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Bristol’s doomsday scenario: could Opdivo start shrinking next year?

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Fears about flattening Opdivo sales were surely a major driver for Bristol's move for Celgene. To keep growing the checkpoint inhibitor needs some big clinical wins.

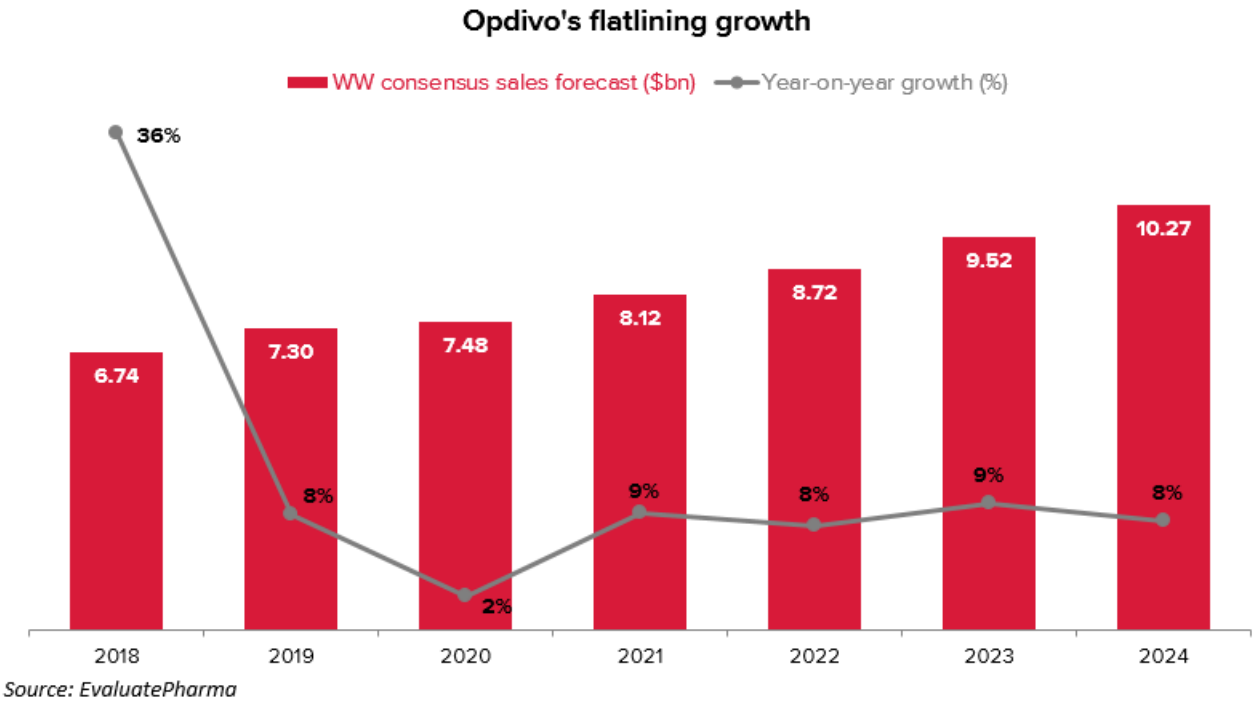
Whether sales of Bristol-Myers Squibb’s Opdivo will fall next year is a question that has been troubling investors and analysts alike for some months now, since well before the company announced a surprise move on Celgene. Consensus among the sellside is that the cancer blockbuster's revenues will inch higher in 2020, not quite going into reverse, then pick up again from 2021.

Some, however, expect a substantial decline next year, a pessimistic stance that is more commonly seen among investors. A more important consideration is what might happen to sales over the longer term, and many are questioning the extent to which demand for the checkpoint inhibitor can pick up again. Could 2019 be the year that Opdivo peaks?

The fast-changing world of immuno-oncology makes this hard to ascertain, and this doomsday scenario is by no means the consensus view, among the analyst community at least. But the consensus view seen in *EvaluatePharma*’s forecasts masks some starkly different opinions.

Morgan Stanley, for example, took a big axe to its numbers last November, and is pretty much alone in predicting a straight-out decline in Opdivo sales in 2020. The analysts do not expect the drug to return to 2019’s level until around 2023, an outlook that stands out as noticeably cautious.

It could be argued that Bristol’s internal projections for Opdivo must have looked similar to the Morgan Stanley numbers for the company's executives to pursue such a divisive acquisition as Celgene. Morgan Stanley is the lead adviser to Bristol on the bid, though the existence of Chinese walls between its equity research and investment banking units means that this can only be a coincidence.



It is Merck & Co's incontrovertible win in first-line lung cancer with Keytruda that will knock the wind from Opdivo's sales next year. To return its product to growth Bristol desperately needs some big clinical wins. Several important readouts are on the horizon, and those analysts pencilling in more weighty numbers – some see sales as high as $12bn in 2024 – must be assuming successes in some of the trials below.

Among the important trials are further readouts from Checkmate-227, in first-line lung cancer. Expectations are low, however, and even with a positive outcome it could be too late for Opdivo to compete seriously.

Meanwhile, a setting where Bristol still has the upper hand, kidney cancer, could soon see Opdivo dethroned by Keytruda and Inlyta, based on stunning results in the Keynote-426 trial. Thus all eyes are on the results of Bristol's Checkmate-9ER study.

The adjuvant setting is a wild card, a space where immuno-oncology has yet to prove itself and in which Bristol has invested heavily. The company is thought to be well positioned in areas like bladder and liver cancers. Combinations with novel mechanisms are also a potential growth area, although the company is also considered lacking here, and hopes are fading for its biggest bet, the Nektar cytokine NKTR-214.

Those forecasting strong future growth for Opdivo must also be assuming that Bristol manages to outmanoeuvre some very motivated competitors; missteps with clinical design have dramatically dented confidence in the company in this regard.

A tempting prospect?

Investors, meanwhile, have been fretting about Opdivo's outlook for some time: Bristol was the worst performing big pharma stock last year, losing 15% of its value, or $14bn. Missed opportunities with the checkpoint inhibitor were largely to blame.

Many fear that Opdivo's growth days are in the past. "I think most investors agree it's a matter of when not if Opdivo flatlines," one told *Vantage*. The possibility of Opdivo sales going into reverse for a year or two was likely one of the reasons why Bristol wanted to buy Celgene, Tim Anderson, an analyst at Wolfe Research, wrote in a note to clients this week.

Dismayed shareholders hoping that an even bigger predator could emerge with a bid for Bristol should bear this issue in mind. It is not inconceivable that sales of Opdivo will peak this year, and buying a product that needs a huge investment just to stay still is not a hugely tempting prospect.

Searching for Opdivo's future sales: trials to watch over the next couple of years				
Study (phase III unless stated)	**Active treatment**	**Setting**	**Timing**	**Trial ID**
Checkmate-227 part 1a	Opdivo + Yervoy	1st-line NSCLC	H1 2019	NCT02477826
Checkmate-227 part 2	Opdivo + chemo	1st-line NSCLC	Mid-2019	NCT02477826
Checkmate-714 (phase II)	Opdivo +/- Yervoy	1st-line SCCHN	H1 2019	NCT02823574
Checkmate-650 (phase II)	Opdivo + Yervoy	Metastatic castration-resistant prostate cancer	H1 2019	NCT02985957
Checkmate-498	Opdivo vs Temodar	1st-line glioblastoma	Mid-2019	NCT02617589
Checkmate-9LA	Opdivo + Yervoy +/- chemo	1st-line NSCLC	H2 2019	NCT03215706
Checkmate-9ER	Opdivo + Cabometyx vs Sutent	1st-line RCC	H2 2019	NCT03141177
Checkmate-459	Opdivo vs Nexavar	1st-line HCC	H2 2019	NCT02576509
Checkmate-816	Opvido + Yervoy or Opdivo + chemo	Neoadjuvant NSCLC	2020	NCT02998528
Checkmate-274	Opdivo	Adjuvant bladder or upper urinary tract cancer	2020	NCT02632409
CheckMate-901	Opdivo + Yervoy or Opdivo + chemo	1st-line inoperable or metastatic urothelial cancer	2020	NCT03036098
Checkmate-648	Opdivo + Yervoy or Opdivo + chemo	1st-line esophageal squamous cell carcinoma	2020	NCT03143153
Checkmate-577	Opdivo	Adjuvant oesophageal or gastroesophageal junction cancer	2020	NCT02743494
Checkmate-274	Opdivo	Adjuvant high-risk invasive bladder cancer	2020	NCT02632409

Note: NSCLC = non-small sell lung sancer; SCCHN = squamous cell carcinoma of the head and neck; RCC = renal cell carcinoma; HCC = hepatocellular carcinoma. Source: company announcements, analyst notes, clinicaltrials.gov.