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| Product | Indication | Primary endpoint | Surrogate/  Biomarker |
| **remdesivir**  Veklury  CMA 03/07/20  EMA/357513/2020 | [T]reatment of coronavirus disease 2019 (COVID-19) in adults and in adolescents (aged 12 to less than 18 years and weighing at least 40 kg) with pneumonia requiring supplemental oxygen | CO-US-540-5776 Phase III Pivotal: The primary clinical endpoint was time to recovery within 29 days after randomisation, defined as either discharged from hospital (with or without limitations of activity and with or without home oxygen requirements) or hospitalised but not requiring supplemental oxygen and no longer requiring ongoing medical care.  GS-US-540-5773 Phase III Safety + Efficacy: The endpoint will be derived by combining the available death, hospital discharge alive and ordinal scale assessment reported by the site, where death supersedes discharge alive and discharge alive suppersedes the ordinal scale score reported by the site.  GS-US-540-5774 Phase III Safety + Efficacy: The primary efficacy endpoint is clinical status assessed by a 7-point ordinal scale on Day 11. | Yes:  Time to recovery (pivotal) |
| **certinib**  Zykadia  CMA 06/05/15  Full MA 26/07/17  EMA/170114/2015 | [T]reatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib. | X2101 Phase I Pivotal: Overall response rate (ORR, CR+PR) and duration of response (DOR) as assessed by the investigator per RECIST 1.0. These endpoints were also derived separately based on BIRC assessment.  X1101 Phase I Supportive: The efficacy endpoints used to evaluate the anti-tumour activity of LDK378 are ORR, DOR and PFS as assessed by the Investigator per RECIST 1.1.  A2201 Phase II Supportive: The primary objective of the study was to demonstrate the anti-tumour activity of ceritinib, as measured by ORR by Investigator assessment.  A2203 Phase II Supportive: The primary objective of the study was to demonstrate the anti-tumour activity of ceritinib, as measured by ORR by Investigator assessment. | Yes:  Overall response rate (pivotal)  Duration of response (pivotal)  Progression-free survival |
| **COVID-19 mRNA vaccine (nucleoside-modified)**  Comirnaty  CMA 21/12/20  EMA/707383/2020 Corr. | Comirnaty is intended for active immunisation against SARS-CoV-2, thereby preventing COVID-19. | C4951001 Phase III Pivotal: First primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2; Second primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2. | Yes:  Incidence of COVID-19 cases from 7 days (pivotal) |
| **COVID-19 mRNA vaccine (nucleoside-modified)**  Spikevax  CMA 06/01/21  EMA/15689/2021 Corr. | The claimed indication of COVID-19 Vaccine Moderna is the prevention of COVID-19 in adults. | P301 Phase III Pivotal: Vaccine efficacy (VE) of mRNA1273 to prevent the first occurrence of COVID-19 in baseline seronegative participants (to prevent confirmed COVID19 starting 14 days after Dose 2) | Yes:  Incidence of COVID-19 cases from 14 days (pivotal) |
| **COVID-19 vaccine (Ad26.COV2-S [recombinant])**  COVID-19 Vaccine Janssen  CMA 11/03/21  EMA/158424/2021 | The claimed indication for COVID-19 Vaccine Janssen is active immunisation for the prevention of coronavirus disease-2019 (COVID-19) in adults greater than or equal to 18 years of age | VAC31518COV3001 Phase III Pivotal: Moderate and severe/critical disease (first occurrence of molecularly confirmed, moderate to severe/critical COVID-19) | Yes:  Severity of disease (pivotal) |
| **crizanlizumab**  Adakveo  CMA 28/10/20  EMA/427120/2020 | Adakveo is indicated for the prevention of recurrent vaso-occlusive crises (VOCs) in sickle cell disease patients aged 16 years and older. It can be given as an add-on therapy to hydroxyurea/hydroxycarbamide (HU/HC) or as monotherapy in patients for whom HU/HC is inappropriate or inadequate. | A2201 Phase II Pivotal: The primary endpoint of this trial was the annual rate of Sickle Cell-Related Pain Crises (SCPC).  A2202 Phase II Supportive: Ongoing | No |
| **bulevirtide**  Hepcludex  CMA 31/07/20  EMA/326446/2020 | [T]reatment of chronic hepatitis delta virus (HDV) infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease. | MYR202 Phase II Pivotal: The primary variable was HDV RNA response, defined as HDV RNA negativation or a decrease in HDV RNA by ≥2 log10 IU/mL from baseline to week 24.  MYR203 Phase II Pivotal: The primary variable was the occurrence of a negative polymerase chain reaction (PCR) result of HDV RNA (HDV RNA negativation) at week 72 (end of the follow up period). | Yes:  HDV RNA response - undetectable or at least 2 log from baseline (pivotal) |
| **andexanet alfa**  Ondexxya  CMA 26/04/19  EMA/347546/2019 | For adult patients treated with a direct factor Xa (FXa) inhibitor (apixaban or rivaroxaban) when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. | 14-503 Phase III Pivotal: Change (%) from baseline in anti-fXa activity at a nadir (after bolus for Part 1 or during infusion for Part 2) was evaluated as the primary endpoint.  14-504 Phase III Pivotal: Change (%) from baseline in anti-fXa activity at a nadir (after bolus for Part 1 or during infusion for Part 2) was evaluated as the primary endpoint.  14-505 Prospective Pivotal: Primary efficacy endpoints were anti-fXa activity and achievement of hemostatic efficacy of stopping a major bleed at 12 hours from end of andexanet infusion | Yes:  Percent change in anti-fXa activity at nadir (pivotal)  Hemostatic efficacy (pivotal) |
| **selinexor**  Nexpovio  CMA 26/03/21  EMA/CHMP/95252/2021 | [T]reatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. | KCP-330-012 Part 2 Phase IIb Pivotal: Primary endpoint: ORR (overall response rate)  Plus nine supportive studies | Yes:  Overall response rate (pivotal) |
| **polatuzumab vedotin**  Polivy  CMA 16/01/20  EMA/CHMP/690748/2019 | Polatuzumab vedotin, is intended in combination with bendamustine and rituximab, for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant. | GO29365 Phase Ib/II Pivotal: Safety (recommended dose), Efficacy (defined complete response (CR) rate using Modified Lugano 2014 Response Criteria (positron emission tomography– computed tomography [PET-CT] criteria) at the time of primary response assessment (6−8 weeks after Cycle 6 Day 1 or last dose of study medication) as defined by the Independent Review Committee (IRC))  DCS4968g Phase I Safety Supportive: The primary objective included the evaluation of the safety and tolerability of polatuzumab vedotin and the determination of the maximum tolerated dose (MTD) and dose-limiting toxicities (DLTs) when administered Q3W in patients with NHL and CLL.  GO27834 Phase II Supportive: Overall response rate  GO29044 Phase Ib/II Supportive: Complete response rate | Yes:  Complete response rate (pivotal)  Overall response rate |
| **larotrectinib**  Vitrakvi  CMA 19/09/19  EMA/CHMP/469135/2019 | VITRAKVI as monotherapy is indicated for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, Assessment report  - who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and  - who have no satisfactory treatment options | LOXO-TRK-14001 Phase I Pivotal: Primary were all safety so N/A  LOXO-TRK-15002 Phase II Pivotal: The primary objective of the study was to determine the overall response rate (ORR) by independent radiology review (IRC)  LOXO-TRK-15003 Phase I/II Pivotal: ORR  Supportive data provided | Yes:  Overall response rate (pivotal) |
| **lorlatinib**  Lorviqua  CMA 06/05/19  EMA/CHMP/182840/2019 | Lorlatinib as monotherapy is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non small cell lung cancer (NSCLC) whose disease has progressed after:  • alectinib or ceritinib as the first ALK tyrosine kinase inhibitor (TKI) therapy; or  • crizotinib and at least one other ALK TKI | PF-06463922 Phase II Pivotal: Primary endpoints: • ORR was defined as the percent of patients with Best Overall Response (BOR) of confirmed Complete Response (CR) or confirmed Partial Response (PR) according to RECIST version 1.1. Confirmed responses were those that persisted on repeat imaging at least 4 weeks after the initial documentation of response. • Intracranial ORR (IC ORR) was defined as the percent of patients with CNS metastases at study entry with Best Overall Intracranial Response of confirmed CR or confirmed PR (considering only the lesions having brain as the disease site).  B7461001 Phase I Supportive: Overall response rate | Yes:  Overall response rate (pivotal) |
| **onasemnogene abeparvovec**  Zolgensma  CMA 18/05/20  EMA/200482/2020 | [T]reatment of patients with 5q spinal muscular atrophy with a bi-allelic mutation in the SMN1 gene and either a clinical diagnosis of type 1 SMA or up to 3 copies of the SMN2 gene. | CL-303 Phase III Pivotal: Proportion of patients that achieve functional independent sitting for at least 30 seconds at the 18 months of age study visit. It is defined by the Bayley Scales of Infant and Toddler Development (Version 3), confirmed by video recording, as a patient who sits up straight with head erect for at least 30 seconds. • Survival at 14 months of age (see study CL-101).  CL-101 Phase I Supportive: Primary endpoint was survival (time from birth to either death or permanent ventilation)  CL-302 Phase 3 Supportive: Ongoing; Determine efficacy by demonstrating achievement of developmental milestone of sitting without support for 10 seconds up to 18 months of age as defined by WHO Motor Developmental Milestones.  CL-304 Phase 3 Supportive: Ongoing; The endpoints per cohort are: Cohort 1 (2 SMN2 copies): proportion of patients achieving milestone of independent sitting for at least 30 seconds at any visit up to 18 months of age. Cohort 2 (3 SMN2 copies): proportion of patients achieving the ability to stand without support for at least 3 seconds at any visit up to 24 months of age. | Yes:  Independent sitting (pivotal)  Stand without support |
| **pretomanid**  Dovprela  CMA 31/07/20  EMA/200048/2020 | [T]reatment of pulmonary extensively drug resistant (XDR), or treatment-intolerant or nonresponsive multidrugresistant (MDR) tuberculosis (TB) | Nix-TB Phase III Pivotal: Primary endpoint is unfavourable rate (Incidence of bacteriologic failure or relapse or clinical failure through follow up until 6 months after the end of treatment.)  NC-006 Phase II Supportive: The primary efficacy endpoint was the incidence of bacteriologic failure or relapse or clinical failure within 12 months from start of therapy in the DS TB group (non-inferiority to control, with an NI margin of 12%).  ZeNix Phase III Supportive: Ongoing | Yes:  Incidence of bacteriologic failure/relapse or clinical failure in 6 months (pivotal)  Same as above in 12 months |
| **selpercatinib**  Retsevmo  CMA 11/02/21  EMA/9037/2021 | Retsevmo as monotherapy is indicated for the treatment of adults with:  – advanced RET fusion positive non small cell lung cancer (NSCLC) who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy  – advanced RET fusion positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib.  Retsevmo as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib. | LOXO-RET-17001 Phase I/II Pivotal: Objective response rate (ORR) by IRC assessment. ORR was defined as the proportion of patients with BOR of confirmed CR or confirmed PR based on RECIST v1.1. BOR was defined as the best response designation for each patient recorded between the date of the first dose of selpercatinib and the data cut-off of 17 June 2019, or the date of documented disease progression per RECIST v1.1 or the date of subsequent therapy or cancer-related surgery. | Yes:  Objective response rate – assessed by IRC (pivotal) |
| **belantamab mafotodin**  Blenrep  CMA 25/08/20  EMA/CHMP/414341/2020 Corr. | BLENREP is indicated as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. | DREAMM-2 Phase II Pivotal: The primary efficacy endpoint of the study was overall response rate (ORR), defined as sCR+CR+VGPR+PR, according to 2016 International Myeloma Working Group (IMWG) Response Criteria (Table 29) and as assessed by Independent Review Committee (IRC) based on intention to treat (ITT) population  DREAMM-1 Phase I Supportive: Primary were all safety | Yes:  Overall response rate (pivotal) |
| **cemiplimab**  Libtayo  CMA 28/06/19  EMA/CHMP/368468/2019 | LIBTAYO as monotherapy is indicated for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation. | R2810-ONC-1540 Phase II Pivotal: The primary efficacy variable for this study was ORR according to independent central review. The following independent central review committees determined ORR separately for Group 1 (mCSCC) and Group 2 (laCSCC)  R2810-ONC-1423 Phase I Supportive: Primary were all safety (checked in clinical registry)  DeCOG Retrospective Supportive: Objective response rate | Yes:  Objective response rate – IRC assessed (pivotal) |
| **ataluren**  Translarna  CMA 31/07/14  EMA/369266/2014 | Translarna is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 5 years and older. | PTC124-GD-007-DMD Phase II Pivotal: Change in 6-minute walk distance from baseline to Week 48  Plus six supportive studies, two ongoing | Yes:  Change in 6-minute walk distance (pivotal) |
| **burosumab**  Crysvita  CMA 19/02/18  EMA/148319/2018 | Treatment of X-linked hypophosphataemia (XLH) in children over 1 year of age and adults. | Paediatric  UX023-CL201 Phase II Pivotal: Change from Baseline in severity of rickets as measured by Rickets Severity Score (RSS)  UX023-CL205 Phase Pivotal: Similar to above, pharmacodynamic: the primary efficacy endpoint is this study is the change from baseline over time in serum phosphorus.  UX023-CL301 Phase II Planned: Same as first.  Adults  UX023-CL303 Phase III Pivotal\*: the proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (0.81 mmol/L) at the mid-point of the dose interval (i.e. Weeks 2, 6, 10, 14, 18 and 22), as averaged across dose cycles between baseline and Week 24.  \*only safety was considered by CHMP | Yes:  Change in RSS score (pivotal)  Pharmacodynamic: Serum phosphorus levels (pivotal) |
| **volanesorsen**  Waylivra  CMA 03/05/19  EMA/180717/2019 | [T]reatment of familial chylomicronemia syndrome (FCS), a genetic based orphan disease characterised by extremely high serum triglycerides (TG) (> 880 mg/dL, 10 mmol/L). | CS6 Phase III Pivotal: The primary endpoint was the percentage change in fasting TG from Baseline to the primary analysis time point at the end of Month 3, where the value was defined as the average of Week 12 (Day 78) and Week 13 (Day 85) fasting assessments.  CS16 Phase III Supportive: Same as above  CS7 Supportive: The primary efficacy endpoints of study CS7 are summarized below: • Percent change and absolute change from Baseline in fasting total ApoC-III, TG and other lipid measurements including total cholesterol, non-HDL-C, apoB, HDL-C, apoA-1 (apoA-1), VLDL-C, and LDL-C, at month 3, 6 and 12. • Frequency and severity of patient reported abdominal pain during the treatment period, • Change from Baseline in Quality of Life (QOL) questionnaires (EQ-5D, SF-36), • Independently adjudicated acute pancreatitis event rate, • Frequency of other symptoms: eruptive xanthoma, lipemia retinalis. | Yes:  Percent change in fasting triglycerides (pivotal) |
| **trastuzumab deruxtecan**  Enhertu  CMA 18/01/21  EMA/2446/2021 | The claimed indication for trastuzumab deruxtecan is monotherapy for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti HER2 based regimens. | DS8201-A-U201 Phase II Pivotal: The primary efficacy endpoint of the study was ORR assessed by an ICR based on tumor scans. Objective response rate was defined as the proportion of subjects who achieved a best overall response (BOR) of complete response (CR) or partial response (PR), with confirmation of response, based on RECIST 1.1.  Unicancer Research Program Supportive  DS8201-PMx004 Meta-Analysis Supportive | Yes:  Overall response rate (pivotal) |
| **pemigatinib**  Pemazyre  CMA 26/03/21  EMA/CHMP/105411/2021 | Pemazyre monotherapy is indicated for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy. | INCB 54828-202 Phase II Pivotal: The primary endpoint of this study is to determine the objective response rate (ORR) in participants with FGFR2 rearrangements or fusions based on the central genomics laboratory results (Cohort A). ORR is defined as the proportion of participants who achieved a complete response (disappearance of all target lesions) or a partial response (≥ 30% decrease in the sum of the longest diameters of target lesions) based on RECIST v1.1. Clinical response is determined by an independent review committee (IRC). | Yes:  Objective response rate (pivotal) |
| **dostarlimab**  Jemperli  CMA 21/04/21  EMA/176464/2021 | Dostarlimab is intended as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen. | 4010-01-001 Phase I Pivotal: The primary endpoints for Cohort A1 were as follows: ORR, defined as the proportion of patients achieving best overall response (BOR) of complete response (CR) or partial response (PR), as assessed per RECIST v1.1 based on BICR; DOR, defined as the time from first documentation of CR or PR, as assessed per RECIST v1.1, until the time of first documentation of PD, as assessed per RECIST v1.1 based on BICR, or death due to any cause  4010-01-001 Part 2B Phase I Supportive: Same as above plus safety endpoints | Yes:  Overall response rate (pivotal)  Duration of response (pivotal) |
| **rucaparib**  Rubraca  CMA 24/05/18  EMA/CHMP/238139/2018 | The revised applied indication for Rubraca is as monotherapy treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum based chemotherapy. | CO-338-010 Phase I/II Pivotal: The primary efficacy endpoint in Part 2A was ORR defined as best confirmed response according to RECIST Version 1.1.  CO-338-017 Phase II Pivotal: Part 1: The primary efficacy endpoint was PFS according to RECIST Version 1.1, as assessed by the investigator, or death from any cause, in molecularly defined HRD subgroups. Part 2: The primary efficacy endpoint was ORR by RECIST Version 1.1 in molecularly defined HRD subgroups. | Yes:  Overall response rate (pivotal)  Progression-free survival (pivotal)\*  \*Put as secondary endpoint in pooled analysis |
| **betibeglogene autotemcel**  Zynteglo  CMA 29/05/19  EMA/56140/2020/Corr. | Zynteglo is indicated for the treatment of patients 12 years and older with transfusiondependent β-thalassaemia (TDT) who do not have a β0/β0 genotype, for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available | HGB-204 Phase I/II, HGB-205 Phase I/II, HGB-207 Phase III Pivotal: The primary endpoint was similar for the pooled analyses with Studies HGB-204, HGB-205, and HGB207, and for study HGB-207: the proportion of patients who meet the definition of transfusion independence (TI).  HGB-204: Percentage of Participants With Sustained Production of >=2.0 Grams Per Deciliter (g/dL) of Hemoglobin A (HbA) Containing βA-T87Q-globin (HbAT87Q) for the Six Months Between Month 18 and Month 24  LTF-303 Long-Term Supportive: Transfusion independence | Yes:  Transfusion independence proportion (pivotal)  Proportion: production of at least 2 g/dL of HbAT87Q (pivotal)\*  \*Not primary endpoint in pooled analysis |
| **entrectinib**  Rozlytrek  CMA 31/07/20  EMA/379739/2020 | Rozlytrek as monotherapy is indicated for the treatment of adult and paediatric patients 12 years of age and older, with solid tumours that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion,  - who have a disease that is locally advanced, f or where surgical resection is likely to result in severe morbidity, and  - who have not received a prior NTRK inhibitor  - who have no satisfactory treatment options (see sections 4.4 and 5.1).  Rozlytrek as monotherapy is indicated for the treatment of adult patients with ROS1-positive, advanced non-small cell lung cancer (NSCLC) not previously treated with ROS1 inhibitors | GO40782 Phase II Pivotal: ORR (confirmed response = persisted on repeated-imaging≥4 weeks after initial documentation of response)  Integrated efficacy analysis (above study, ALKA, STARTRK-1): primary endpoints ORR, BOR, DOR | Yes:  Overall response rate (pivotal)  Best overall response (pivotal)  Duration of response (pivotal) |
| **COVID-19 Vaccine (ChAdOx1-S [recombinant])**  Vaxzevria  CMA 29/01/21  EMA/94907/2021 | The claimed indication for AZD1222 vaccine is active immunisation of individuals ≥18 years of age to prevent coronavirus disease 2019 (COVID-19). | COV001 Phase I/II Pivotal: Virologically-confirmed symptomatic cases of COVID-19  COV002 Phase II/III, COV003 Phase III Pivotal: The primary efficacy endpoint was the incidence of COVID-19 obtained by measuring the first case of SARSCoV-2 virologically-confirmed COVID-19 occurring ≥ 15 days post second dose of study intervention, with at least one of the following symptoms: objective fever (defined as ≥ 37.8°C), cough, shortness of breath, anosmia, or ageusia.  COV005 Phase I/II Pivotal: efficacy not included in MAA | Yes:  Incidence of COVID-19 at least 15 days post second dose (pivotal) |
| **bedaquiline**  Sirturo  CMA 05/03/14  EMA/CHMP/329898/2013 | SIRTURO is indicated for use as part of an appropriate combination regimen for pulmonary multidrug resistant tuberculosis (MDR TB) in adult patients when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability | C208 Phase II Pivotal: The primary efficacy endpoint was time to sputum culture conversion (SCC) during treatment with bedaquiline or placebo. This parameter was based on the qualitative assessment of culture growth in MGIT using spot sputum samples.  C209 Phase IIb Supportive: Same as above. | Yes:  Time to sputum culture conversion (pivotal) |
| **Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured**  Tecartus  CMA 14/12/20  EMA/588798/2020 | [T]reatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after two or more lines of systemic therapy including a Bruton’s tyrosine kinase (BTK) inhibitor. | ZUMA-2 Phase II Pivotal: ORR, defined as CR or PR using central assessment per Lugano Classification (Cheson 2014)  Meta-Analysis Supportive | Yes:  Objective response rate (pivotal) |
| **imlifidase**  Idefirix  CMA 25/08/20  EMA/372587/2020 Rev 1 | [D]esensitisation treatment of highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor. | 06 Phase II Pivotal: efficacy defined as imlifidase ability to create a negative CXM test within 24 hours after imlifidase dosing.  04 Phase I/II Supportive: Primary Endpoints • Number and levels of DSAs prior to transplantation • Number and levels of DSA levels post transplantation • Incidence of allograft rejections • Renal function by creatinine, eGFR, and urine protein measurements • Biopsy pathology evaluation • Safety parameters (AEs, laboratory assessments, vital signs, ECG) | Yes:  Negative CXM test post-dosing (pivotal)  DSA number and level  Incidence of allograft rejections  Creatinine/eGFR/  urine protein |
| **brentuximab vedotin**  Adcetris  CMA 25/10/12  EMA/702390/2012 | ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL): 1. following autologous stem cell transplant (ASCT) or  2. following at least two prior therapies when ASCT or multi-agent chemotherpay are not a treatment option  ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL). | SG035-003 Phase II Pivotal: Objective Response Rate per Independent Review Facility (IRF)  SG035-004 Phase II Pivotal: Same as above  SG035-001 Phase I Supportive: Primary were safety endpoints  SG035-002 Phase I Supportive: Primary were safety endpoints | Yes:  Objective response rate per IRF (pivotal) |
| **vandetanib**  Caprelsa  CMA 16/02/12  EMA/128076/2012 | [T]reatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease. 'For patients in whom rearranged during transfection (RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision | D4200C00058 Phase III Pivotal: Progression-free survival (PFS), defined from the date of randomization to the date of objective progression or death (by any cause in the absence of progression), provided death was within 3 months from the last evaluable RECIST assessment, using data from RECIST assessments performed at baseline, during treatment and during the follow-up period. The PFS assessment was based on an independent radiological review.  Phase II Supportive: Preliminary results of a phase II, placebo controlled randomised study (study 79) of vandetanib 300 mg in 145 patients with locally advanced or metastatic papillary or follicular thyroid carcinoma failing or unsuitable for radioiodine therapy found a HR of 0.62 (0.43,0.92), p=0.017 on the primary endpoint PFS without any significant difference on the secondary endpoints. | Yes:  Progression-free survival (pivotal) |
| **cabozantinib**  Cometriq  CMA 21/03/14  EMA/97103/2014 | Cometriq is indicated for the treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. | XL184-301 Phase III Pivotal: Progression-free survival (IRC determined) defined as the time from randomization to documented PD per mRECIST criteria or death due to any cause, whichever occurred first.  XL184-001 Phase I Supportive: Primary were safety | Yes:  Progression-free survival (pivotal) |
| **delamanid**  Deltyba  CMA 27/04/14  EMA/55567/2014 | Delamanid is indicated for the treatment of multidrug-resistant tuberculosis (MDR-TB) in combination with an optimised background regimen (OBR) according to WHO guidelines in adult patients. | 242-07-204 Phase II Pivotal: The primary efficacy endpoint was the proportion of the subset of MITT subjects (sputum culture positive for MDR-TB at baseline) that achieved SCC using the MGIT system by Day 57. The time to SCC was based on the collection of the first sputum specimen with MGIT culture negative for growth of MTB that was followed by at least one additional sputum specimen with no MTB growth in MGIT at least 27 days after the first negative specimen and not followed by any sputum specimens with MGIT growth of MTB at any point during the remainder of the 84 day study period. | Yes:  Proportion achieved sputum culture conversion (pivotal) |
| **ixazomib**  Ninlaro  CMA 21/11/16  EMA/CHMP/594718/2016 | NINLARO in combination with lenalidomide and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy | C16010 Phase III Pivotal: The primary efficacy endpoint was PFS defined as the time from the date of randomization to the date of first documentation of disease progression, based on central laboratory results and IMWG criteria, or death due to any cause, whichever occurred first  Plus three supportive studies (safety/pharmacokinetics) | Yes:  Progression-free survival (pivotal) |
| **parathyroid hormone**  Natpar  CMA 24/04/17  EMA/180882/2017 | Natpar is indicated as adjunctive treatment of adult patients with chronic hypoparathyroidism who cannot be adequately controlled with standard therapy alone. | REPLACE Phase III Pivotal: The primary efficacy variable was the percentage of subjects who met the triple efficacy endpoint at Week 24, based on investigator-prescribed data. A subject met the triple efficacy endpoint if he/she achieved: o At least a 50% reduction from the baseline oral calcium supplementation dose and o At least a 50% reduction from the baseline active vitamin D metabolite/analog dose and o An albumin-corrected total serum calcium concentration that was maintained or normalized compared to the baseline value (≥ 1.875 mmol/L) and did not exceed the upper limit of the laboratory normal range.  PAR-C10-008, PAR-C10-009 Phase III Supportive: Primary was safety | Yes:  Reduction from baseline calcium/vitamin D dose or serum calcium concentration (pivotal) |
| **bosutinib**  Bosulif  CMA 27/03/13  EMA/70979/2013 | Bosulif is indicated for the treatment of adult patients with chronic phase (CP), accelerated phase (AP), and blast phase (BP) Philadelphia chromosome positive chronic myelogenous leukaemia (Ph+ CML) previously treated with one or more tyrosine kinase inhibitor(s) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. | 3160A4-200-WW Phase I/II Pivotal: Clinical evaluation of efficacy CP CML patients who were resistant to imatinib: • MCyR (PCyR or CCyR) at 24 weeks  Compassionate use supportive study  3000-WW Phase III Supportive\*: CCyR rate at 1 year based on ITT population.  \*originally pivotal but 200-WW better | Yes:  Major cytogenic response (pivotal)  Complete cytogenic response rate |
| **obeticholic acid**  Ocaliva  CMA 12/12/16  EMA/725757/2016 | OCALIVA is indicated for the treatment of primary biliary cholangitis (also known as primary biliary cirrhosis) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. | 747-301 Phase III Pivotal: Percentage of subjects (OCA 10 mg vs. placebo) achieving composite endpoint at Month 12. (Defined as the percentage of subjects reaching an ALP <1.67x ULN and a ≥15% reduction in ALP and a total bilirubin ≤ULN)  747-205 Phase II Supportive: the efficacy variables were related with different lipid metabolism parameters (HDLc concentration, total cholesterol, etc.).  Plus three LTSE supportive studies | Yes:  Composite: ALP< 1.67 x ULN and a ≥15% reduction in ALP and a total bilirubin ≤ULN (pivotal)  Change in HDLc concentration/  particle concentration |
| **ex vivo expanded autologous human corneal epithelial cells containing stem cells**  Holoclar  CMA 17/02/15  EMA/25273/2015 | Non-drug based so N/A | N/A | N/A |
| **venetoclax**  Venclyxto  CMA 05/12/16  Full MA 20/10/18  EMA/725631/2016 | Venclyxto monotherapy is indicated for the treatment of chronic lymphocytic leukaemia (CLL) in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor.  Venclyxto monotherapy is indicated for the treatment of CLL in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor. | M13-982 Phase II Pivotal: The assessment of ORR by IRC was performed once after 107 subjects had completed the 36 week disease assessment, had progressed prior to the 36-week disease assessment, discontinued study drug for any reason, or after all treated subjects had discontinued venetoclax, whichever was earlier.  M14-032 Phase II Supportive: ORR  M13-365 Supportive: Primary was safety | Yes:  Overall response rate by IRC (pivotal) |
| **pandemic influenza vaccine (H5N1) (live attenuated, nasal)**  Pandemic influenza vaccine H5N1 AstraZeneca  CMA 20/05/16  EMA/CHMP/323530/2016 | Prophylaxis of influenza in an officially declared pandemic situation in children and adolescents from 12 months to less than 18 years of age | CIR 217, CIR 239 Phase I Pivotal: In P/LAIV studies CIR 217 (ca A/Vietnam/1203/2004 [H5N1] vaccine) and CIR 239 (ca A/Hong Kong/213/2003 [H5N1] vaccine), antibody responses were measured by assays for serum haemagglutination inhibition (HAI), microneutralisation (MN), immunoglobulin G (IgG), and immunoglobulin A (IgA) and nasal IgA assays.  CIR 277 Pivotal: Primary was safety | Yes:  Antibody responses – serum AI, MN, IgG, (nasal) IgA assays (pivotal) |
| **avapritinib**  Ayvakyt  CMA 24/09/20  EMA/451735/2020 | Ayvakyt is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation. | BLU-285-1101 Phase I Pivotal: The primary endpoints were: • ORR, defined as the rate of centrally confirmed CR or PR by mRECIST version 1.1 Overall safety profile of avapritinib, as assessed by the type, frequency, severity, timing, and relationship to study drug of any AEs, SAEs, and changes in vital signs, ECGs, and safety laboratory tests.  BLU-285-1002 Retrospective Supportive: The efficacy analysis across the first-line treatment, second-line treatment, and third-line treatment populations was based principally on best overall response/ORR, DOR, and PFS with OS investigated as a secondary efficacy endpoint  BLU-285-1303 Phase III Supportive: The primary efficacy endpoint was PFS by blinded, independent central radiology review, based on mRECIST v1.1 criteria for GIST  BLU-285-1105 Phase I/II Supportive: Ongoing | Yes:  Overall response rate (pivotal)  Duration of response  Progression-free survival |
| **Ebola Zaire Vaccine (rVSV∆G-ZEBOV-GP, live)**  Ervebo  CMA 11/11/19  Full MA 14/11/21  EMA/606159/2019 | Ervebo is indicated for active immunization of individuals 18 years of age or older to protect against Ebola Virus Disease (EVD) caused by Zaire Ebola virus (see sections 4.2, 4.4 and 5.1). The use of Ervebo should be in accordance with official recommendations. | V920-010 Phase III Pivotal: The primary efficacy endpoint was confirmed EVD, defined as: • any probable or suspected case from whom a blood sample taken was laboratory confirmed as positive for EVD; or • any deceased individual with probable EVD, from whom a post-mortem sample taken within 48 hours after death was laboratory confirmed as positive for EVD | No |
| **pazopanib**  Votrient  CMA 14/06/10  Full MA 01/07/13  EMA/CHMP/248579/2010 | Votrient is indicated for the first line treatment of advanced Renal Cell Carcinoma (RCC) and for patients who have received prior cytokine therapy for advanced disease | VEG105192 Phase III Pivotal: The primary efficacy endpoint was PFS, defined as the interval between the date of randomization and the earliest date of disease progression or death due to any cause. The RECIST criterion for the assessment of progression of solid tumours was used.  VEG102616 Phase II Supportive: EPAR emphasised of PFS comparison (secondary endpoint) whilst primary efficacy endpoint of this study was overall response  VEG107769 Supportive: Same as above (PFS emphasis) except primary were different | Yes:  Progression-free survival (pivotal) |
| **fampridine**  Fampyra  CMA 20/07/11  Full MA 22/05/17  EMA/555661/2011 | Fampyra is indicated for the improvement of walking in adult patients with multiple sclerosis with walking disability (EDSS 4-7) | MS-F203, MS-F204 Phase III Pivotal: Primary efficacy endpoint was the proportion of ‘consistent’ responders defined as patients with higher walking speed for at least three out of four visits during the double-blind period as compared to the maximum value among the non-treatment visits  MS-F20-F201 Supportive Study | Yes:  Responder rate in walking speed (pivotal) |
| **pixantrone dimaleate**  Pixuvri  CMA 10/05/12  EMA/309145/2012 | Pixuvri is indicated as monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive Non Hodgkin B cell Lymphomas (NHL). The benefit of pixantrone treatment has not been established in patients when used as fifth line or greater chemotherapy in patients who are refractory to last therapy. | PIX301 Phase III Pivotal: CR or CRu rate (ITT) assessed by the Independent Assessment Panel (IAP) based on the Report of the International Workshop to Standardize Response Criteria. These criteria are also known as the International Working Group (IWG) criteria (Cheson 1999).  AZA-II-01 Phase II Supportive: Primary: ORR (CR and PR) in ITT population according to investigator assessment | Yes:  Confirmed and unconfirmed complete response (pivotal)  Overall response rate |
| **stiripentol**  Diacomit  CMA 04/01/07  Full MA 08/01/14 | Diacomit is indicated for use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet’s syndrome) whose seizures are not adequately controlled with clobazam and valproate. | No Public Assessment Report, used Scientific Discussion report.  BC-299, BC-385 Pivotal: 50% Seizure reduction  STEV Phase II Supportive: Change in Seizure freq  STILON Open Supportive (Compassionate Use) | Yes:  Proportion with at least 50% seizure reduction (pivotal) |
| **blinatumomab**  Blincyto  CMA 23/11/15  Full MA 18/06/18  EMA/CHMP/469312/2015 | BLINCYTO in treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL) | MT103-211 Phase II Pivotal: The primary efficacy endpoint was the CR/CRh\* rate calculated as the number of subjects with either a CR or CRh\* response within the first two treatment cycles divided by the total number of subjects in the analysis set. CR was defined as having ≤ 5% blasts in the bone marrow, no evidence of disease, and full recovery of peripheral blood counts (platelets > 100,000/μL and absolute neutrophil count (ANC) > 1,000/μL) and CRh\* was defined as having ≤ 5% blasts in the bone marrow, no other evidence of disease, and partial recovery of peripheral blood counts (platelets > 50,000/μL and ANC > 500/μL).  MT103-206 Phase II Supportive: Same as above.  Other supportive studies include historical comparator, meta-analysis | Yes:  Complete response/CR with partial haematological recovery rate (pivotal) |
| **osimertinib**  Tagrisso  CMA 02/02/16  Full MA 24/04/17  EMA/CHMP/15445/20165 | TAGRISSO is indicated for the treatment of adult patients with locally advanced or metastatic EGRF T790 mutation-positive non-small cell lung cancer (NSCLC) | AURA Phase I/II, AURA2 Phase II Pivotal: In both studies, the primary efficacy endpoint variable was the ORR according to RECIST 1.1 by BICR using the evaluable for response analysis set. | Yes:  Objective response rate (pivotal) |
| **raltegravir**  Isentress  CMA 20/12/07  Full MA 14/07/09 | ISENTRESS is indicated in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in treatment-experienced adult patients with evidence of HIV-1 replication despite ongoing anti-retroviral therapy | No Public Assessment Report, used Scientific Discussion report.  BENCHMRK 1, 2 Phase III Pivotal: The primary measurement for efficacy in the study was the percentage with < 400 copies/ml and the primary time point for evaluation of efficacy was Week 16. | Yes:  Percentage with viral load <400 copies/mL (pivotal) |
| **avelumab**  Bavencio  CMA 18/09/17  Full MA 19/08/20  EMA/496529/2017 | Bavencio is indicated as monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (MCC) | EMR100070-003 Phase II Pivotal: ORR according to RECIST 1.1 as determined by an IERC ORR definition: proportion of subjects with a confirmed BOR of CR or PR, based on independent tumor assessment according to RECIST 1.1  Above study Part B Supportive: Interim efficacy data with ORR also  100070-Obs001 Observational Supportive: The primary endpoint was the patients’ BOR to their line of systemic chemotherapy. | Yes:  Objective response rate (pivotal)  Best overall response |
| **lapatinib**  Tyverb  CMA 10/06/08  Full MA 17/02/15  EMEA/H/C/795 | [T]reatment of: Patients with advanced or metastatic breast cancer whose tumours overexpress ErbB2 (HER2). Patients should have progressive disease following prior therapy which must include anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting | EGF100151 Phase III Pivotal: Time to progression (TTP, disease progression or death due to breast cancer prior to progression), was established by an independent review committee (IRC), who were blinded to study treatment, after radiological assessment including a chest CT (or MRI) scan including liver or alternatively, separate chest and abdominal CT (or MRI) scan and a bone scan  EGF30001 Phase III Supportive: TTP  EGF103659 Open Supportive: BOR | Yes:  Time to progression (pivotal)  Best overall response |
| **panitumumab**  Vectibix  CMA 03/12/07  Full MA 15/01/15 | [M]onotherapy for the treatment of patients with EGFR expressing metastatic colorectal carcinoma with non-mutated (wild-type) KRAS after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens | No Public Assessment Report, used Scientific Discussion report.  20020408 Phase III Pivotal: Progression free survival  20030167, 20030250, 20025405 Phase II Supportive: Objective tumour response | Yes:  Progression-free survival (pivotal)  Objective tumour response |
| **sunitinib**  Sutent  CMA 19/07/06  Full MA 11/01/07 | [T]reatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour after failure of imatinib mesylate treatment due to resistance or intolerance, and in the treatment of advanced and/or metastatic metastatic renal cell carcinoma after failure of cytokine-based therapy | No Public Assessment Report, used Scientific Discussion report.  GIST  A6181004 Phase III Pivotal: For the pivotal trial, Study A6181004, TTP was the primary endpoint, defined as the time from the first dose of study medication to first documentation of PD.  RTKC-0511-013 Phase I/II Supportive: Primary were safety  MRCC  A6181006 Phase II Pivotal: The primary endpoint for the studies was ORR.  RTKC-0511-014 Phase II Supportive: Same as above. | Yes:  For GIST: time to progression (pivotal)  For MRCC: objective response rate (pivotal) |
| **everolimus**  Votubia  CMA 02/09/11  Full MA 16/11/15  EMA/646111/2011 | [T]reatment of patients aged 3 years and older with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) who require therapeutic intervention but are not amenable to surgery | RAD001 Phase II Pivotal: The primary efficacy endpoint was the change from baseline in volume of the primary SEGA lesion at 6 months after the start of treatment (or at the last available assessment if a patient ended treatment prior to this timepoint) as determined by central radiology review.  M2301 Phase III Supportive: The primary efficacy endpoint was the SEGA response rate as defined as the proportion of patients with a best overall SEGA response as per Independent Central Radiological Review | Yes:  Change in SEGA volume (pivotal)  SEGA response rate |
| **daratumumab**  Darzalex  CMA 20/05/16  Full MA 28/04/17  EMA/278085/2016 | [T]reatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy | MMY2002 Phase II Pivotal: The primary endpoint was the overall response rate (ORR), which was defined as the proportion of subjects who achieved PR or better according to the IMWG criteria (Durie 2007, Rajkumar 2011).  GEN 501 Phase I/II Pivotal: The primary efficacy endpoint was overall response rate (ORR), which was defined as the proportion of patients who achieved a partial response (PR) or better. Objective response evaluations were made based on assessments from a computerized algorithm using the International Multiple Myeloma Working Group (IMWG) Response Criteria for Multiple Myeloma (Durie 2006, Rajkumar 2011).  GEN503 Phase I/II Supportive: Same as above | Yes:  Overall response rate (pivotal) |
| **etravirine**  Intelence  CMA 28/08/08  EMEA/H/C/000900 | INTELENCE, in combination with a boosted protease inhibitor and other antiretroviral medicinal products, is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-experienced adult patients | C206, C216 Phase III Pivotal: Proportion of subjects with plasma viral load i.e. < 50 copies / mL at week 24  C203 Phase IIb Supportive: Primary was safety  C223 Phase IIb Supportive: Change in log10 plasma viral load at Week 24 | Yes:  Proportion with viral load <50 copies/mL (pivotal)  Change in log plasma viral load |
| **aztreonam**  Cayston  CMA 21/09/09\*  \*originally not granted CMA  EMEA/H/C/000996 | [S]uppressive therapy of chronic pulmonary infections due to Pseudomonas aeruginosa in patients with cystic fibrosis (CF) aged 18 years and older | CP-AI-005 Phase III Pivotal: The primary endpoint was time to need for IV or inhaled anti-PA antibiotics other than trial drug with documented symptom(s) predictive of pulmonary exacerbation (such as decreased exercise tolerance, increased cough, increased sputum/chest congestion, decreased appetite) following start of blinded study drug  CP-AI-007 Phase III Pivotal: The primary endpoint was change from Day 0 (baseline) to Day 28 in clinical symptoms as assessed by the respiratory domain of the CFQ-R). The CFQ-R was administered at Days 0, 14, 28, and 42/ Early Termination in a similar fashion as in study CP-AI-005.  CP-AI-006 Phase III Supportive: Ongoing, safety  CP-AI-003 Phase II Supportive: The primary efficacy variable was the percent change from pretreatment Day 0 to Day 14 in FEV1 | Yes:  Time to need for IV/other antibiotics (pivotal)  Percent change in FEV1 |
| **tafasitamab**  Minjuvi  CMA 26/08/21  EMA/426468/2021  \*\*\*Systematic review up to 13/08/21\*\*\*\* | [I]n combination with lenalidomide followed by Minjuvi monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT). | MOR208C203 Phase II Pivotal: The proportion of patients with CR and PR (CR+PR) as assessed by the Investigators and central read by independent reviewers, using the revised IWG Response Criteria (Cheson et al. 2007).  MOR208C201 Phase IIa Supportive: Overall response rate also  MOR208C206 Observational Supportive: Overall response rate also | Yes:  Overall response rate (pivotal) |
| **idecabtagene vicleucel**  Abecma  CMA 18/08/21  EMA/409800/20212021 | [T]reatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti CD38 antibody and have demonstrated disease progression on the last therapy | MM-001 Phase II Pivotal: Overall Response Rate (ORR), defined as the percentage of subjects who achieved partial response (PR) or better (stringent CR (sCR) + CR + VGPR + PR) as assessed by an Independent Response Committee (IRC) according to International IMWG response criteria (Kumar, 2016). The primary efficacy analysis was conducted based on the mITT (infused) patient population.  **Systematic literature review was carried out and found 36 trials**  CRB-401 Phase I Supportive: Primary objective is safety not efficacy | Yes:  Overall response rate (pivotal) |
| **selumetinib**  Koselugo  CMA 17/06/21  EMA/549867/2021 | [M]onotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and above | SPRINT Phase II Pivotal: The primary outcome variable pre-specified in the protocol was objective response rate (ORR), defined as the percentage of patients with a complete response (CR) or confirmed partial response (PR is target PN volume decrease from baseline ≥20%, confirmed when documented by subsequent volumetric MRI within 3 to 6 months)  01-C-0222 Phase II Supportive: placebo only analysis: primary outcome is time-to-progression clinicaltrials.gov/ct2/show/NCT00021541 | Yes:  Objective response rate (pivotal)  Time-to-progression |
| The following were in “conditional marketing authorization” or “conditional marketing authorisation” search queries despite unconditional MA  BeneFIX, Vazkepa, Imbruvica, Hyrimoz, Opdivo, Yervoy, Enspryng, Kesimpta, Trulicity, Tivicay, Hefiya, Saxenda, Tysabri, Inrebic, Ponvory, Pradaxa, Sarclisa, Drovelis, Lydisilka, Doptelet, Perjeta, Tafinlar, Plegridy, Alprolix, Rapamune, Tobi Podhaler, Kovaltry, Livogiva, Tremfya, Isturisa, Imvanex, Mepsevii, Zeposia, Palforzia, Phesgo, Xofluza, Evkeeza, Rekambys, Lumoxiti, Sogroya, Klisyri, Ryeqo, Imcivree, Bylvay, Byooviz, Bimzelx, Voxzogo, Regkirona, Ronapreve, Vumerity, Maviret, Leqvio, Jivi, Evotaz, Libmeldy, Xarelto | N/A | N/A | N/A |
| **trametinib**  Mekinist  MA 30/06/14  \*was in “conditional marketing authorization” search query despite unconditional  EMA/CHMP/258608/2014 | The Applicant requested with the Day 121 responses consideration of a conditional marketing authorisation approval. The results of the ongoing phase III confirmatory trial exploring activity of dabrafenib in combination with trametinib in the proposed target population are expected in late 2013, and could be assessed within the timeframe of this procedure, the request for conditional marketing authorisation was therefore not endorsed by the CHMP. | N/A | N/A |
| **crizotinib**  Xalkori  CMA 23/10/12  EMA/CHMP/497137/2012 | XALKORI is indicated for the treatment of adults with previously treated anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). | A8081001 Phase I Pivotal: The primary efficacy endpoint in this cohort was ORR: ORR was defined as the percent of patients in the Response Evaluable (RE) population achieving a confirmed CR or confirmed PR according to RECIST.  1005 Phase II Supportive: Same as above  1007 Phase III Supportive: Primary efficacy criteria (PFS) | Yes:  Objective response rate (pivotal)  Progression-free survival |
| **vismodegib**  Erivedge  CMA 12/07/13  EMA/297688/2013 | [T]reatment of adult patients with:  - Symptomatic metastatic basal cell carcinoma  - Locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy | SHH4476g Phase II Pivotal: ORR per IRF assessment  SHH3925g Phase I Supportive: Safety, pharmacokinetics, and determination of the MTD  Plus two safety supportive studies | Yes:  Objective response rate (pivotal) |
| **alectinib**  Alecensa  CMA 16/02/17  EMA/197343/2017 | Alecensa as monotherapy is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib | NP28761 Phase I/II Pivotal: ORR (IRC assessed) - Proportion of patients achieving confirmed CR or PR  NP28673 Phase I/II Pivotal: ORR as per central IRC using RECIST v1.1 in the overall population (with and without prior exposure of cytotoxic chemotherapy treatments). • ORR as per central IRC using RECIST v1.1 in patients with prior exposure of cytotoxic chemotherapy treatments.  AF-001JP Phase I/II Supportive: The primary endpoint of the phase 2 was the proportion of patients who had an objective response.  JO28928 Phase III Supportive: Ongoing | Yes:  Objective response rate (pivotal) |
| **darunavir**  Prezista  CMA 12/02/07 | PREZISTA, co-administered with 100 mg ritonavir in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in highly pre-treated adult patients who failed more than one regimen containing a protease inhibitor (PI) | No Public Assessment Report, used Scientific Discussion report.  TMC-114-C202, TMC-114-C213 Phase IIb Pivotal: Following amendment of the objective of the studies, the primary endpoint was switched from change in viral load from baseline, to virologic response defined as at least 1.0 log10 decrease in viral load versus baseline at week 24.  C208, C215 Phase IIb Supportive: Primary changed from efficacy to safety | Yes:  At least 1 log decrease in viral load (pivotal) |