EDISON

The post-ASCO IO pecking order

What it means for smaller biotech companies

Thematic notes

27 June 2018

Immunotherapy has become one of the most relevant areas at the American Society of Clinical Oncology (ASCO) Annual Meeting and the leaders have emerged. Immunotherapies for cancer include a number of technologies such as immune checkpoint inhibitors (ICIs), T-cell-based therapies, oncolytic viruses or cancer vaccines. Several ICIs have been approved across the world for a number of cancer types. Still, a significant number of patients do not benefit from ICI therapies, so combinations with other agents have become increasingly popular. In 2017, 469 clinical trials with such combinations were initiated. This year clinical data in lung cancer were of special relevance, setting a new standard of care in first-line advanced squamous lung cancer and exposing the gaps in improved combinations.

Harness the immune system to fight disease

The field of immunotherapy for cancer has experienced significant growth over the last few years. ICIs target molecules that inhibit the immune system, releasing the brakes on the immune system to fight cancer. In particular, antibodies targeting CTLA-4 and PD-1/L1 from Merck, Bristol-Myers Squibb and Roche have been approved and are on the market. However, some patients do not respond to current immunotherapies and subgroups (according to biomarkers) and combinations are being investigated extensively to find the best therapeutic options for patients. Additionally, chimeric antigen receptor T-cell (CAR-T) therapies from Novartis and Gilead gained regulatory approval in 2017, and are now commercialised for acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL).

Themes that generate the most attention

There are hundreds of clinical trials with combinations that use an ICI as a backbone. As Incyte and Nektar Therapeutics have shown, not all combinations will succeed. We see two means of playing the space:

- **Large-cap companies.** This year's ASCO showed that Merck, Bristol-Myers Squibb (BMS) and Roche are consolidating as the main players in lung cancer and more broadly, in the immunoncology space.
- **Smaller players** with unique approaches such as oncolytic viruses, cell immunotherapies and cancer vaccines, albeit at a higher risk. For instance, Transgene's Pexa-Vec (oncolytic virus) and TG4010 (vaccine), Immunicum's cell therapy ilixadencel or Targovax's oncolytic virus ONCOS.

The companies shown above do not translate into buys and sells as other themes may conflict with this one.

From the street

Immunotherapy is perhaps the most exciting innovation opportunity in healthcare. In particular, immunoncology has gone from being relatively unknown just a few years ago to being a major area of research. It attempts to use the body's immune system to fight cancer, by either turning on mechanisms to fight tumour cells, or turning off the mechanism in tumour cells that impedes a natural immune system response. Citigroup analysts predict that immunoncology drugs could be generating $35bn in annual sales over the medium term and will constitute 60% of cancer treatments by 2023 (from 3% today). This would make immunotherapy the biggest market in medicine and transform the face of cancer treatment as we know it (source: Fidelity International).

Edison investment themes

As one of the largest issuer sponsored research firms, we're known for our bottom-up work on individual stocks. However, our thinking does not stop at the company level. Through our regular dialogue with management teams and investors we consider the broad themes in which the companies we follow operate. Edison investment Themes looks to identify the big issues likely to shape company strategy and portfolios in the years ahead.

Analyst

Juan Pedro Serrate +44 (0)20 3681 2534

healthcare@edisongroup.com

Differentiation key for a slice of the first-line NSCLC market

Merck's Keytruda, best in patients expressing high PD-L1

Merck continues its lead in first-line immunotherapy in non-small cell lung cancer (NSCLC). The company presented data from the Phase III **Keynote-042** trial with Keytruda (an approved PD-1 inhibitor) in monotherapy vs chemotherapy alone in patients with different levels of PD-L1 expression: (1) PD-L1 ≥ 1%; (2) PD-L1 ≥ 20%; and (3) PD-L1 ≥ 50% in advanced, squamous or non-squamous NSCLC. As expected, the best results were seen in the high PD-L1 group. The results are shown on Exhibit 1.

Exhibit 1: Summary of Keynote-042 data

Endpoint	PD-L1 ≥ 50%		PD-L1 ≥ 20%;		PD-L1 ≥ 1%		PD-L1 ≥ 1-49%	
	Keytruda	Chemo	Keytruda	Chemo	Keytruda	Chemo	Keytruda	Chemo
Median OS (months)	20	12.2	17.7	13	16.7	12.1	13.4	12.1
HR and p value	0.69 (0.0003)		0.77 (0.002)		0.81 (0.0018)		0.92 (not shown)	
ORR	39.5%	32%	33.4%	28.9%	27.3%	26.5%	16.6%	21.7%

Source: Edison Investment Research, Merck & Co. Note: Median OS = overall survival; HR = hazard ratio and ORR = objective response rate.

The median duration of response (DOR) for patients in the Keytruda arm was more than double that of the chemotherapy arm: 20.2 months vs 8.3 months respectively. Grade 3-5 treatment-related adverse events occurred in 17.8% of patients in the Keytruda group and in 41% in the chemotherapy group.

The best data were shown in the high PD-L1 ≥50% patients (median overall survival [mOS] of 20 months in Keytruda arm vs 12.2 months in chemo arm); survival and response rate data in expressers between 1% and 49% were similar. We therefore view it as unlikely that Keytruda will be used as monotherapy, unless potentially in the ≥50% expressers.

EvaluatePharma's consensus forecast for Keytruda is $12.1bn sales in 2022.

For Roche and BMS the potential lies in subsets

Roche presented data from the **IMpower150** trial testing Tecentriq (atezolizumab, approved PD-L1 inhibitor) plus Avastin (bevacizumab, approved anti-VEGF) and chemotherapy (called the ABCP group) vs Avastin and chemotherapy (BCP group) in first-line **non-squamous NSCLC**. Median OS was 19.2 months in the ABCP group vs 14.7 months in the BCP group (p=0.02, HR 0.78). Progression-free survival (PFS) was 8.3 months in the ABCP group vs 6.8 months in the BCP group (p<0.001, HR 0.62). Grade 3-5 treatment-related adverse events were 59% in the ABCP arm vs 50% in the BCP arm. Roche showed data in the subgroup of EGFR/ALK+ patients (survival not reached in ABCP group vs 17.5 months in the BCP group, HR=0.54). Following these data, we believe that Roche's combination could be an alternative in patients that have failed EGFR/ALK inhibitors.

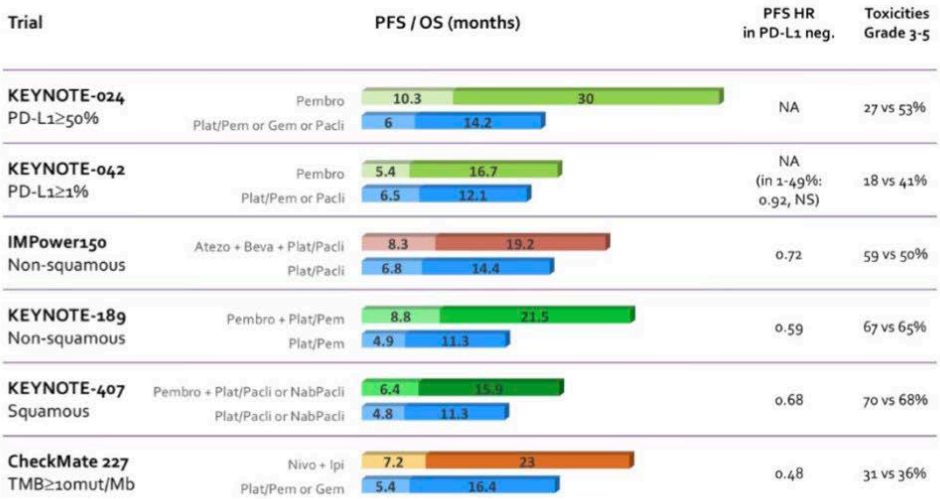
Roche data from the **IMpower-131** study testing Tecentriq plus chemo vs chemo in **squamous NSCLC** were underwhelming. It met the co-primary endpoint of PFS (6.3 months atezo + chemo vs 5.6 months chemo, HR=0.71), but has so far missed on OS. This compares with Merck's **Keynote-407** trial in the same setting, which met both co-primary endpoints of PFS and OS. Median OS was 15.9 months in the Keytruda + chemo arm vs 11.3 months in chemo arm, HR=0.64. Following these data, Keytruda plus chemotherapy is now the new standard of care in first-line metastatic squamous NSCLC. EvaluatePharma projects $6.86bn Keytruda sales in NSCLC in 2022.

EvaluatePharma's consensus forecast is global sales of $4.5bn for Tecentriq in 2022 across all indications.

BMS's **Checkmate-227** trial had three arms comparing (1) Opdivo (nivolumab) plus Yervoy (ipilimumab) vs (2) Opdivo plus chemotherapy vs (3) chemotherapy alone in patients with PD-L1 ≤1% expression and high (≥10mut/Mb) or low (<10mut/Mb) tumour mutational burden (TMB) expression. TMB is a biomarker that BMS has developed according to its own standards and claims can be used to better select subgroups of patients. In this trial the best data came from the combination of nivolumab and ipilimumab: PFS was 7.7 months in this arm vs 6.2 months of nivo plus chemo and 5.3 months of chemo alone. Despite this, we believe the combination of Keytruda plus chemo will be favoured in this setting, from both clinical (better efficacy and fewer side effects) and commercial perspectives (potential lower costs).

EvaluatePharma's consensus forecast is global sales of $8.5bn for Opdivo in 2022 across all indications.

Exhibit 2: PFS/OS data across trials



Source: Solange Peters via twitter. Note: This is for illustration purposes only and comparing different trials is challenging as populations, indications and other characteristics vary.

More options in SCLC

Lung cancer is divided into two main groups: NSCLC and SCLC. SCLC cells are not only smaller, but also tend to grow quicker, respond faster to treatment and relapse quickly, becoming more aggressive and resistant to treatments. SCLC is about 15% of all lung cancers. There were 1.8 million cases of lung cancer in the world in 2012 (source: Globocan). We present the main findings from Merck's Phase II basket study **Keynote-158** with Keytruda as monotherapy in PD-L1 positive (≥1%) and PD-L1 negative patients (<1%), AbbVie's **Trinity** study with Rova-T according to delta-like protein 3 (DLL3) expression and PharmaMar's **Phase II** with lurbinectedin as monotherapy.

Exhibit 3: Data summary

	Merck – Keynote-158		AbbVie – Trinity		PharmaMar – Phase II basket	
Endpoint	PD-L1+ (n=42)	PD-L1- (n=50)	DLL3 high (3L)	All dosed (3L)	CTFI<90d (n=27)	**CTFI≥90d** (n=34)
ORR (%)	35.7	6.0	19.7 (INV)	18.0 (INV)	33.3	44.1
mPFS (months)	2.1	1.9	3.9	N/A	3.4	4.2
mOS (months)	14.9	5.9	5.6	N/A	8.1	15.8
AEs: Any/Gr 3-4	60%/12% (n=107)		91%/40% (n=339; Gr 3+, drug related)		39% Gr 3-4 neutropenia; 9% febrile neutropenia.	

Source: Merck & Co, AbbVie, PharmaMar, Edison Investment Research.

PharmaMar's data were divided according to the chemotherapy-free interval (CTFI), which is the time elapsed since completing a platinum-based therapy. In general, the longer the CTFI, the more likely patients are to respond to retreatment. In PharmaMar's Phase II, patients with 90 days or more chemo-free had a median OS of 15.8 months, which we view as very encouraging. The company is running the ATLANTIS Phase III trial in SCLC comparing lurbinectedin (transcription inhibitor) plus chemo vs chemo alone. Recruitment will complete in Q218 and final data are expected in H219. Our previous coverage on PharmaMar can be found here.

We view Merk's data in PD-L1+ patients as positive, with median OS over other immunotherapies (eg nivolumab and nivolumab plus ipilimumab combination) in this setting. AbbVie's data are interesting, given that patients were in the third or fourth line of treatment where there are no other options, and are in line with other targeted agents for relapsed SCLC, eg sorafenib or sunitinib. We advise caution in making cross-trial comparisons, as patient population, selection criteria or previous therapies, among other factors, usually differ.

T-cell immunotherapies remain a hot area

Bluebird's CAR-T continues to impress in multiple myeloma

Last year one of the main highlights at ASCO was chimeric antigen receptor (CAR) T-cell therapies. This year the main dataset came from bluebird bio's bb2121, partnered with Celgene. The CAR-T targeting the B-cell maturation antigen (BCMA) showed an increase of one-year PFS in multiple myeloma patients who had received more than three previous lines of therapy. There was a positive dose response: ORR was 80.6% in patients who received a dose of at least 150m cells (43% CR), 95.5% for patients receiving more than 150m cells (50% CR) and 100% in the 450m cell level (37.5% CR) in low BCMA expressers. On the safety front, there were 63% cases of cytokine release syndrome (CRS) in 43 evaluable patients. Furthermore, there were four additional deaths in addition to two previous ones, driving the total number to six. Safety is important to move the product to earlier-stage patients, as the company intends. We see these data as positive as bb2121 provides validation for a new target (BCMA) in a new indication, multiple myeloma (MM), away from leukaemia and lymphoma, for which anti-CD19 CARTs from Novartis and Gilead are approved. Bluebird continues recruitment in Phase II KarMMa, in heavily pre-treated MM patients (94 expected) with the aim of filing in 2019.

T-cell receptor therapies: Adaptimmune and Immunocore

Adaptimmune presented data from three pilot studies. The first data were an oral presentation of the pilot study of NY-ESO-SPEAR T-cells in advanced myxoid/round cell liposarcoma (MRCLS). With eight patients treated, the best overall responses include three confirmed PRs, one unconfirmed PR and three SD. There were four serious AEs reported by three patients: one Grade 3 CRS, two Grade 2 CRS (resolved) and one Grade 2 pleural effusion. Secondly, two pilot studies tested NY-ESO-SPEAR, which targets MAGE-A10, in NSCLC and the triple tumour study in bladder, melanoma, and head & neck cancers. In these initial data there were no responses. One

patient received 90m cells and seven patients received 100m cells in both cohorts. There were no signs of anti-tumour effect, which we view as disappointing. In terms of safety, there were two complete responses (CRs) (one Grade 1, one Grade 4 in the NSCLC cohort, both resolved). Further data will be presented later this year.

Immunocore presented a poster on a Phase I trial in patients with metastatic uveal melanoma (mUM) treated with IMCgp100. In 17 evaluable patients, ORR was 18% (all PRs) and a one-year OS rate was 74% at the time of data cut-off. Patients who responded showed a duration of response of 19.1 months and median OS has not yet been reached. All 19 patients evaluable for safety had treatment-related adverse events, with 15 of them (73%) experiencing Grade 3 or higher. There were no deaths.

T-cell receptor-based immunotherapies are showing some early signs of activity, although patients still have serious side effects. We look forward to these therapies moving towards advanced stages. We elaborate more on this exciting field in our report on T-cell cancer therapies.

Targeted therapies: Comeback confirmed

The comeback of targeted therapies seems to have been confirmed by results from Loxo Oncology and Deciphera. Loxo presented data with its RET-targeted kinase inhibitor, LOXO-292. Response rates in both NSCLC and medullary thyroid cancer (MTC) were 77% and 45% respectively, improving from 65% and 14% previously. Loxo has seen no relapses among patients who have responded to treatment. We view these data as encouraging.

Deciphera presented updated data from its ongoing Phase I clinical trial with DCC-2618, a broad-spectrum KIT and PDGFR-α inhibitor, in patients with gastrointestinal stromal tumours (GIST). Across all treatment lines, in 145 patients, DCC-2618 generated a 15% ORR and 70% disease control rate (DCR) at three months. The company intends to start the Phase III trial, INTRIGUE, in second-line GIST later this year. The ORR in second-line GIST was 24% in the Phase I study, which compares favourably to 7% of sunitinib, with the obvious limitations of cross-trial comparison. Please see poster for more details.

Data from companies under coverage

Oncology Venture: Phase I data from 2X-121

The main data came from a Phase I study of its dual PARP-1/2 and TNKS-1/2 inhibitor, 2X-121, as a single agent in patients with advanced solid tumours (link to abstract). Two patients achieved partial response (PR) and 13 patients had stable disease (SD), which was maintained for over 24 weeks. Survival was measured according to the company's proprietary method of identifying drug responders and non-responders. Median overall survival was greater than 800 days for the predicted sensitive/responder group and 208 days for the non-responder group, respectively (HR=0.26, p=0.07). The company plans to start a Phase II trial this year.

In addition to this, Oncology Venture published an electronic abstract on its ongoing single-arm, open-label focused Phase II study investigating LiPlaCis in heavily pre-treated mBC patients and another electronic abstract on the characterisation of resistance to APO010 in human myeloma cell lines. The company plans to initiate a Phase II trial with LiPlaCis this year, with top-line data in H119.

For a detailed analysis of the data, read our update report here.

Chi-Med: Fruquintinib benefit irrespective of previous VEGF/EGFR therapy

Hutchison China MediTech (Chi-Med) presented a subgroup analysis of patients according to prior anti-VEGF and anti-EGFR therapy in the Phase III FRESCO trial. The study tested fruquintinib (oral VEGFR 1, 2, and 3 inhibitor) in 416 Chinese patients with advanced metastatic colorectal cancer (mCRC). Data were previously presented at ASCO 2017 where in the total treatment population it demonstrated a statistically significant improvement in overall survival. This follow-up analysis demonstrated that previous treatment with targeted therapy (anti-VEGF and anti-EGFR therapy or both) had no clinically meaningful effect on the magnitude of the response when compared to those who had not previously received targeted therapy (link to poster). This validates the applicability of fruquintinib across a range of patient populations. An application for fruquintinib in mCRC is currently under review by the Chinese National Drug Administration (CDNA). We expect approval and launch in China in H218.

The company also presented a poster on Quality-adjusted time without symptoms or toxicity (Q-TWiST) in the FRESCO trial. Data demonstrated that patients treated with fruquintinib had an improvement in Q-TWiST compared with patients treated with placebo (link to poster). This manifested as patients having a longer duration before progression and without adverse events than those on placebo.

Our coverage on Chi-Med can be found here.

Transgene: First data of Pexa-Vec in the neo-adjuvant setting

Pexa-Vec was administered in a single intravenous (iv) infusion to nine patients (three with metastatic melanoma and six with liver metastasis from CRC) prior to surgery. Pexa-Vec produced one complete pathological response (no signs of viable tumour cells in the tissues that previously had tumours) and one partial pathological response among four evaluable patients with CRC metastasis in the liver (poster). Furthermore, Pexa-Vec triggered the activation of immune cells, increasing the expression of PD-L1, and the induction of a cytokine and chemokine profile associated with an inflammatory response. These data show the presence and activity of the virus in the tumour after iv injection and the trigger of an innate and adaptive immune response specific to the tumour. Transgene states that this increase of PD-L1 expression provides mechanistic rationale for combination with PD-1 inhibitors.

In the second half of 2018 Transgene plans to present data from its five products:

- Pexa-Vec + nivolumab in first-line HCC.
- Pexa-Vec + cyclophosphamide in advanced breast cancer.
- TG4010 + nivolumab in second-line NSCLC.
- TG4010 + nivolumab + chemotherapy in first-line NSCLC.
- TG4001 + avelumab in HPV+ head and neck cancer.
- TG1050 in chronic hepatitis B.
- TG6002 in glioblastoma.

Our coverage on Transgene can be found here.

ASLAN: Additional varlitinib data presented

ASLAN presented two posters at ASCO's annual conference. Firstly, the company presented data from an ongoing Phase Ib clinical trial that tests varlitinib with and without Herceptin (trastuzumab, Roche) in combination with carboplatin and paclitaxel. Patients were enrolled across a range of cancers and had a median of three prior therapies; the majority (20/37) were HER2+ metastatic

breast cancer patients. On the efficacy front, a disease control rate of 81% in evaluable patients and 56% on an intent-to-treat basis was observed. For comparison, disease control using Herceptin and paclitaxel in the first line is 79%, so we find the results from this study to be compelling. The highest amount of dose-limiting toxicities was observed at the initial high doses, but no toxicities in patients receiving Herceptin at the optimal varlitinib dose (300mg dosed twice a day four days on, three days off), which opens the possibility of combination therapy.

Secondly, a poster described the company's ongoing pivotal TREETOP study of varlitinib in biliary tract cancer (BTC), which did not provide any new clinical data.

Our report on the ASCO data can be found here.

Targovax moves away from TG01 for resected pancreatic cancer after new FOLFIRINOX data

Targovax did not publish data at ASCO this year, but an important piece of news at ASCO made the company revisit one of its programmes. New data from the PRODIGE 24 Phase III trial backed by a French and Canadian consortium showed an almost two-year improvement in OS in the modified FOLFIRINOX arm compared to gemcitabine. Median overall survival in this study was approaching five years. Citing this substantially increased hurdle, Targovax made the decision to discontinue its cancer vaccine TG01 in resected pancreatic cancer even though encouraging Phase I/II data with TG01 were presented at ASCO 2017 and updated again recently. We believe this is a sensible move from the company as mFOLFIRINOX could quickly become the standard of care in resected pancreatic cancer and it is important to maximise resources. Targovax ramped up its focus on other platforms in the pipeline based on its oncolytic virus technology, ONCOS. Our analysis of the announcement can be downloaded here. Our coverage on Targovax can be found here.

Data from other companies on our radar

BerGenBio, a key player in AXL inhibition

The company presented interim Phase II data from several clinical trials with its inhibitor of the AXL receptor tyrosine kinase bemcentinib.

- Bemcentinib in combination with Keytruda in advanced NSCLC. Of 15 evaluable patients, three had a PR, nine had SD and three had progressive disease, which is a 20% ORR and 80% DCR. The data presented at ASCO showed a response according to AXL and PD-L1 status in some patients. Seven PD-L1 negative patients had an ORR of 29% and DCR of 89%. Five AXL positive patients had an ORR of 20% and DCR of 80%.
- Bemcentinib as monotherapy in r/r AML and Myelodisplastic Syndrome (MDS). The highest response rates were observed in patients with low soluble AXL, 43% and 50% ORR, and 86% and 100% DCR in AML and MDS patients respectively. Total ORR (in AML and MDS patients) was 46% and DCR was 92%.
- Bemcentinib in combination with either Keytruda or Tafinlar/Mekinist (dabrafenib/trabetinib, D/T) in metastatic melanoma. This was an investigator-sponsored Phase Ib/II trial. In bemcentinib+D/T treated patients there were two CRs, three PRs and two SDs. One patient treated with D/T alone had a PR. In Keytruda monotherapy there was one PR and two SDs and in the Keytruda+bemcentinib arm there were three PDs, two SDs and two PRs. Several serum biomarkers were assessed for pharmacodynamics and patient benefit, including sAXL.
- Biomarker data. The company concluded that sAXL is predictive of patient benefit in bemcentinib monotherapy treatment in AML and MDS. Furthermore, sAXL levels increase and are correlated with exposure to bemcentinib. The company is developing a predictive AXL immunohistochemistry (IHC) assay.

- Bemcentinib plus Keytruda in triple negative breast cancer (TNBC). Most patients (14/18) were AXL negative and 12/15 were PD-L1 negative. There was a PR in the 18 patients analysed.
- Electronic abstract (link). Phase I/II dose escalation of bemcentinib with docetaxel in advanced non-squamous NSCLC. Out of the first seven patients evaluated, two PRs (29%) and two SDs (29%) were reported.

We believe that, although early, these data show activity of bemcentinib as monotherapy or in combination with other products. We look forward to full data from these trials late next year, in particular further biomarker and efficacy data.

A link to the posters can be found here.

Erytech: Pharmacodynamic data from Phase II/III trial

Erytech presented pharmacodynamic data from its Phase II/III trial of eryaspase in combination with chemotherapy for the treatment of relapsed acute lymphoblastic leukaemia (ALL). Eryaspase is L-asparaginase (ASNase, a key product in the treatment of ALL, but limited by toxicities, mainly hypersensitivity) encapsulated in erythrocytes (red blood cells). The objective of the trial is to obtain the mean duration of activity of ASNase at a dose of 100u/L and hypersensitivity reactions in the induction phase. The company reported that the mean duration of ASNase activity was significantly higher with eryaspase (18.9 ± 5.3 days) compared with native ASNase (8.5 ± 6.6 days). Here is a link to the abstract.

Key takeaways

- Merck is the leader in front-line NSCLC and the combination of Keytruda plus chemotherapy has become the standard of care in non-squamous NSCLC.
- Roche's Tecentriq combo with Avastin and chemo may be the product of choice in EGFR/ALK resistant patients, while more data are needed from BMS's Opdivo to assess the validity of the TMB biomarker.
- Other immune-based therapies like CAR-T and TCR continue their progress with more mature data.
- Targeted therapies continue to strive with mounting positive data.
- Most combinations have an anti-PD-1 as backbone, but not all will be successful. Earlier this year a Phase III trial with Incyte's epacadostat (anti-IDO) plus Keytruda failed to show a survival benefit in melanoma. Nektar Therapeutics' IL-2 product did not produce additional responses in combination with Keytruda, as the market expected, so gaps remain.
- Other combinations in small, uncontrolled trials have shown signs of activity, but it is not possible to assess the magnitude of the effect the test drug brings to the combination, if any. Hence the need for larger, controlled trials.

Edison is an investment research and advisory company, with offices in North America, Europe, the Middle East and AsiaPac. The heart of Edison is our world-renowned equity research platform and deep multi-sector expertise. At Edison Investment Research, our research is widely read by international investors, advisers and stakeholders. Edison Advisors leverages our core research platform to provide differentiated services including investor relations and strategic consulting. Edison is authorised and regulated by the Financial Conduct Authority. Edison Investment Research (NZ) Limited (Edison NZ) is the New Zealand subsidiary of Edison. Edison NZ is registered on the New Zealand Financial Service Providers Register (FSP number 247505) and is registered to provide wholesale and/or generic financial adviser services only. Edison Investment Research Inc (Edison US) is the US subsidiary of Edison and is regulated by the Securities and Exchange Commission. Edison Investment Research Pty Limited (Edison Aus) [46085869] is the Australian subsidiary of Edison. Edison Germany is a branch entity of Edison Investment Research Limited [4794244]. www.edisongroup.com

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
295 Madison Avenue, 18th Floor
10017, New York
US

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia