	52.62	53.12	53.63	54.17	54.63	55.10	55.59	56.10	56.62
25.1%	51.29	51.76	52.24	52.74	53.25	53.79	54.25	54.73	55.22	55.73	56.25
25.6%	50.90	51.37	51.85	52.35	52.87	53.41	53.87	54.35	54.84	55.35	55.87
26.1%	50.50	50.97	51.45	51.96	52.48	53.02	53.48	53.96	54.45	54.96	55.48
26.6%	50.10	50.56	51.05	51.55	52.08	52.62	53.08	53.56	54.06	54.57	55.09

Source: Barclays Research, company reports.

We have also conducted a similar analysis of MRK's Keytruda. For 2015, we model Keytruda sales at $502m, in line with the consensus mean of $493m. As with Opdivo, Keytruda's sales are expected to ramp sharply through 2020E with our estimate at $5.3bn compared to approximately $3.6bn for consensus. Our model assumes the successful launch of Keytruda into lung cancer, both refractory and front line patients, together with expansion in front-line melanoma and new indications including TNBC, head & neck cancer and bladder cancer. The slower sales ramp relative to Opdivo is a function of BMY's head-start in lung cancer including combination approaches, MRK's more deliberate focus on thoroughly exploring Keytruda as a monotherapy and the company's relative reliance on multiple external assets for its combination studies. We think that the difference with consensus estimates reflects differing penetration assumptions, the initial labelling for lung, and timing of label expansion for other indications beyond melanoma and NSCLC. Given the limited sample size in the Bloomberg estimates, we believe that the company's internal consensus model based on aggregated sell-side model projects 2020 Keytruda sales closer to $4.6bn, which would be a 15% difference relative to our estimate.

FIGURE 23 **Keytruda Estimates**

$ millions	2015E	2016E	2017E	2018E	2019E	2020E
Consensus	493	1,142	1,836	2,564	3,070	3,550
Barclays	502	1,650	3,235	4,520	5,102	5,357
Delta	2%	44%	76%	76%	66%	51%

Source: Barclays Research, Bloomberg.

Given that MRK has a more diversified revenue mix, Keytruda is likely to be a smaller contributor to the company's sales than Opdivo will be for BMY. For 2015E, we estimate Keytruda will be 1% of sales with it becoming a larger portion at 14% by 2023E. On the earnings side, Merck should be able to leverage Keytruda through its oncology sales force and increase its earnings contribution from 2% this year to 18% of earnings by 2023E.

FIGURE 24

Estimated Keytruda Sales and Earnings Contribution

$ millions	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Total Revenue	39,867	42,298	44,719	46,313	47,267	47,705	48,204	47,223	44,970
Keytruda	502	1,650	3,235	4,520	5,102	5,357	5,625	5,906	6,201
% of Total Revenue	1%	4%	7%	10%	11%	11%	12%	13%	14%
EPS	3.50	3.86	4.45	4.88	5.13	5.27	5.37	5.18	5.13
Keytruda Contribution	0.06	0.20	0.42	0.62	0.72	0.78	0.83	0.88	0.94
% of EPS	2%	5%	9%	13%	14%	15%	15%	17%	18%

Source: Barclays Research, company reports.

We have conducted a sensitivity analysis on the impact of different Keytruda sales ramps assumptions on MRK's valuation. Given that potential leverage that could be generated by incremental sales, we have also varied the SG&A assumptions relative to the level of sales as the other variable. However, for MRK we have used 20 bps increments rather than 100 bps as with BMY given the larger portion of fixed costs and SG&A requirements for its other product lines. Based on these assumptions, our analysis indicates that a faster ramp resulting in an incremental $1 billion in Keytruda sales by 2023E would increase MRK's valuation by nearly $2.0/share while a slower sales ramp would decrease it by approximately $1.5/share.

FIGURE 25

MRK DCF Valuation Sensitivity Analysis

	2023E Keytruda Sales										
2023E SG&A as % of Sales	$5.2B	$5.4B	$5.6B	$5.8B	$6.0B	$6.2B	$6.4B	$6.6B	$6.8B	$7.0B	$7.2B
24.0%	68.75	69.02	69.60	69.61	69.91	70.25	70.60	70.96	71.35	71.76	72.18
24.2%	68.60	68.87	69.15	69.45	69.77	70.10	70.45	70.82	71.20	71.61	72.03
24.4%	68.45	68.72	69.00	69.30	69.61	69.95	70.30	70.67	71.05	71.46	71.88
24.6%	68.30	68.57	68.85	69.15	69.46	69.80	70.15	70.51	70.90	71.31	71.73
24.8%	68.15	68.42	68.70	69.00	69.31	69.64	69.99	70.36	70.75	71.15	71.58
25.0%	68.00	68.27	68.55	68.85	69.16	69.52	69.84	70.21	70.60	71.00	71.43
25.2%	67.85	68.12	68.40	68.70	69.01	69.34	69.69	70.06	70.44	70.85	71.28
25.4%	67.70	67.97	68.25	68.55	68.86	69.19	69.53	69.90	70.29	70.70	71.12
25.6%	67.55	67.82	68.10	68.40	68.71	69.03	69.38	69.75	70.14	70.54	70.97
25.8%	67.40	67.66	67.95	68.24	68.55	68.88	69.23	69.59	69.98	70.39	70.82
26.0%	67.24	67.51	67.79	68.09	68.40	68.73	69.07	69.44	69.83	70.23	70.66

Source: Barclays Research, company reports.

ANALYST(S) CERTIFICATION(S):

We, Mark Purcell, Michael Leuchten, Simon Mather, Olivia Capra, Atsushi Seki and Geoff Meacham, Ph.D., hereby certify (1) that the views expressed in this research report accurately reflect our personal views about any or all of the subject securities or issuers referred to in this research report and (2) no part of our compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed in this research report.

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Primary Stocks (Ticker, Date, Price)

AstraZeneca (AZN.L, 12-Aug-2015, GBP 42.89), Underweight/Neutral, C/D/J/K/L/M/N

Bristol-Myers Squibb (BMY, 12-Aug-2015, USD 62.39), Equal Weight/Neutral, A/C/D/J/K/L/M/N

Merck & Co. (MRK, 12-Aug-2015, USD 58.26), Equal Weight/Neutral, C/D/E/J/K/L/M/N/O

Roche (ROG.VX, 12-Aug-2015, CHF 270.60), Overweight/Neutral, A/C/D/J/K/L/M/N

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IMPORTANT DISCLOSURES CONTINUED

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Guide to the Barclays Fundamental Equity Research Rating System:

Our coverage analysts use a relative rating system in which they rate stocks as Overweight, Equal Weight or Underweight (see definitions below) relative to other companies covered by the analyst or a team of analysts that are deemed to be in the same industry (the "industry coverage universe").

In addition to the stock rating, we provide industry views which rate the outlook for the industry coverage universe as Positive, Neutral or Negative (see definitions below). A rating system using terms such as buy, hold and sell is not the equivalent of our rating system. Investors should carefully read the entire research report including the definitions of all ratings and not infer its contents from ratings alone.

Stock Rating

Overweight - The stock is expected to outperform the unweighted expected total return of the industry coverage universe over a 12-month investment horizon.

Equal Weight - The stock is expected to perform in line with the unweighted expected total return of the industry coverage universe over a 12-month investment horizon.

Underweight - The stock is expected to underperform the unweighted expected total return of the industry coverage universe over a 12-month investment horizon.

Rating Suspended - The rating and target price have been suspended temporarily due to market events that made coverage impracticable or to comply with applicable regulations and/or firm policies in certain circumstances including where the Investment Bank of Barclays Bank PLC is acting in an advisory capacity in a merger or strategic transaction involving the company.

Industry View

Positive - industry coverage universe fundamentals/valuations are improving.

Neutral - industry coverage universe fundamentals/valuations are steady, neither improving nor deteriorating.

Negative - industry coverage universe fundamentals/valuations are deteriorating.

Below is the list of companies that constitute the "industry coverage universe":

European Pharmaceuticals

Actelion (ATLN.VX)	Almirall SA (ALM.MC)	AstraZeneca (AZN.L)
Bayer AG (BAYGn.DE)	GlaxoSmithKline (GSK.L)	Hikma Pharmaceuticals (HIK.L)
Ipsen (IPN.PA)	Merck KGaA (MRCG.DE)	Novartis (NOVN.VX)
Novo Nordisk (NOVOb.CO)	Roche (ROG.VX)	Sanofi (SASY.PA)
Shire (SHP.L)	Stada (STAGn.DE)	UCB SA (UCB.BR)
Vectura (VEC.L)		

Japan Biopharmaceuticals

Acucela, Inc. (4589.T)	Alfresa Holdings Corp. (2784.T)	Astellas Pharma Inc. (4503.T)
Chugai Pharmaceutical Co., Ltd. (4519.T)	Daiichi Sankyo Co., Ltd. (4568.T)	Eisai Co., Ltd. (4523.T)
Kyowa Hakko Kirin Co., Ltd. (4151.T)	Medipal Holdings Corp. (7459.T)	Mitsubishi Tanabe Pharma Co. (4508.T)
Nichi-Iko Pharmaceutical Co., Ltd. (4541.T)	Ono Pharmaceutical Co., Ltd. (4528.T)	Otsuka Holdings Co., Ltd. (4578.T)
Santen Pharmaceutical Co., Ltd. (4536.T)	Sawai Pharmaceutical Co., Ltd. (4555.T)	Shionogi & Co., Ltd. (4507.T)
Sumitomo Dainippon Pharma (4506.T)	Suzuken Co., Ltd. (9987.T)	Taisho Pharmaceutical Holdings (4581.T)
Takeda Pharmaceutical Co. (4502.T)	Towa Pharmaceutical Co., Ltd. (4553.T)	

IMPORTANT DISCLOSURES CONTINUED

U.S. Major Pharmaceuticals

AbbVie Inc. (ABBV)	Bristol-Myers Squibb (BMY)	Eli Lilly & Co. (LLY)
Johnson & Johnson (JNJ)	Merck & Co. (MRK)	Pfizer Inc. (PFE)

Distribution of Ratings:

Barclays Equity Research has 2692 companies under coverage.

43% have been assigned an Overweight rating which, for purposes of mandatory regulatory disclosures, is classified as a Buy rating; 53% of companies with this rating are investment banking clients of the Firm.

41% have been assigned an Equal Weight rating which, for purposes of mandatory regulatory disclosures, is classified as a Hold rating; 46% of companies with this rating are investment banking clients of the Firm.

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Top Picks:

Barclays Equity Research's "Top Picks" represent the single best alpha-generating investment idea within each industry (as defined by the relevant "industry coverage universe"), taken from among the Overweight-rated stocks within that industry. Barclays Equity Research publishes global and regional "Top Picks" reports every quarter and analysts may also publish intra-quarter changes to their Top Picks, as necessary. While analysts may highlight other Overweight-rated stocks in their published research in addition to their Top Pick, there can only be one "Top Pick" for each industry. To view the current list of Top Picks, go to the Top Picks page on Barclays Live (https://live.barcap.com/go/keyword/TopPicksGlobal).

To see a list of companies that comprise a particular industry coverage universe, please go to http://publicresearch.barclays.com.

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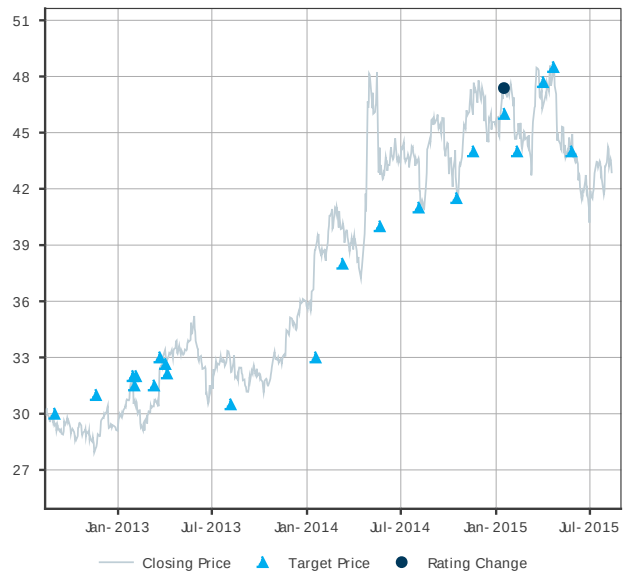
IMPORTANT DISCLOSURES CONTINUED

AstraZeneca (AZN LN / AZN.L)

	Stock Rating	Industry View
GBP 42.89 (12-Aug-2015)	**UNDERWEIGHT**	**NEUTRAL**

Rating and Price Target Chart - GBP (as of 12-Aug-2015) **Currency=GBP**



Date	Closing Price	Rating	Adjusted Price Target
26-May-2015	43.74		44.00
21-Apr-2015	48.55		48.50
01-Apr-2015	46.41		47.70
10-Feb-2015	44.88		44.00
16-Jan-2015	47.15	Underweight	46.00
17-Nov-2014	45.97		44.00
16-Oct-2014	42.25		41.50
04-Aug-2014	43.63		41.00
21-May-2014	44.20		40.00
10-Mar-2014	39.90		38.00
17-Jan-2014	38.75		33.00
06-Aug-2013	32.72		30.50
05-Apr-2013	32.83		32.15
02-Apr-2013	33.40		32.65
22-Mar-2013	32.36		33.00
11-Mar-2013	30.39		31.50
04-Feb-2013	30.41		32.00
01-Feb-2013	30.69		31.50
29-Jan-2013	31.68		32.00
19-Nov-2012	28.18		31.00
31-Aug-2012	29.37		30.00

Source: Thomson Reuters, Barclays Research

Historical stock prices and price targets may have been adjusted for stock splits and dividends.

Source: IDC, Barclays Research

Link to Barclays Live for interactive charting

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Valuation Methodology: We value AstraZeneca through a DCF valuation assuming a risk-free rate derived from the yield curve, an equity risk premium of 5%, an asset beta of 0.9, pre-tax cost of debt based on CDS spreads and a target debt ratio of 25%. Beyond our explicit forecast period we assume returns fade to cost of capital in the long term and we adjust AZ's reported capital base by capitalising and expensing R&D over an assumed 12-year asset life. These assumptions result in our price target of GBP44.00.

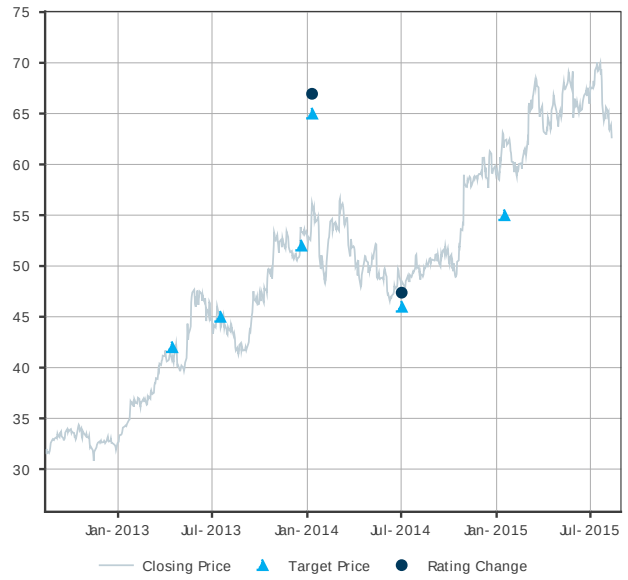
Risks which May Impede the Achievement of the Barclays Research Price Target: Risks and opportunities relate to outcomes for development pipeline projects. Commercial success of Brilinta (acute coronary syndromes), Bydureon (diabetes) and Symbicort (asthma/ COPD) are also important drivers.

IMPORTANT DISCLOSURES CONTINUED

Bristol-Myers Squibb (BMY)

	Stock Rating	Industry View
USD 62.39 (12-Aug-2015)	**EQUAL WEIGHT**	**NEUTRAL**

Rating and Price Target Chart - USD (as of 12-Aug-2015) **Currency=USD**



Date	Closing Price	Rating	Adjusted Price Target
16-Jan-2015	62.31		55.00
02-Jul-2014	48.24	Equal Weight	46.00
10-Jan-2014	56.18	Overweight	65.00
20-Dec-2013	53.37		52.00
17-Jul-2013	44.51		45.00
15-Apr-2013	40.75		42.00

Source: Thomson Reuters, Barclays Research

Historical stock prices and price targets may have been adjusted for stock splits and dividends.

Source: IDC, Barclays Research

Link to Barclays Live for interactive charting

A: Barclays Bank PLC and/or an affiliate has been lead manager or co-lead manager of a publicly disclosed offer of securities of Bristol-Myers Squibb in the previous 12 months.

C: Barclays Bank PLC and/or an affiliate is a market-maker and/or liquidity provider in equity securities issued by Bristol-Myers Squibb or one of its affiliates.

D: Barclays Bank PLC and/or an affiliate has received compensation for investment banking services from Bristol-Myers Squibb in the past 12 months.

J: Barclays Bank PLC and/or an affiliate trades regularly in the securities of Bristol-Myers Squibb.

K: Barclays Bank PLC and/or an affiliate has received non-investment banking related compensation (including compensation for brokerage services, if applicable) from Bristol-Myers Squibb within the past 12 months.

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Valuation Methodology: We value BMY through a DCF valuation assuming a risk-free rate derived from the yield curve, an equity risk premium of 5%, an asset beta of 0.6, pre-tax cost of debt of 5.2% and a target debt ratio of 20%. These assumptions result in a dynamic cost of capital averaging 5.2%, peaking at 6.0% in 2040, and yield a price target of $55.

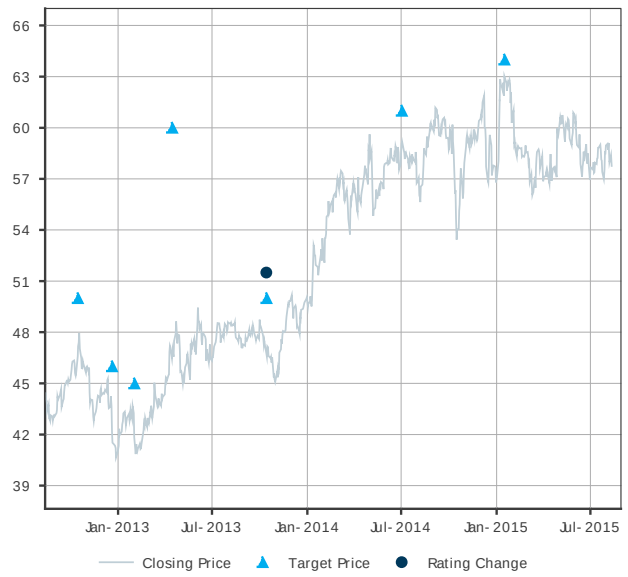
Risks which May Impede the Achievement of the Barclays Research Price Target: As BMY's growth prospects increasingly depend on the delivery of its immunoncology pipeline, any setbacks or delays could pose risk to the stock. The field of immunoncology is getting increasingly competitive and BMY's leadership is being challenged by other major players. Any competitive disadvantage in terms of clinical development or regulatory timeline could put pressure on the stock.

IMPORTANT DISCLOSURES CONTINUED

Merck & Co. (MRK)

	Stock Rating	Industry View
USD 58.26 (12-Aug-2015)	**EQUAL WEIGHT**	**NEUTRAL**

Rating and Price Target Chart - USD (as of 12-Aug-2015) **Currency=USD**



Date	Closing Price	Rating	Adjusted Price Target
16-Jan-2015	63.03		64.00
02-Jul-2014	59.05		61.00
14-Oct-2013	46.75	Equal Weight	50.00
15-Apr-2013	46.46		60.00
01-Feb-2013	41.83		45.00
20-Dec-2012	42.16		46.00
15-Oct-2012	46.59		50.00

Source: Thomson Reuters, Barclays Research

Historical stock prices and price targets may have been adjusted for stock splits and dividends.

Source: IDC, Barclays Research

Link to Barclays Live for interactive charting

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D: Barclays Bank PLC and/or an affiliate has received compensation for investment banking services from Merck & Co. in the past 12 months.

E: Barclays Bank PLC and/or an affiliate expects to receive or intends to seek compensation for investment banking services from Merck & Co. within the next 3 months.

J: Barclays Bank PLC and/or an affiliate trades regularly in the securities of Merck & Co..

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Valuation Methodology: We value MRK using a DCF valuation assuming a dynamic cost of capital based on CDS, an equity risk premium of 5%, asset beta of 0.60, pre-tax cost of debt of 5.50%, and a target debt ratio of 10%. These assumptions result in a cost of capital averaging 5.18% - with a peak value of 6.0% in 2040 - and our price target of $64.

Risks which May Impede the Achievement of the Barclays Research Price Target: Competitive pressure and market maturation for MRK's diabetes, immunology and vaccines franchise could cause slowdown of growth in the core business. MRK's key pipeline assets, HCV and anti-PD1 are both in highly competitive markets. Any setback in clinical development of these assets could cause concerns over long term growth.

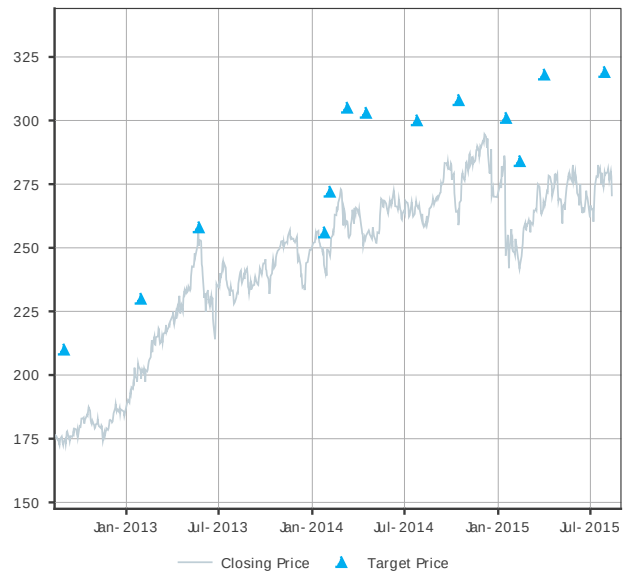
IMPORTANT DISCLOSURES CONTINUED

Roche (ROG VX / ROG.VX)

CHF 270.60 (12-Aug-2015)

Stock Rating	Industry View
OVERWEIGHT	**NEUTRAL**

Rating and Price Target Chart - CHF (as of 12-Aug-2015) **Currency=CHF**



Date	Closing Price	Rating *	Adjusted Price Target
28-Jul-2015	276.70		319.00
01-Apr-2015	267.40		318.00
12-Feb-2015	241.70		284.00
16-Jan-2015	247.20		301.00
15-Oct-2014	258.90		308.00
25-Jul-2014	267.00		300.00
16-Apr-2014	254.20		303.00
10-Mar-2014	260.50		305.00
04-Feb-2014	247.50		272.00
24-Jan-2014	243.30		256.00
23-May-2013	250.70		258.00
29-Jan-2013	201.40		230.00
31-Aug-2012	173.80		210.00

Source: Thomson Reuters, Barclays Research

Historical stock prices and price targets may have been adjusted for stock splits and dividends.

*The rating for this security remained Overweight during the relevant period.

Source: IDC, Barclays Research

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N: Roche is, or during the past 12 months has been, a non-investment banking client (non-securities related services) of Barclays Bank PLC and/or an affiliate.

Valuation Methodology: We value Roche on a DCF basis applying a risk-free rate derived from the yield curve, a 5% risk premium, an asset beta of 0.9, cost of debt derived from the CDS curve and a target debt ratio of 10%. This yields a dynamic cost of capital. In the long-run we are feeding incremental ROCE back towards the company's long term cost of capital. This approach yields our price target of CHF319.

Risks which May Impede the Achievement of the Barclays Research Price Target: Risks to our stance near term include R&D failures and more aggressive than anticipated margin pressure. The key downside risk to long-term forecasts and the defensive perception of Roche's future cash flows remains biosimilar competition to Rituxan and Herceptin.

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