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Equity Research
23 October 2015

U.S. Major Pharmaceuticals

Opdivo/Keytruda heading into Q3

Market data point to a strong Opdivo Q3'15 performance: IMS Health revenue and prescription data suggest a strong Q3'15 US performance for Opdivo and Keytruda US revenues in-line with Q2'15. **We estimate that BMY should report US Opdivo revenues of circa $220m based on these data projections, with IMS MIDAS data trends implying an additional $25m in Opdivo international revenues**. Opdivo's performance suggests that either the average duration of treatment is increasing beyond 3 months and / or off-label usage is emerging from indications such as renal cancer, and we will look for commentary in this regard on the Q3 results Tuesday 27 October. For Keytruda, IMS data imply Q3'15 sales of circa $82m in the US compared to $86m Q2'15. Whilst our analysis is clearly supportive of near-term Opdivo consensus estimates, longer-term prospects remain dependent on ex-US execution and US revenues in the increasingly competitive first-line NSCLC setting. Phase 1 data emerging for novel agents combined with anti-PD(L)-1 agents remains a key competitive focus over the next 9 months, starting with the Keytruda plus INCB2430-202 data at the SITC meeting 6 November.

Opdivo/Keytruda rapidly becoming standard of care, does this provide an important first-mover advantages?: Proprietary prescribing data from AlphaImpactRx highlight that the adoption of Opdivo and Keytruda has been very rapid, with the two drugs combined capturing 61% and 71% of the on-label indications in refractory melanoma and squamous NSCLC, respectively. Triangulating these data with Q2 results commentary and a relatively short 3 month 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. Opdivo off-label penetration in the refractory non-squamous NSCLC setting has risen to 24% from 12% in Q2'15, with FDA approval of both Opdivo and Keytruda in this setting early October setting up an intriguing market share battle. In front-line melanoma, Keytruda patent penetration has accelerated from 17% to 29% in September, with tolerability concerns seemingly limiting the adoption of Opdivo plus Yervoy to a 7% patient share.

Top-down assumptions support our $21bn immunoncology company sales forecasts, but a number of key variables remain unanswered: Combining our individual US and EU Pharma company models together we currently forecast immunoncology 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 and assuming an eligibility rate of 65% would trim our immunoncology revenues by circa $5.5bn.

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PLEASE SEE ANALYST CERTIFICATION(S) AND IMPORTANT DISCLOSURES BEGINNING ON PAGE 13.

INDUSTRY UPDATE

U.S. Major Pharmaceuticals
NEUTRAL
Unchanged

For a full list of our ratings, price target and earnings changes in this report, please see table on page 2.

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Summary of our Ratings, Price Targets and Earnings Changes in this Report (all changes are shown in bold)

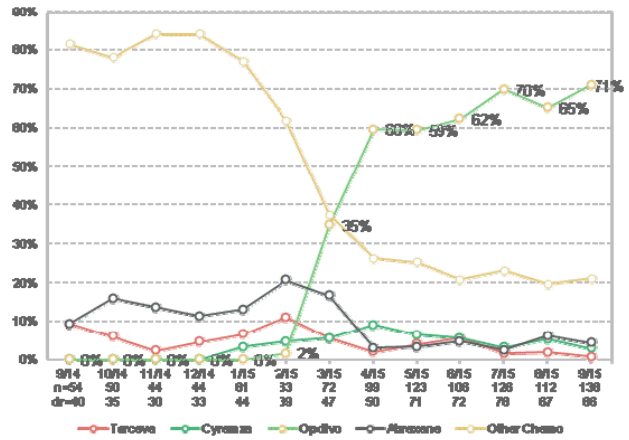
Company	Rating		Price	Price Target			EPS FY1 (E)			EPS FY2 (E)		
	Old	New	21-Oct-15	Old	New	%Chg	Old	New	%Chg	Old	New	%Chg
U.S. Major Pharmaceuticals	Neu	Neu										
AbbVie Inc. (ABBV)	OW	OW	53.83	73.00	73.00	-	4.28	4.28	-	4.96	4.96	-
Bristol-Myers Squibb (BMY)	EW	EW	62.51	55.00	55.00	-	1.79	1.79	-	2.30	2.30	-
Eli Lilly & Co. (LLY)	EW	EW	77.01	75.00	75.00	-	3.28	3.28	-	3.70	3.70	-
Johnson & Johnson (JNJ)	EW	EW	97.63	101.00	101.00	-	6.19	6.19	-	6.49	6.49	-
Merck & Co. (MRK)	EW	EW	50.59	64.00	64.00	-	3.50	3.50	-	3.86	3.86	-
Pfizer Inc. (PFE)	EW	EW	33.46	34.00	34.00	-	2.06	2.06	-	2.23	2.23	-

Source: Barclays Research. Share prices and target prices are shown in the primary listing currency and EPS estimates are shown in the reporting currency.
FY1(E): Current fiscal year estimates by Barclays Research. FY2(E): Next fiscal year estimates by Barclays Research.
Stock Rating: OW: Overweight; EW: Equal Weight; UW: Underweight; RS: Rating Suspended
Industry View: Pos: Positive; Neu: Neutral; Neg: Negative

Executive summary

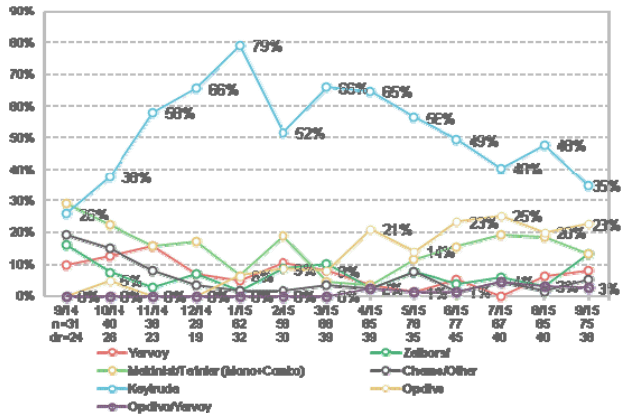
BMY's Opdivo and MRK's Keytruda on track for US revenues of $1.7bn in melanoma and refractory lung cancer, but is this enough to meet heightened expectations?: We triangulated comments made on the Q2 earnings calls, reported and the latest IMS estimated revenue data and proprietary AlphaImpactRx prescribing data from September 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 61% and 71% of the on-label indications in refractory melanoma and squamous NSCLC, respectively. **However the duration of treatment remains relatively short** and a key debating point - using a 3 month treatment duration, we estimate that the melanoma indication will likely generate $715m in US sales and the refractory NSCLC indication $1.0bn in US revenues.

FIGURE 1
Opdivo has captured a 71% patient share of the refractory squamous mNSCLC opportunity



Source: Barclays Research, AlphaImpactRx

FIGURE 2
Keytruda and Opdivo have captured a 61% patient share of the refractory metastatic melanoma opportunity



Source: Barclays Research, AlphaImpactRx

Whilst 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. Key take-aways from our updated analysis for Q3 2015:

- **IMS Health revenue and prescription data suggest a strong Q3'15 US performance for Opdivo, with reported revenues circa $220m vs $107m Q2'15**. IMS MIDAS data for July-August suggest that Opdivo international could contribute revenues of circa $25m.
- **IMS Health revenue and prescription data suggest Keytruda Q3'15 US revenues will be broadly in-line with Q2** (circa $82m compared to $89m Q2'15).
- **Opdivo has reached a 71% penetration rate in refractory squamous NSCLC patients**, an incremental jump from the 61% penetration rate achieved during Q2'15. **Opdivo off-label penetration in the refractory non-squamous NSCLC setting has risen to 24% from 12% in Q2'15**.
- **Across all lines of melanoma, MRK's Keytruda franchise has maintained a 27% patient share in Q3'15**. BMY's Opdivo franchise (including use in combination with Yervoy) has increased from a 9% to a 17% patient share in Q3'15, offsetting a corresponding decline in the Yervoy franchise from a 24% patient share in Q2'15 to a 15% share in September 2015.

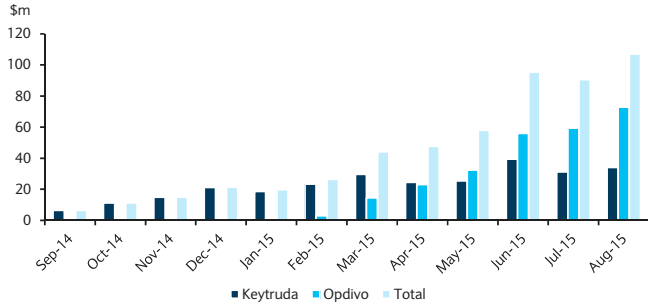
Lung cancer has driven an acceleration in I/O revenues

IMS data point to a strong Opdivo Q3 performance in the US

Our analysis of IMS Health revenue and prescription data suggest a strong Q3'15 US performance for Opdivo and Keytruda US revenues in-line with Q2'15. IMS has reported Opdivo revenues of $132m in July-August and reflecting weekly prescription trends, Q3'15 Opdivo revenues should reach circa $230m (circa $220m as reported) with IMS MIDAS data suggesting an additional $25m Opdivo contribution from outside the US. For Keytruda, IMS data imply Q3'15 sales of circa $85m (circa $82m as reported).

As a reminder, BMY reported Opdivo revenues of $122m in Q2'15, with the majority of sales from the US ($107m) where IMS estimated Q2'15 revenues of $112m. The majority of Merck's Keytruda revenues were also generated in the US, $86m from a Q2 total of $122m which correlated closely with the IMS Q2'15 revenue estimate of $89m.

FIGURE 3
Lung cancer drives Opdivo/Keytruda revenue growth



Source: Barclays Research, IMS Health

FIGURE 4
Opdivo/Keytruda Q3 revenues estimates in the US

	Q3'14	Q4'14	Q1'15	Q2'15	*Q3'15E*
Keytruda IMS estimated	7	47	72	89	*85*
Keytruda reported		44	66	86	*82*
Opdivo IMS estimated	-	0	19	112	*230*
Opdivo reported		1	38	107	*220*
Yervoy rep	191	199	181	136	

Source: Barclays Research, IMS Health, company data

Therefore combined Opdivo/Keytruda revenues appear to have accelerated from June onwards 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. Given how rapidly Opdivo has been adopted in 2L+ squamous NSCLC, which represents a risk to "undifferentiated" fast-follower strategies, the recent FDA approvals of Keytruda in 2L NSCLC (2 October) and Opdivo in 2L non-squamous NSCLC (9 October) emphasizes the importance of the October performance data.

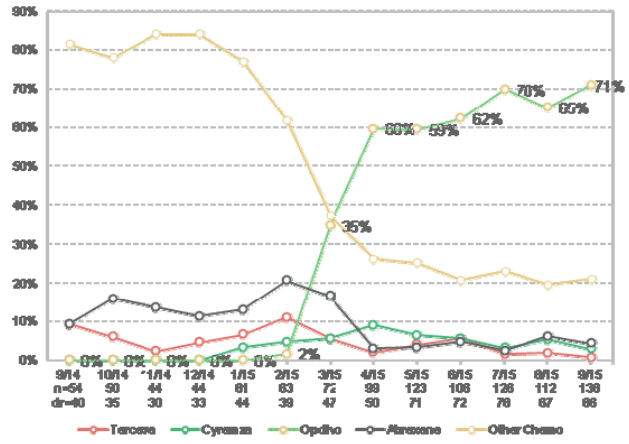
AlphaImpactRx data demonstrate rapid uptake in lung cancer…

Proprietary physician-level data from AlphaImpactRx 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 has reached a 71% penetration rate in refractory squamous NSCLC patients, an incremental jump from the 61% penetration rate achieved during Q2'15. It is unclear whether the 30% of patients not treated with Opdivo, the majority of which are receiving chemotherapy), 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 24% from 12% in Q2'15 following the presentation of the CHECKMATE-057 data at ASCO and subsequent endorsement by the NCCN. The uptake of Opdivo has contributed to a decline in Alimta's market share in this setting (12% Sept'15 vs 15% Q2'15) and is reflected in LLY's Q3'15 results comment that volumes are under competitive pressure. Whilst MRK

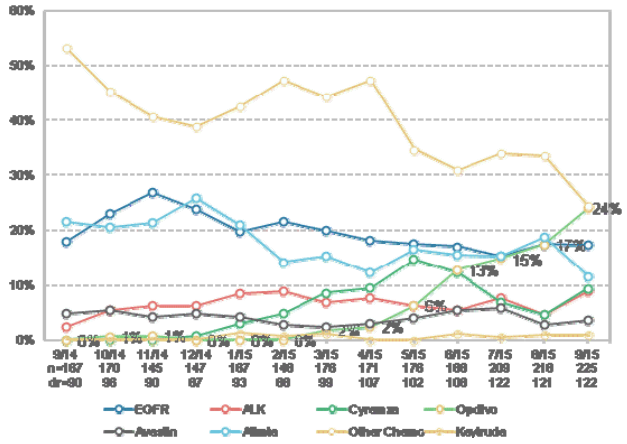
reported that 15% of Keytruda revenues were in lung cancer in Q2'15, AlphaImpactRx data suggest a 1% penetration rate for Keytruda in 2L+ non-squamous patients.

FIGURE 5
Refractory squamous mNSCLC patient share



Source: Barclays Research, AlphaImpactRx

FIGURE 6
Refractory non-squamous mNSCLC patient share



Source: Barclays Research, AlphaImpactRx

…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 had a 60% patient share in Yervoy-refractory melanoma and was the No.1 melanoma drug overall. The latest AlphaImpactRx data suggest that the overall picture in melanoma has not changed substantially from Q2'15, but treatment trends remain dynamic on an individual indication perspective as pivotal data and regulatory approvals drive changes in treatment practice.

FIGURE 7
Immuno-oncology approvals in melanoma

Est. Timing	FDA approval	Importance
1 Oct	*Approved*	*FDA approval of Opdivo+Yervoy 1L BRAF V600 wild-type melanoma (CM-069 trial)*
Nov	Pending	FDA approval decision Tefinlar+Mekinist 1L melanoma (COMBI-D trial)
27 Nov	Pending	FDA approval decision Opdivo vs decarbazine 1L melanoma (CM-066 trial)
19 Dec	Pending	FDA approval decision Keytruda 1L melanoma (KN-006 trial)

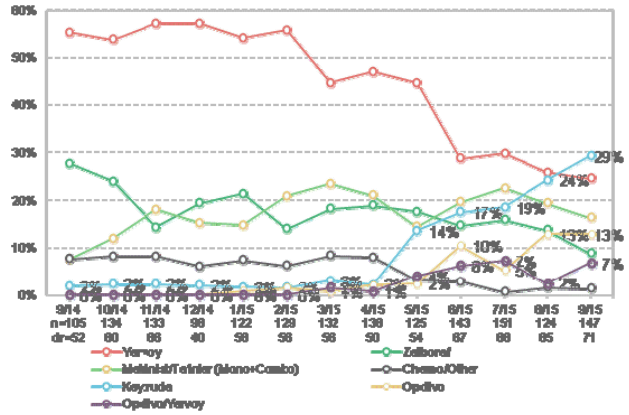
Source: Barclays Research, company data

Across all lines of melanoma, MRK's Keytruda franchise has maintained a 27% patient share in Q3'15. BMY's Opdivo franchise (including use in combination with Yervoy) has increased from a 9% to a 17% patient share in Q3'15, offsetting a continued decline in the Yervoy franchise from a 24% patient share in Q2'15 to a 15% share in September 2015. In the first-line setting, Keytruda has gained significant share supported by positive data from the KN-006 trial which was presented in April – patient share has risen from circa 17% in Q2'15 to 29% in September. These share gains have been mirrored by patient share losses in the second-line setting, where Keytruda's share has fallen from circa 56% in Q2'15 to 35% in September.

Patient share for the Opdivo franchise in first-line melanoma has risen from 9% in Q2'15 to 20% in September 2015, with circa one third of patient share driven by use in combination with Yervoy. Patient from the Opdivo franchise in second-line melanoma has risen modestly from 20% in Q2'15 to 26% in September'15. The Opdivo plus Yervoy combination is used in

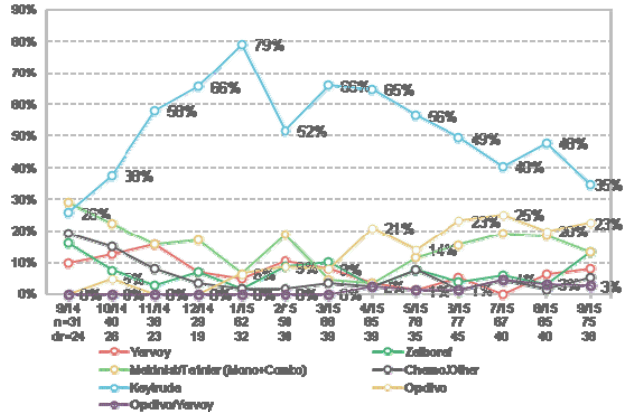
just 3% of second-line melanoma patients, perhaps reflecting tolerability concerns, so uptake of this combination in October following FDA approval will be a key focus. In first line patients with BRAF mutations, Mekinist/Tafinlar and Zelboraf have continued to hold >50% of patient starts ahead of the FDA COMBI-D approval decision.

FIGURE 8
First line metastatic melanoma share



Source: Barclays Research, AlphaImpactRx

FIGURE 9
Refractory metastatic melanoma share



Source: Barclays Research, AlphaImpactRx

Triangulating I/O revenues & proprietary market share data

We 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 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.

We have used the same approach ahead of the BMY and MRK Q3 results to be released Tuesday 27 October. Using an average duration of therapy of 3 months, the AlphaImpactRx data suggest that Opdivo Q3'15 total patient penetration rates have increased to 69% (vs 61%) in the second-line squamous setting, increased to19% (vs 7%) in the second-line non-squamous setting and increased to 16% (vs 9%) in the first-line melanoma setting. Taken together revenues would projected to rise from $107m Q2'15 to $167m Q3'15. With IMS revenue data implying reported US Opdivo revenues of circa $220m, this suggests that the average duration of Opdivo treatment might have increased towards an average of 4 months and/or Opdivo might be generating revenues in other indications such as renal cancer following the early stop of the CHECKMATE-025 trial 20 July because of a significant overall survival benefit relative to Affinitor.

Using an average duration of therapy of 3 months, the AlphaImpactRx data suggest that Keytruda Q3'15 total patient penetration rates have increased to 24% (vs 11%) in the first-line melanoma setting and decreased to 41% (vs 57%) in the second-line melanoma setting. Assuming that the Keytruda NSCLC revenue contribution has not changed quarter over quarter would imply US Keytruda revenues of $101m in Q3'15 compared to $86m in Q2'15. IMS revenue data imply reported US Keytruda revenues of closer to $82m, with the

difference being the implied lung cancer revenue contribution, which in isolation implies that duration of treatment with Keytruda might be less than 3 months.

FIGURE 10
Opdivo US revenue estimates

	Total	Melanoma	1L melanoma	2L+ melanoma	NSCLC	2L+ Sq NSCLC	2L+ Non-sq NSCLC
Opdivo Q1	38						
Opdivo Q2	107	43	21	22	64	48	16
Opdivo Q3	167	66	39	27	101	54	47
Opdivo Q4	229	116	85	31	113	51	62
Total	541						
Peak Opdivo quarterly	272	130	97	33	142	43	99
Peak Opdivo annual	1,089	521	390	132	568	173	395
Steady state penetration rates							
Opdivo Q2			9%	20%		61%	7%
Opdivo June			16%	24%		62%	13%
Opdivo Q3			16%	25%		69%	19%
Opdivo Q4			35%	28%		65%	25%
Opdivo peak			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

FIGURE 11
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 Q3	101	88	50	38	14	4	10
Keytruda Q4	152	117	86	31	35	8	27
Total	405						
Peak Keytruda quarterly	157	83	41	42	74	12	62
Peak Keytruda annual	627	332	165	167	294	47	247
Steady state penetration rates							
Keytruda Q2			11%	57%		*4%*	*4%*
Keytruda June			17%	49%		*na*	*na*
Keytruda Q3			24%	41%		5%	4%
Keytruda Q4			19%	47%		9%	11%
Keytruda peak			20%	45%		15%	25%

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

Key modelling questions

Duration of treatment

AlphaImpactRx data demonstrated 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. Whilst 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 steadily increased to just 71% in September. 25% of patients continue to receive chemotherapy in this setting, with 3% of patients treated with Cyramza and 1% 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 interstitional 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.

FIGURE 12

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

Patient triaging

The key debate emerging at the ASCO 2015 meeting and about to heat up with the 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.

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 priorisation 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.

FIGURE 13

Immunoncology 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 14

Immunoncology 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 15

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 16

Immunoncology 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

U.S. Major Pharmaceuticals — **Industry View: NEUTRAL**

Bristol-Myers Squibb (BMY)

Stock Rating: EQUAL WEIGHT

Income statement ($mn)	2014A	2015E	2016E	2017E	CAGR
Revenue	15,879	15,781	17,210	19,080	6.3%
EBITDA (adj)	3,935	3,649	4,761	6,013	15.2%
EBIT (adj)	3,468	3,257	4,191	5,401	15.9%
Pre-tax income (adj)	3,884	3,780	4,778	6,016	15.7%
Net income (adj)	3,085	2,987	3,817	4,842	16.2%
EPS (adj) ($)	1.85	1.79	2.30	2.95	16.8%
Diluted shares (mn)	1,670.0	1,667.5	1,655.3	1,644.0	-0.5%
DPS ($)	1.45	1.49	1.53	1.57	2.7%

Margin and return data					Average
EBITDA (adj) margin (%)	24.8	23.1	27.7	31.5	26.8
EBIT (adj) margin (%)	21.8	20.6	24.4	28.3	23.8
Pre-tax (adj) margin (%)	24.5	24.0	27.8	31.5	26.9
Net (adj) margin (%)	19.4	18.9	22.2	25.4	21.5
ROIC (%)	12.4	14.9	19.3	25.1	18.0
ROA (%)	7.7	9.2	12.3	15.5	11.2
ROE (%)	20.4	20.2	27.2	34.6	25.6

Balance sheet and cash flow ($mn)					CAGR
Tangible fixed assets	4,417	5,146	5,519	5,932	10.3%
Intangible fixed assets	9,695	9,116	9,116	9,116	-2.0%
Cash and equivalents	7,435	5,191	4,906	5,448	-9.8%
Total assets	33,749	31,326	30,487	31,970	-1.8%
Short and long-term debt	7,832	7,296	7,296	7,296	-2.3%
Other long-term liabilities	618	475	475	475	-8.4%
Total liabilities	18,766	16,709	17,057	17,377	-2.5%
Net debt/(funds)	397	2,105	2,390	1,848	67.0%
Shareholders' equity	14,983	14,617	13,430	14,593	-0.9%
Change in working capital	201	-646	-304	N/A	N/A
Cash flow from operations	3,148	2,587	3,779	N/A	N/A
Capital expenditure	-526	-536	-533	N/A	N/A
Free cash flow	2,622	2,052	3,246	N/A	N/A

Valuation and leverage metrics					Average
P/E (adj) (x)	33.8	34.9	27.2	21.2	29.3
EV/sales (x)	6.5	6.7	6.1	5.5	6.2
EV/EBITDA (adj) (x)	26.3	28.9	22.2	17.5	23.7
Equity FCF yield (%)	2.3	2.8	4.0	4.9	3.5
P/BV (x)	7.0	7.1	7.7	7.0	7.2
Dividend yield (%)	2.3	2.4	2.4	2.5	2.4
Total debt/capital (%)	34.3	33.3	35.2	33.3	34.0
Net debt/equity (%)	2.6	14.4	17.8	12.7	11.9

Selected operating metrics					Average
SG&A/sales (%)	29.7	29.3	26.9	24.3	27.5
R&D/sales (%)	24.6	26.0	22.7	20.9	23.6
R&D growth (%)	5.3	5.0	-5.0	2.2	1.9
SG&A growth (%)	-4.2	-2.1	0.3	0.0	-1.5

Source: Company data, Barclays Research
Note: FY End Dec

Price (21-Oct-2015) USD 62.51
Price Target USD 55.00

Why Equal Weight? BMY retains one of the better revenue and EBIT recovery rates among peers in the post-expiry period of 2015-20. The oncology pipeline appears to be one of the most productive among industry peers. The company is undergoing the trough year of performance with upcoming expiries of Abilify and Sustiva, but the opportunity in oncology drives the valuation.

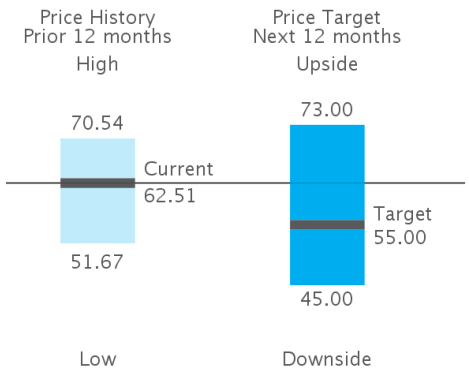
Upside case USD 73.00

Upside including successful development of the immunoncology portfolio including nivolumab and other checkpoint inhibitors. Combination data are expected to be better than single agent, and could potentially expand the indications.

Downside case USD 45.00

Downside case including in clinical risks in the development of anti-PD1, additional data might not meet the expectation, or drug combinations might not produce additional benefits to expand the market.

Upside/Downside scenarios



U.S. Major Pharmaceuticals — **Industry View: NEUTRAL**

Merck & Co. (MRK)

Stock Rating: EQUAL WEIGHT

Income statement ($mn)	2014A	2015E	2016E	2017E	CAGR
Revenue	42,210	39,867	42,298	44,719	1.9%
EBITDA (adj)	21,580	21,071	21,245	22,044	0.7%
EBIT (adj)	13,667	13,351	14,289	15,982	5.4%
Pre-tax income (adj)	13,772	13,054	13,934	15,764	4.6%
Net income (adj)	10,188	9,979	10,848	12,276	6.4%
EPS (adj) ($)	3.49	3.50	3.86	4.45	8.4%
Diluted shares (mn)	2,927.8	2,851.4	2,814.9	2,761.8	-1.9%
DPS ($)	1.77	1.81	1.84	1.88	2.1%

Margin and return data					Average
EBITDA (adj) margin (%)	51.1	52.9	50.2	49.3	50.9
EBIT (adj) margin (%)	32.4	33.5	33.8	35.7	33.8
Pre-tax (adj) margin (%)	32.6	32.7	32.9	35.3	33.4
Net (adj) margin (%)	24.1	25.0	25.6	27.5	25.6
ROIC (%)	-8.5	-8.5	-8.8	-9.7	-8.9
ROA (%)	10.2	10.2	10.9	12.3	10.9
ROE (%)	20.2	20.4	22.3	24.9	21.9

Balance sheet and cash flow ($mn)					CAGR
Tangible fixed assets	13,136	11,569	9,959	8,904	-12.2%
Intangible fixed assets	33,378	36,913	33,497	30,442	-3.0%
Cash and equivalents	29,234	30,106	32,202	35,577	6.8%
Total assets	98,335	102,914	101,624	101,182	1.0%
Short and long-term debt	14,783	15,480	15,480	15,480	1.5%
Other long-term liabilities	18,843	23,135	22,446	19,852	1.8%
Total liabilities	49,544	53,805	53,393	50,821	0.9%
Net debt/(funds)	5,684	6,969	4,184	-1,785	N/A
Shareholders' equity	48,791	49,108	48,231	50,361	1.1%
Change in working capital	1,824	2,397	1,344	269	-47.2%
Cash flow from operations	7,860	11,020	13,878	15,745	26.1%
Capital expenditure	-1,317	-1,548	-1,868	-1,976	N/A
Free cash flow	6,543	9,472	12,011	13,769	28.1%

Valuation and leverage metrics					Average
P/E (adj) (x)	14.5	14.5	13.1	11.4	13.4
EV/sales (x)	3.8	4.1	3.8	3.4	3.8
EV/EBITDA (adj) (x)	7.5	7.7	7.5	7.0	7.4
Equity FCF yield (%)	14.8	12.9	7.9	10.0	11.4
P/BV (x)	3.0	2.9	3.0	2.8	2.9
Dividend yield (%)	3.5	3.6	3.6	3.7	3.6
Total debt/capital (%)	32.8	32.6	29.1	27.0	30.4
Net debt/equity (%)	11.6	14.2	8.7	-3.5	7.7

Selected operating metrics					Average
SG&A/sales (%)	26.0	24.9	25.0	24.2	25.0
R&D/sales (%)	15.5	16.8	15.5	14.9	15.7
R&D growth (%)	-8.3	2.8	-2.4	1.6	-1.6
SG&A growth (%)	-5.9	-9.6	6.5	2.3	-1.7

Source: Company data, Barclays Research
Note: FY End Dec

Price (21-Oct-2015) USD 50.59
Price Target USD 64.00

Why Equal Weight? Though the LOEs are annualizing, we do see some weakness in MRK's key brands, especially the Januvia/Janumet franchise, that causes near to mid-term revenue pressure. However, we believe that MRK has an attractive pipeline (e.g. Odanacatib, Anacetrapib, BACE inhibitor) that supports long-term growth.

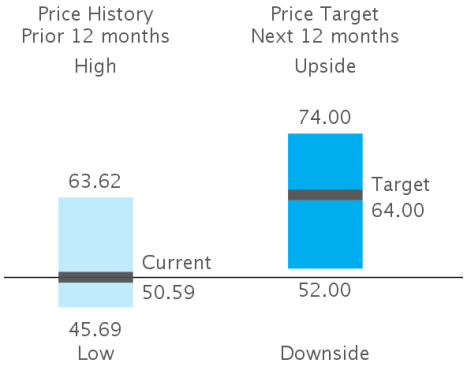
Upside case USD 74.00

Strong data from pipeline assets support higher-than-expected top-line growth from 2013E-17E, including anti-PD-1, BACE inhibitors, etc. De-risking of pipeline could provide upside and drive the stock.

Downside case USD 52.00

Continued weakness in core brands coupled with pipeline setbacks depress the revenue estimates in the long term. Further delays/failures of odanacatib and suvorexant may create additional pressure.

Upside/Downside scenarios



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AstraZeneca (AZN.L, 21-Oct-2015, GBP 39.47), Underweight/Neutral, C/D/J/K/L/M/N

Bristol-Myers Squibb (BMY, 21-Oct-2015, USD 62.51), Equal Weight/Neutral, A/C/D/J/K/L/M/N

Merck & Co. (MRK, 21-Oct-2015, USD 50.59), Equal Weight/Neutral, C/D/J/K/L/M/N/O

Merck KGaA (MRCG.DE, 21-Oct-2015, EUR 77.76), Equal Weight/Neutral, A/D/E/J/K/L/M/N

Pfizer Inc. (PFE, 21-Oct-2015, USD 33.46), Equal Weight/Neutral, C/D/J/K/L/M/O

Roche (ROG.VX, 21-Oct-2015, CHF 253.30), Overweight/Neutral, A/D/J/K/L/M/N

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Materially Mentioned Stocks (Ticker, Date, Price)

AbbVie Inc. (ABBV, 21-Oct-2015, USD 53.83), Overweight/Neutral, A/C/D/J/K/L/M/O

Eli Lilly & Co. (LLY, 21-Oct-2015, USD 77.01), Equal Weight/Neutral, A/C/D/J/K/L/M/O

Johnson & Johnson (JNJ, 21-Oct-2015, USD 97.63), Equal Weight/Neutral, C/J/K/M/N

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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)		
U.S. Major Pharmaceuticals		
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