



**GlobalData»**  
PharmaPoint

**MELANOMA –  
GLOBAL DRUG FORECAST AND MARKET ANALYSIS  
TO 2023**

## Executive Summary

Melanoma: Key Metrics in Eight Major Pharmaceutical Markets	
<b>2013 Epidemiology</b>	
Melanoma incident cases	69,992
<b>2013 Market Sales</b>	
US	\$864m
5EU	\$373m
Japan	\$0
Australia	\$131m
<b>Total</b>	<b>\$1.37bn</b>
<b>Pipeline Assessment</b>	
Number of drugs in Phase III	7
<b>Most Promising Pipeline Drugs</b>	<b>Peak-Year Sales</b>
Cobimetinib	\$233m
Binimetinib	\$123m
Talimogene laherparepvec	\$76m
Encorafenib	\$57m
<b>Key events (2013–2023)</b>	<b>Level of Impact</b>
Label expansion of Tafenlar and Mekinist as a combination in the metastatic setting in 2014	↑↑↑
Launch of Keytruda in the second-/third-line metastatic setting in 2014	↑↑↑
Launch of Opdivo in the BRAF wild-type first-line metastatic setting in Europe in 2015	↑↑↑
Label expansion of Tafenlar and Mekinist in the adjuvant setting in 2016	↑↑↑
Label expansion of Yervoy and Opdivo as a combination in the first-line metastatic setting in 2017	↑↑↑
<b>2023 Market Sales</b>	
US	\$3.21bn
5EU	\$2.01bn
Japan	\$63.5m
Australia	\$358m
<b>Total</b>	<b>\$5.64bn</b>
Source: GlobalData	
5EU = France, Germany, Italy, Spain, and UK	

Table above presents the key metrics for melanoma in the eight major pharmaceutical markets (8MM) (US, France, Germany, Italy, Spain, UK, Japan, and Australia) during the forecast period from 2013–2023.

### Robust Growth in the Melanoma Market Expected from 2013 Through 2023

GlobalData estimates that the value of the melanoma market in the US, 5EU (France, Germany, Italy, Spain, and the UK), Japan, and Australia in 2013 was \$1.34 billion. This market is defined as sales of the major branded drugs commonly prescribed for melanoma patients across the 8MM. 62% of these sales, \$836m, were generated in the US, with the 5EU representing the next largest region by sales with an estimated \$373m (28%). Australia contributed the smallest proportion (10%) of sales to the global melanoma market, with 2013 sales of \$131m. There were no branded sales for melanoma in Japan, as none of the major branded drugs were approved in the base year of this forecast.

By 2023, the end of the forecast period, GlobalData projects melanoma sales to rise to \$5.64 billion in the 8MM, at a robust Compound Annual Growth Rate (CAGR) of 15.5%. In particular, GlobalData expects the 5EU melanoma market to grow most rapidly, increasing to \$2.01 billion (a 36% share) by 2023, at a robust CAGR of 18.3%. Sales in the other regions are expected to increase by the end of the forecast period, however, the proportion of sales from the US and

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Australia are forecast to decrease to 57% and 6%, respectively, while market share in Japan will increase to 1% by 2023.

Major drivers of the growth of the melanoma market over the forecast period include:

- Melanoma incident cases are increasing in all the markets covered. Overall, across the 8MM, the incidence of melanoma is expected to increase by an Annual Growth Rate (AGR) of 3.0% from 2013–2023. GlobalData expects there to be nearly 87,900 cases in 2023, rising from just under 70,000 in 2013. This increase, coupled with an anticipated increase in branded therapy prescription, will drive growth of the global melanoma market over the forecast period.
- The launch of premium-priced metastatic therapies, such as anti-PD-1 immunotherapy and BRAF/MEK inhibitor combinations, will extend treatment duration and replace cheaper, generic, chemotherapy regimens. GlobalData expects Bristol-Myers Squibb's (BMS') Yervoy (ipilimumab) and Opdivo (nivolumab) to garner label extension as a combination treatment for first-line patients, increasing the uptake of both agents in the first-line setting. Overall, GlobalData expects these novel therapies to replace generic, chemotherapy-only regimens in the early lines of therapy and extend the number of lines of treatment available for patients, thus driving the overall growth of the melanoma market.

- GlobalData expects branded drugs for metastatic disease, including BMS' Yervoy and Novartis' (formerly GlaxoSmithKline's [GSK's]) Tafinlar/Mekinist (dabrafenib/trametinib) combination, to garner label expansion in the adjuvant setting for high-risk early-stage resected patients. These premium-priced agents will not only begin to replace interferon therapy, but are also expected to facilitate the gradual increase in the number of patients receiving branded therapy in this setting and thus increase the market size of this segment and the overall market.

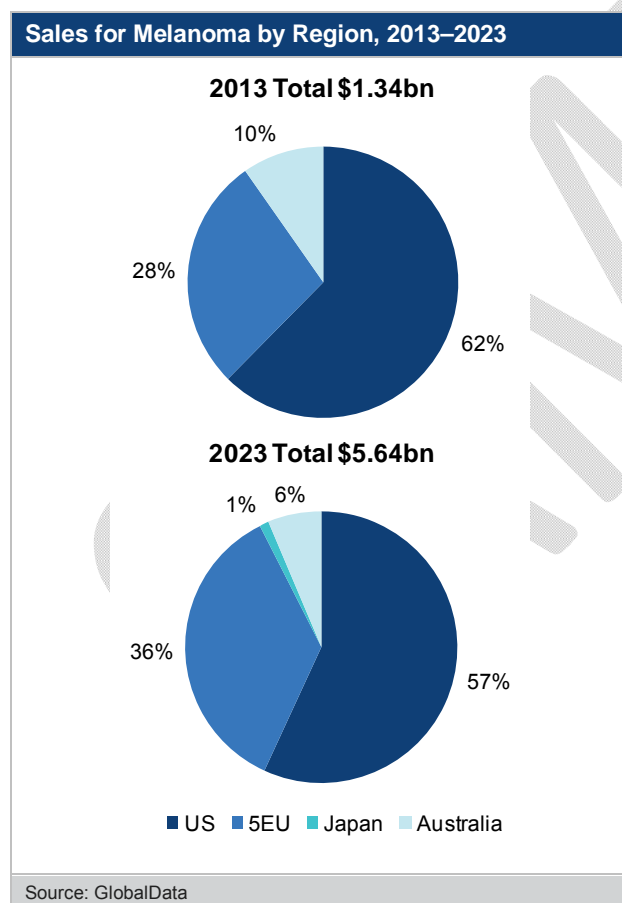
Major barriers of the growth of the melanoma market over the forecast period include:

- Increasing cost-consciousness will limit premium pricing opportunities for pipeline agents in the melanoma market. Healthcare austerity measures are being incorporated across the major markets, and drug companies will need to consider the changing reimbursement landscape when determining pricing strategies for their drugs. GlobalData expects that this era of austerity and healthcare reform will negatively affect pharmaceutical companies' ability to gain reimbursement approval for their new melanoma therapies.
- With the many recent drug launches, GlobalData expects the melanoma market to become increasingly crowded during the forecast period. GlobalData estimates that the

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checkpoint immunotherapy and BRAF/MEK drug classes will represent more than 97% of the global melanoma market by 2023. GlobalData expects the barrier to entry for this market to become increasingly difficult for developers of future pipeline agents, resulting in the targeting of smaller, niche populations and fewer approvals towards the end of the forecast period.

Figure below illustrates the global sales for melanoma by region during the forecast period.



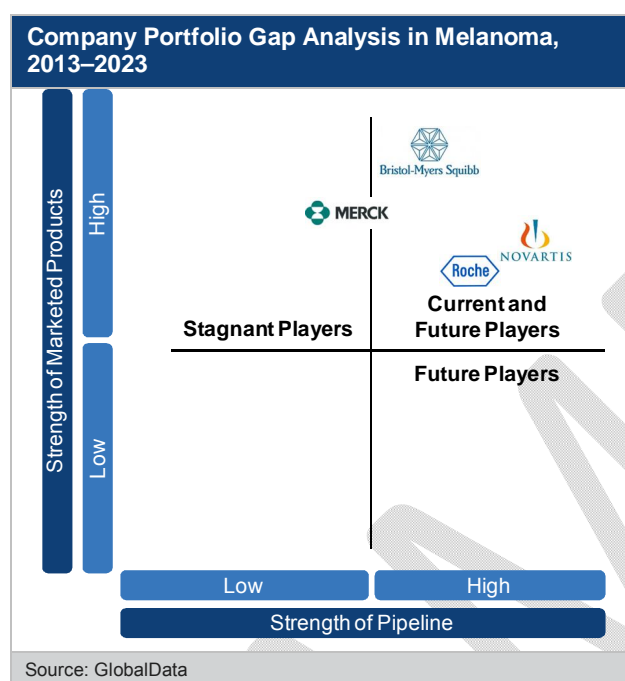
### Despite Strong Competition, Bristol-Myers Squibb to Remain the Leader of the Checkpoint Immunotherapy and Overall Melanoma Market

The 2011 launch of Yervoy propelled BMS onto the melanoma market and positioned the company as the premier immuno-oncology player. Yervoy has rapidly become the best-selling brand in melanoma, approaching blockbuster status in 2013, with growth fuelled by recent label extension in the first-line setting in Europe. With the launch of its second melanoma asset, the anti-PD-1 antibody, Opdivo (nivolumab), GlobalData expects BMS to further strengthen its position in the checkpoint immunotherapy and melanoma market. However, competition in this drug class is becoming intense as Merck's Keytruda (pembrolizumab), which was approved in the US in 2014, is also expected to obtain first-line approval and garner uptake across the major markets. To circumvent this threat, BMS is actively developing its trump card, the combination of Yervoy and Opdivo, which has demonstrated promise in terms of increasing response rates and OS. GlobalData expects this combination to launch in 2017 and to wrest away significant patient share from anti-PD-1 monotherapy treatment in the first line, including Keytruda. In particular, GlobalData expects the approval of the Yervoy/Opdivo combination to drive robust growth of Yervoy's sales, retaining Yervoy's position as the market leader. Overall, GlobalData expects the checkpoint immunotherapy drug class to dominate the melanoma market, both BRAF

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wild-type and mutation-positive, with an overall 67% share of the melanoma market in 2023.

Figure below presents the gap analysis for the forecast period of major companies in the melanoma space.



### High Unmet Needs Remains for Efficacious Treatment Options for BRAF Wild-Type Patients

As they are ineligible for treatment with BRAF/MEK inhibitors, BRAF wild-type advanced melanoma patients have fewer treatment options compared to BRAF mutation-positive patients. Mainstay of treatment is immune checkpoint inhibitors, however, despite the potential durable response offered by CTLA-4 and PD-1 immunotherapies, the

majority of patients do not respond to these agents. Non-responders to immunotherapy have no further treatment options except largely ineffective chemotherapy or biochemotherapy regimens. Although there have been clinical studies to investigate the use of targeted agents for NRAS- or c-KIT-mutated patients, the results have not greatly enthused interviewed Key Opinion Leaders (KOLs). GlobalData does not expect any pipeline agent to substantially improve upon the current treatment options for BRAF wild-type patients, thus the unmet need for this segment is expected to remain high throughout the forecast period.

### High Commercial Opportunity for Adjuvant Treatments that Improve Cure Rates in Early-Stage, Resectable Melanoma Patients

GlobalData's KOLs report disappointment with the efficacy of current adjuvant interferon treatments for high-risk stage II and III melanoma patients. GlobalData primary research confirms that a large proportion of these patients receive surgery alone with no drug treatment, or enter clinical trials. Interviewed KOLs report that despite the availability of interferon adjuvant therapy, a significant proportion of these patients will ultimately recur or progress to metastatic disease. Because of this unmet need and the large patient pool, the melanoma adjuvant setting represents a lucrative setting for drug developers. BMS (Yervoy), Novartis (Tafinlar/Mekinist), and Roche (Zelboraf) are aiming to expand their metastatic



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melanoma therapeutics into the adjuvant setting, and these label expansions are expected to be won in the second half of the forecast period. However, interviewed experts remain unconvinced by these drugs, particularly when considering their efficacy in light of the potential safety concerns with these agents. Overall, GlobalData expects there to remain high commercial reward for developers of efficacious and well-tolerated drugs that can improve the cure rate and cater to this large population of patients.

### **Innovative Immune Checkpoint Inhibitor Combinations Required to Penetrate the Crowded Melanoma Market**

As the melanoma markets becomes increasingly saturated with the development of anti-PD-1 immunotherapies across the various lines of treatment, GlobalData expects developers of this drug class to focus on PD-1's combination with other targeted agents to improve response rate and treatment outcome, and to differentiate their asset from competitors. Interviewed KOLs are enthusiastic about the potential efficacy of the dual checkpoint inhibitor combination, Yervoy and Opdivo, however, the increased toxicity associated with the combination remains a concern. GlobalData expects the development of safe and effective drug combinations involving anti-PD-1 immunotherapy to become a significant R&D strategy for developers looking to compete with BMS during and beyond the forecast period. For example, Merck is collaborating with GSK (now

Novartis) to investigate the combination of its anti-PD-1 Keytruda with the BRAF/MEK inhibitor combination Tafinlar/Mekinist, and with Amgen to test the combination of Keytruda and talimogene laherparepvec (T-VEC). In addition, Merck is also running clinical trials to combine Keytruda with its own Sylatron or BMS' Yervoy. Roche is also looking to enter the immune checkpoint melanoma market and is investigating its anti-PD-L1 asset, atezolizumab (MPDL3280A), in combination with Zelboraf and cobimetinib in an early-stage clinical study in melanoma. As anti-PD-1 immunotherapies hold the promise of long, durable response for metastatic patients, a safe combination that can improve response rate will have the potential to attract patient share even in an increasingly crowded melanoma market.

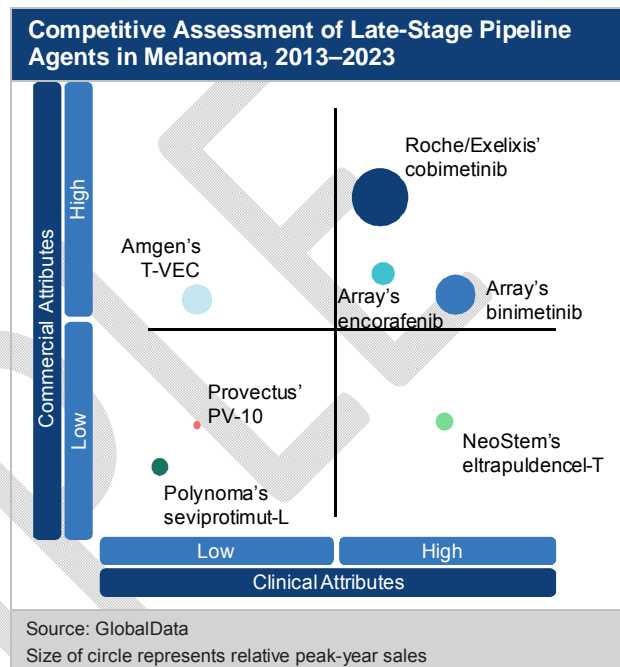
### **Late-Stage Pipeline Agents to Have Limited Impact on the Future Melanoma Landscape**

GlobalData expects the approval of seven pipeline agents over the forecast period, however, none of these are expected to have a major impact on the overall melanoma market. Of these pipeline agents, Exelixis' MEK inhibitor cobimetinib represents the sales leader with peak-year sales of \$233m in 2023. Cobimetinib will garner uptake in combination with Roche's Zelboraf, with this regimen expected to be the first-to-market BRAF/MEK inhibitor combination in Europe. However, without perceived efficacy advantage over Novartis' Tafinlar/Mekinist, GlobalData does not expect this combination to have great impact

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on the US and Australian markets, where Novartis' combination has already been marketed from early 2014. The second highest-selling pipeline agent, Array's binimetinib is a MEK inhibitor that produces clinical responses in NRAS-mutated advanced melanoma patients, who currently have no mutation-specific targeted treatment. However, KOLs are not enthusiastic about its efficacy in this setting, and GlobalData, therefore, expects limited uptake of binimetinib despite its first-to-market status. Overall, the sales of binimetinib are estimated to peak at \$123m in 2023, with \$45m coming from sales in the NRAS setting and \$78m from combination with Array's (formerly Novartis') BRAF inhibitor encorafenib. Other pipeline agents include Amgen's T-VEC, NeoStem's eltrapuldencel-T, encorafenib, Polynoma's seviprotimut-L, and Provectus' PV-10; however, GlobalData forecasts these to have little impact on the overall melanoma market.

Figure below provides a competitive assessment of the most promising agents for melanoma during the forecast period.



### What Do the Physicians Think?

KOLs expect anti-PD-1 immunotherapies to garner approval for first-line use and to soon become the standard of care for advanced melanoma.

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*“PD-1 was surprisingly approved for pembrolizumab in US early, and nivolumab was approved in Japan already, so my expectation is that both drugs will be on the market next year in Europe... At the moment, I would see them clearly in the first-line treatment, although pembrolizumab has been approved for the second line after ipilimumab failure in the US, but I don’t see that an issue. I would say they are both well working in the first line.”*

OUS Key Opinion Leader, September 2014

*“It’s likely that early next year, we’ll actually see PD-1 antibodies approved as a first-line therapy, at least in BRAF wild-type patients.”*

US Key Opinion Leader, December 2014

*“My rough guess is about [a] 70% chance the patient will get, probably start with PD-1 in the future, when PD-1 becomes a first-line agent... regardless of BRAF status.”*

US Key Opinion Leader, August 2014

*“I think PD-1 is definitely going to be the main treatment... whether it’s PD-1 alone or PD-1 plus the combinations.”*

OUS Key Opinion Leader, November 2014

Interviewed experts reported that high unmet need remains for BRAF wild-type melanoma patients.

*“I have not seen any new approach for BRAF wild-type patients.”*

OUS Key Opinion Leader, September 2014

*“[The clinical unmet needs are] something with a decent response rate in the BRAF wild-type patients... We haven’t got access to PD-1 yet. It may be going to be good enough, but that’s the group of patients, with ipilimumab, there isn’t a great response rate.”*

OUS Key Opinion Leader, December 2014

*“What is getting sort of lost is that the response rate of these PD-1 agents is still in the range of 30% to 40% in highly screened and highly selected patients that go on to clinical trials.”*

US Key Opinion Leader, December 2014

Interviewed KOLs call for novel adjuvant therapies to reduce the risk of relapse for resected melanoma and treatment-related toxicities, and enthuse about the potential to develop anti-PD-1 immunotherapy in the adjuvant setting.

*“Oncologists have lost the confidence in [the] efficacy of these drugs [interferons]... Also, the oncologists are struggling because we are very concerned about the toxicity of interferons.”*

OUS Key Opinion Leader, November 2014



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*"I would think that adjuvant therapy is going to be anti-PD-1 in the future. And there are two trials that will likely happen; one is the intergroup trial of pembrolizumab vs. interferon which will, I think, inform us of the role of pembrolizumab but that will be six years [from now] before it's done."*

US Key Opinion Leader, November 2014

*"At the moment, we certainly would be happy to actively participate in clinical trials [for adjuvant therapies], and potentially going to do so with anti-PD-1, because I think immunotherapy in the adjuvant setting may well be beneficial... Certainly with the clinical data in the metastatic setting, you would hope the PD-1 in the adjuvant setting will be as effective [as] or better than the ipilimumab."*

OUS Key Opinion Leader, December 2014

Experts are excited about the potential of combination therapies involving immune checkpoint inhibitors, such as Yervoy plus Opdivo.

*"I'm a believer in combination of treatment, so I believe PD-1 antibodies plus targeted therapies might be an issue, and also PD-1 plus ipilimumab is a big issue."*

OUS Key Opinion Leader, September 2014

*"My guess is that the combo [of ipilimumab and nivolumab] will be more effective, and at least in the big teaching hospitals or the big oncology centers, the combo will probably be the treatment of choice."*

OUS Key Opinion Leader, November 2014

*"We certainly, I think, are ending the era of the single agent treatments and are moving into the era where it's all going to be combinations."*

US Key Opinion Leader, December 2014

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## Introduction

## 2 Introduction

### 2.1 Catalyst

Melanoma is the deadliest and most aggressive form of skin cancer. Melanoma is rare compared to other major cancer indications, but the incident cases are increasing because of the aging population and changes in lifestyle that result in more ultraviolet (UV) exposure. Although only 3–7% of patients in the major markets (US, France, Germany, Italy, Spain, UK, and Australia; excludes Japan) are diagnosed with unresectable stage III or stage IV metastatic disease, which has poor prognoses, a significant proportion of resectable stage III diseases (47–57%) progresses to metastatic melanoma. In 2011 the first two targeted therapies were approved, Yervoy (ipilimumab) and Zelboraf (vemurafenib); they have revolutionized the treatment landscape of melanoma, which previously was heavily dependent on generic chemotherapy. Though these new treatments have extended the survival of metastatic patients compared to chemotherapy-only regimens, high unmet needs remain for the non-responders to these targeted treatments, especially BRAF wild-type patients.

The melanoma market is expected to grow robustly due to the uptake of novel treatments approved in 2014, including Novartis' (formerly GlaxoSmithKline's [GSK's]) Tafinlar/Mekinist (dabrafenib/trametinib) combination, Bristol-Myers Squibb's (BMS') Opdivo (nivolumab), and Merck's Keytruda (pembrolizumab). These agents will be utilized in early lines of metastatic therapy, and will push the use of chemotherapy to later lines of treatment. Furthermore, GlobalData expects the label expansion of Yervoy and Opdivo as a combination treatment for the first-line metastatic setting. This premium-priced combination is expected to be the main driver for the melanoma market in the second half of the forecast period. Ultimately, however, GlobalData expects unmet needs to remain, particularly for early-stage patients, and anticipates that novel, innovative approaches, such as safer immune checkpoint inhibitor combinations, will provide the best opportunity for substantial improvement in the prognosis of advanced melanoma patients.

## Introduction

### 2.2 Related Reports

- GlobalData (2015). HER2-Negative Breast Cancer – Global Drug Forecast and Market Analysis to 2023, January 2015, GDHC92PIDR
- GlobalData (2014). Colorectal Cancer – Global Drug Forecast and Market Analysis to 2023, November 2014, GDHC95PIDR
- GlobalData (2014). HER2-Positive Breast Cancer – Global Drug Forecast and Market Analysis to 2023, September 2014, GDHC86PIDR
- GlobalData (2014). Non-Hodgkin's B-Cell Lymphoma – Opportunity Analysis and Forecast to 2018, August 2014, GDHC035POA
- GlobalData (2014). Chronic Lymphocytic Leukemia (CLL) – Opportunity Analysis and Forecasts to 2018, June 2014, GDHC017POA
- GlobalData (2014). Non-Small Cell Lung Cancer (NSCLC) – Global Drug Forecast and Market Analysis to 2022 – Event-Driven Update, April 2014, GDHC002EPIDR
- GlobalData (2014). Pancreatic Cancer – Opportunity Analysis and Forecasts to 2017, March 2014, GDHC016POA

### 2.3 Upcoming Related Reports

- GlobalData (2015). Multiple Myeloma – Global Drug Forecast and Market Analysis to 2023
- GlobalData (2015). Renal Cell Carcinoma – Global Drug Forecast and Market Analysis to 2023
- GlobalData (2015). Prostate Cancer – Global Drug Forecast and Market Analysis to 2023



## Appendix

### 11.8 About GlobalData

GlobalData is a leading global provider of business intelligence in the Healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

GlobalData has offices in New York, Boston, London, India and Singapore.

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