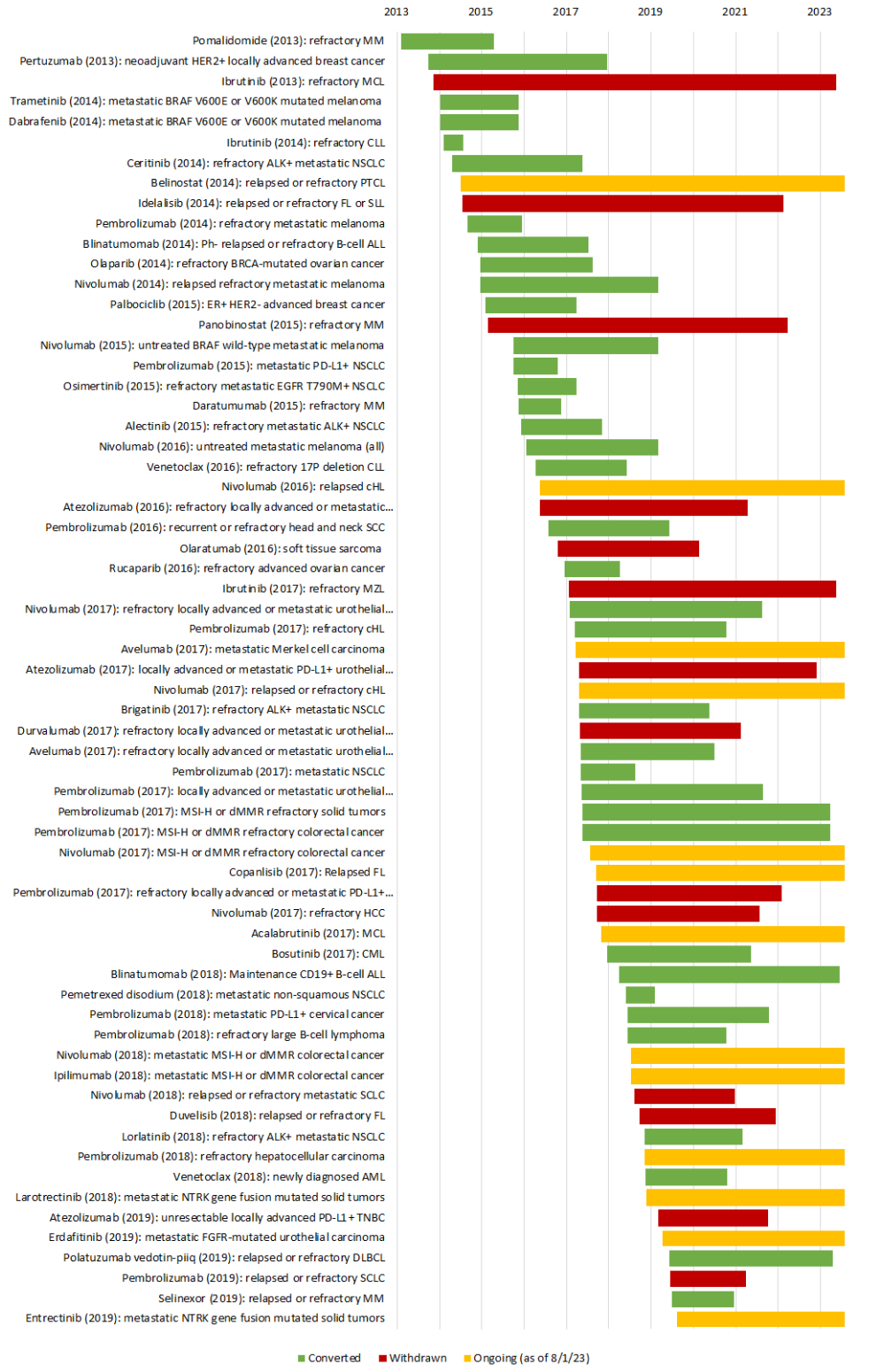
Supplemental Online Content

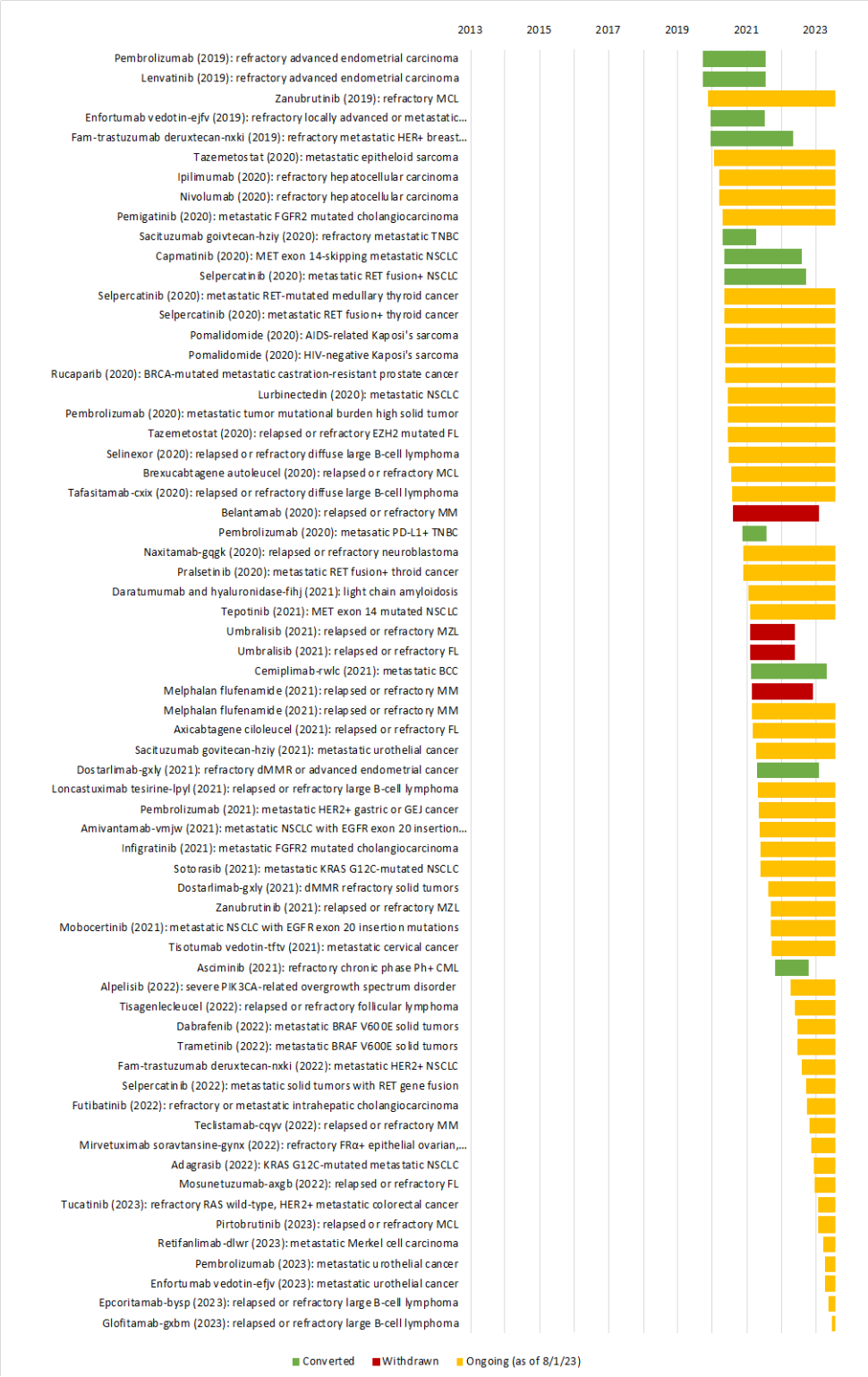
Liu ITT, Kesselheim AS, Cliff ERS. Clinical benefit and regulatory outcomes of cancer drugs receiving accelerated approval. *JAMA*. doi:10.1001/jama.2024.2396

This supplemental material has been provided by the authors to give readers additional information about their work.

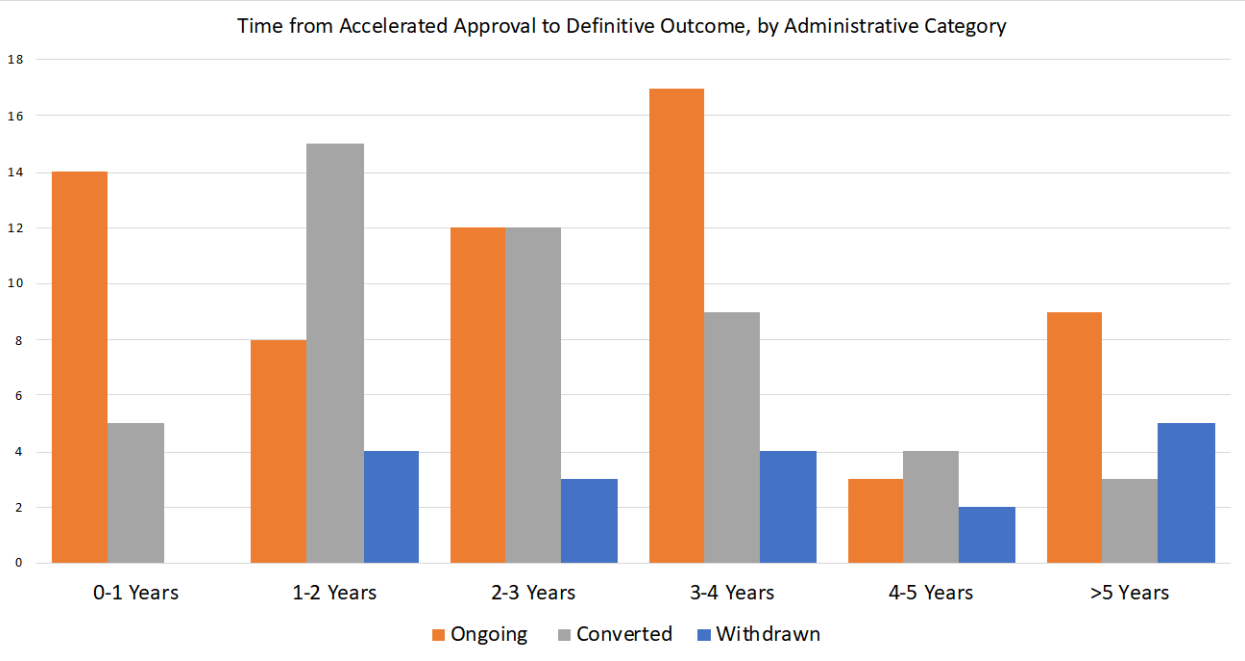
eFigure 1A. Cancer drugs granted accelerated approval between January 2013 and July 2023 and administrative status.



eFigure 1B. Cancer drugs granted accelerated approval between January 2013 and July 2023 and administrative status.

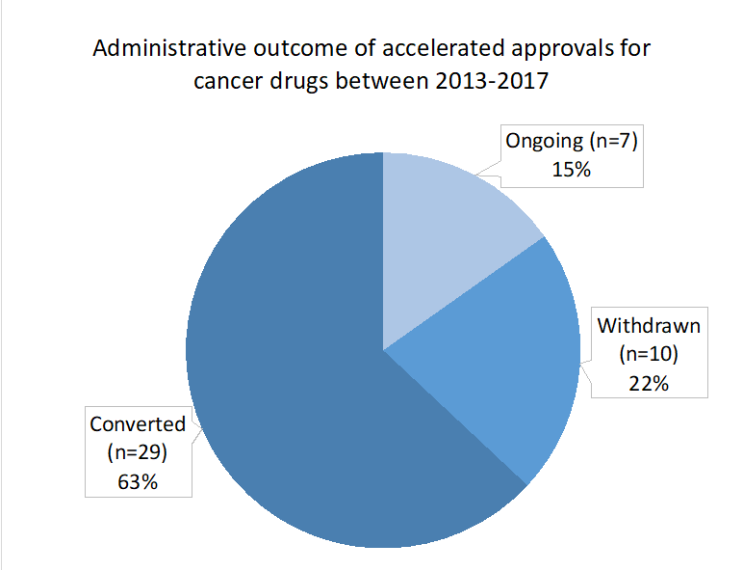


eFigure 2. Time from accelerated approval to definitive outcome for cancer drugs granted accelerated approval between 2013 and August 2023, by administrative status.

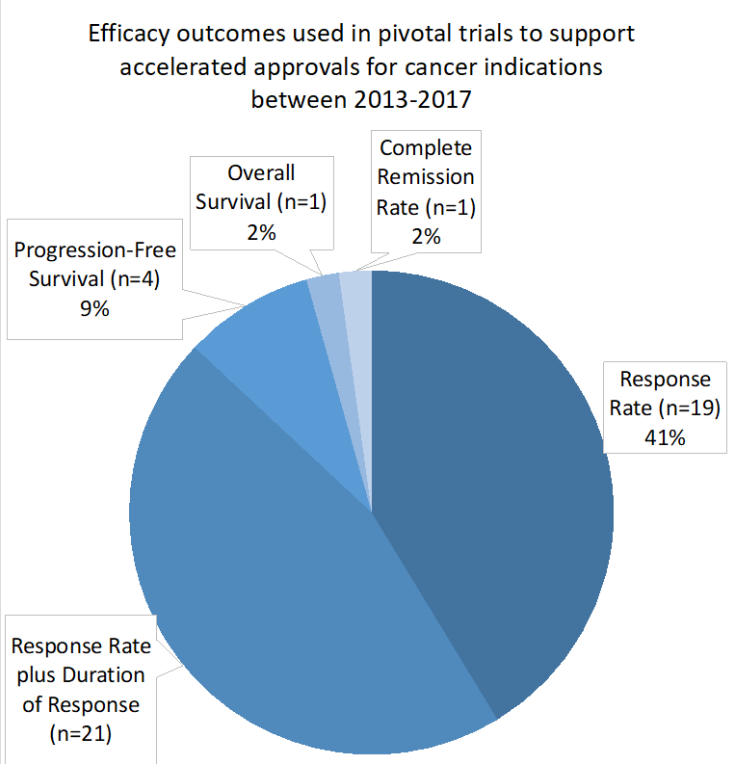


Note: Definitive outcome date for “ongoing” accelerated approvals set at August 1, 2023.

eFigure 3A. Administrative outcome of accelerated approvals for cancer drugs between 2013-2017.



eFigure 3B. Efficacy outcomes used in pivotal trials to support accelerated approvals for cancer indications between 2013-2017.



eFigure 4. Projected time to required study completion following accelerated approval for cancer indications approved between 2013-2017.

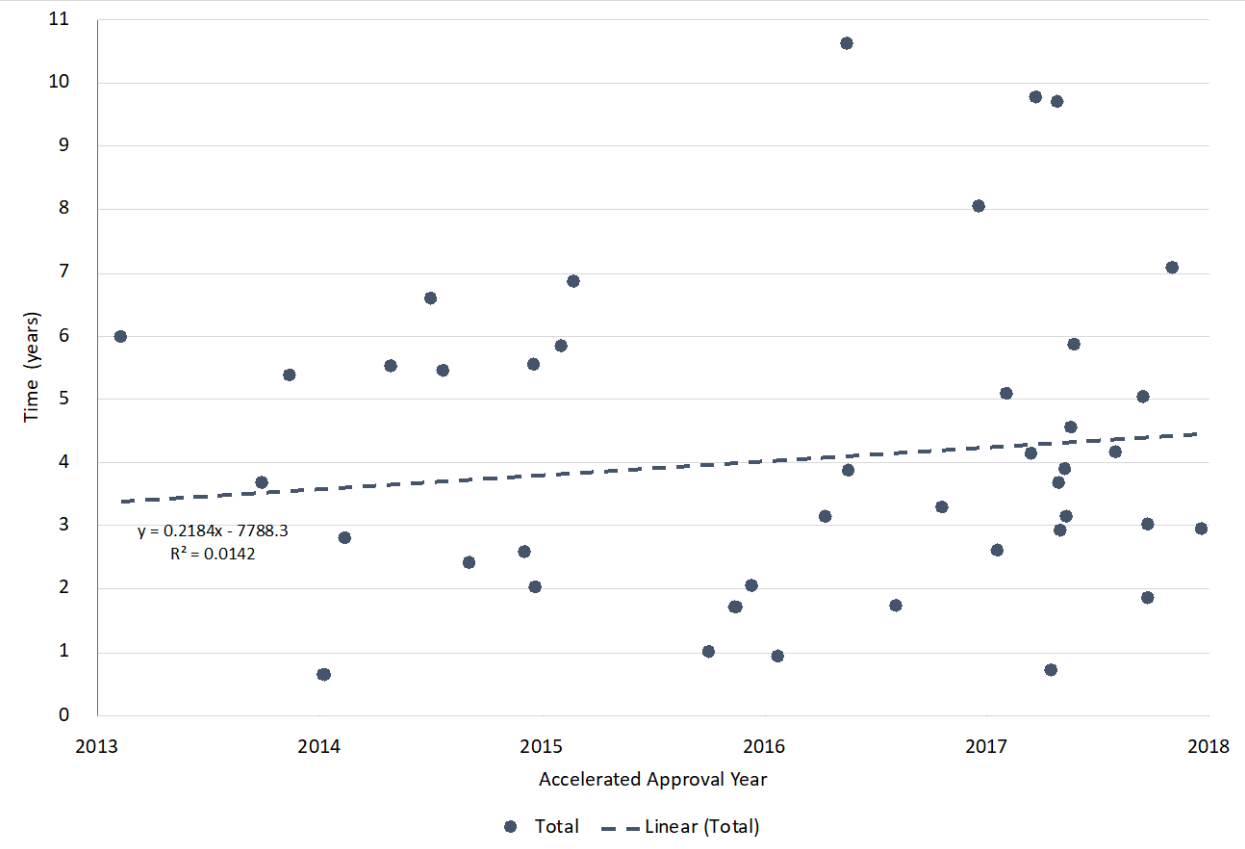


Figure legend: The duration from accelerated approval to projected confirmatory trial completion at the time of initial approval increased from 3.4 years for approvals in 2013 to 4.5 years in 2017 accelerated approvals.

eFigure 5. Time between accelerated approval and definitive outcome for cancer indications approved between 2013 and 2017.

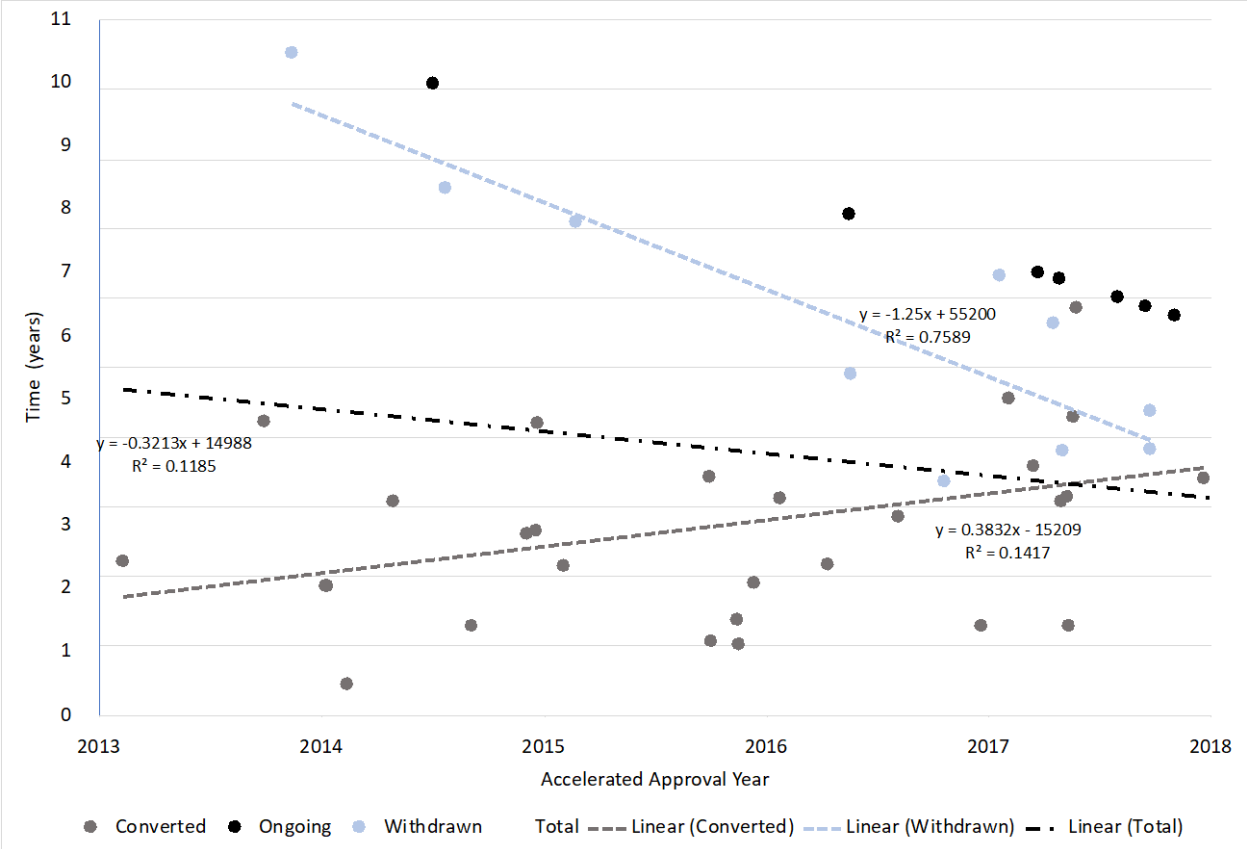


Figure legend: For the 29 converted indications, duration from accelerated approval to conversion increased from 1.6 years in 2013 to 3.6 years in 2017 approvals. For the 10 withdrawn indications, the duration between accelerated approval and withdrawal date decreased from 9.9 years in 2013 to 3.6 years in 2017.

eFigure 6. Difference between projected and actual definitive outcome for accelerated approval cancer indications approved between 2013-2017.

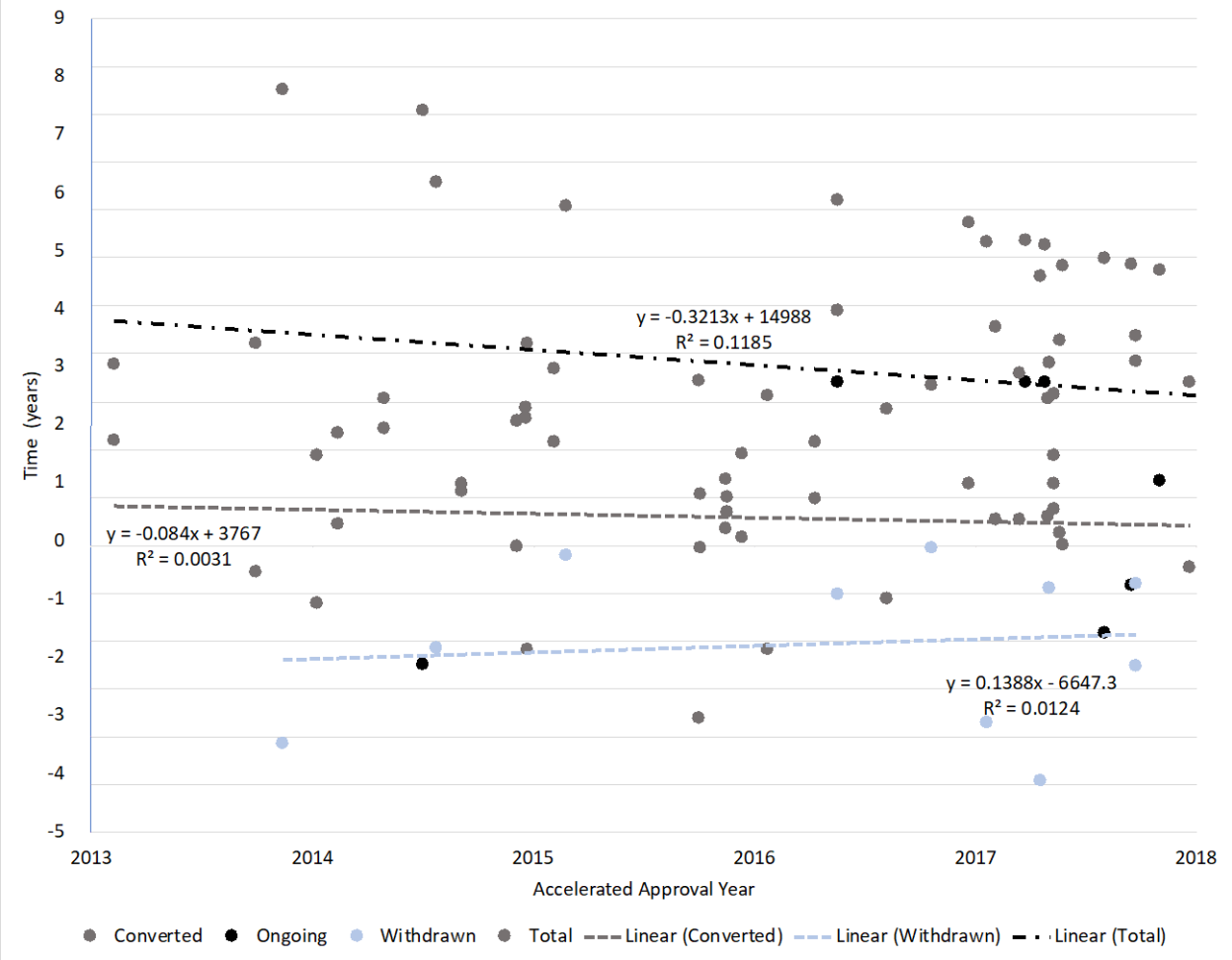
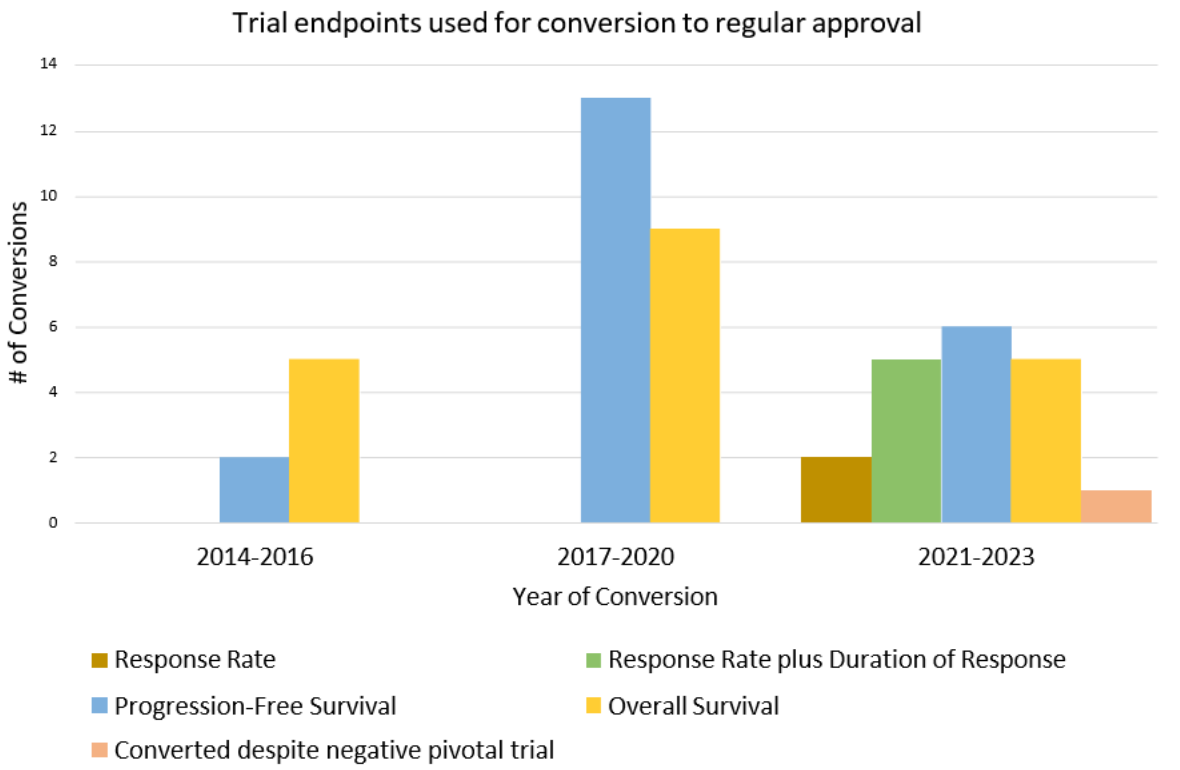


Figure legend: The time from projected trial completion to withdrawal or conversion narrowed slightly over time (50 days/year).

eFigure 7. Confirmatory trial endpoints used for conversion to regular approval



Accelerated approvals for cancer indications converted to regular approval with trial endpoint used to support conversion.

eTable 1. Clinical benefit of accelerated approval drug-indication pairs granted between 2013 and 2017, later converted to regular approval, no. (%)

	All converted indications (n=29)	Original indications (n=14)	Supplemental indications (n=15)
Confirmed overall survival or quality of life benefit	20 (69)	11 (79)	9 (60)
No confirmed overall survival or quality of life benefit	9 (31)	3 (21)	6 (40)

e**Table 2.** Examples of indication changes between accelerated and regular approval.

Category	Drug name	Accelerated approval indication	Regular approval indication	Summary of change(s)
Same indication /no change	Bosutinib	Adults with newly-diagnosed chronic phase Philadelphia chromosome positive chronic myeloid leukemia		None
Earlier line of therapy	Alectinib	Anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) that progressed on or is intolerant to crizotinib	ALK-positive metastatic NSCLC, as detected by an FDA-approved test	2nd line to 1st line
Broadened – not earlier line of therapy	Venetoclax	Chronic lymphocytic leukemia (CLL) with 17p deletion as detected by an FDA-approved test, after at least one prior therapy	Chronic lymphocytic leukemia or small lymphocytic lymphoma, with or without 17p deletion, who have received at least one prior therapy	Includes CLL without 17p deletion, remains 2nd line (Note: Subsequently also approved in the 1st line setting)
Narrowed	Pemetrexed disodium	In combination with pembrolizumab and carboplatin for first-line treatment of metastatic non-squamous NSCLC	In combination with pembrolizumab and platinum chemotherapy for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.	Narrowed to patients whose tumors do not have EGFR or ALK mutations
Other	Pembrolizumab	Metastatic PD-L1 positive NSCLC, as determined by an FDA-approved test, with progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab.	Patients with metastatic NSCLC whose tumors have high PD-L1 expression (Tumor Proportion Score (TPS) ≥50%), with no EGFR or ALK genomic tumor aberrations, and no prior chemotherapy for metastatic NSCLC; and patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%), with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression for these aberrations prior to pembrolizumab.	Moved from second to first line, but only for patients whose disease has high PD-L1 expression (≥50%)

eTable 3. Indications of oncology drugs receiving accelerated and regular approval between January 2013 and converted by July 2023

Brand name (generic name)	Accelerated approval indication	Regular approval indication	Indication change category
Bosulif (bosutinib)	Adults with newly diagnosed chronic phase Philadelphia chromosome positive CML	Adults with newly-diagnosed chronic phase Ph+ chronic myelogenous leukemia (CML)	Same
Keytruda (pembrolizumab)	Treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options	adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options	Same
Keytruda (pembrolizumab)	Metastatic MSI-H or dMMR colorectal cancer that have progressed following treatment with a fluoropyrimidine, oxaliplatin and irinotecan	First-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.	Earlier line
Keytruda (pembrolizumab)	For patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy and locally-advanced or metastatic urothelial carcinoma ineligible for cisplatin-containing chemotherapy	for the treatment of patients with locally-advanced or metastatic urothelial carcinoma who: are not eligible for any platinum-containing chemotherapy, or who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum- containing chemotherapy.	Same
Keytruda (pembrolizumab)	In combination with pemetrexed and carboplatin for first-line treatment of metastatic non-squamous NSCLC	In combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.	Narrowed
Bavencio (avelumab)	Locally-advanced or metastatic urothelial carcinoma following disease progression on platinum-containing chemotherapy or disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy	Patients with locally-advanced or metastatic urothelial carcinoma who: • Have disease progression during or following platinum-containing chemotherapy. • Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	Same
Alunbrig (brigatinib)	Patients with ALK-positive metastatic NSCLC that have progressed or are intolerant to crizotinib	treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.	Earlier line
Keytruda (pembrolizumab)	Adult and pediatric patients with refractory classical Hodgkin	for the treatment of adult patients with relapsed or	Earlier line

	Lymphoma or who have relapsed after 3 or more prior lines of therapy	refractory cHL. (1.5) • for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.	
Opdivo (nivolumab)	locally-advanced or metastatic urothelial carcinoma that: • progressed during or following platinum-containing chemotherapy • progressed within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy	patients with locally-advanced or metastatic urothelial carcinoma who: • have disease progression during or following platinum-containing chemotherapy • have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	Same
Rubraca (rucaparib)	Deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer treated with 2 or more chemotherapies and whose tumors have a specific gene mutation (deleterious BRCA) as identified by and FDA-approved companion diagnostic test	for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. (1.1) • for the treatment of adult patients with deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for RUBRACA.	Broadened-not earlier line
Keytruda (pembrolizumab)	Recurrent or metastatic head and neck squamous cell carcinoma that progressed on or after platinum-containing chemotherapy	in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC. (1.3) · as a single agent for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test. (1.3, 2.1)	Earlier line
Venclexta (venetoclax)	Chronic lymphocytic leukemia with 17P deletion as detected by an FDA-approved test, after at least one prior therapy	For the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy.	Broadened-not earlier line
Opdivo (nivolumab)	Unresectable or metastatic melanoma and progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor	for the treatment of patients with unresectable or metastatic melanoma, as a single agent or in combination with (ipilimumab).	Earlier line
Opdivo (nivolumab)	1) In combination with ipilimumab for unresectable or	for the treatment of patients with unresectable or metastatic	Earlier line

	metastatic melanoma to remove the restriction for treatment of only patients with BRAF wild-type melanoma; 2) As a single agent for BRAF V600 mutation positive unresectable or metastatic melanoma to remove the restriction that such patients should have disease progression following ipilimumab and a BRAF inhibitor	melanoma, as a single agent or in combination with (ipilimumab).	
Alecensa (alectinib)	ALK-positive metastatic NSCLC that progressed on or is intolerant to crizotinib	for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test	Earlier line
Darzalex (daratumumab)	Multiple myeloma after at least 3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent or double refractory to a proteasome inhibitor and an immunomodulatory agent	combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.	Earlier line
Tagrisso (osimertinib)	Metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, that progressed on or after EGFR TKI therapy	treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.	Same
Keytruda (pembrolizumab)	Metastatic PD-L1 positive NSCLC, as determined by an FDA-approved test, with progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.	patients with metastatic NSCLC whose tumors have high PD-L1 expression [(Tumor Proportion Score (TPS) ≥50%)] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC. (1.2) · patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA	Other
Opdivo (nivolumab)	In combination with ipilimumab for BRAF V600 wild-type unresectable or metastatic melanoma	for the treatment of patients with unresectable or metastatic melanoma, as a single agent or in combination with (ipilimumab).	Broadened-not earlier line
Ibrance (palbociclib)	In combination with letrozole for postmenopausal women	treatment of hormone receptor (HR) positive, human epidermal	Same

	with ER-positive, HER2-negative advanced breast cancer as initial endocrine-based therapy for metastatic disease	growth factor receptor 2 (HER2) negative advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women.	
Lynparza (olaparib)	Deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer after treatment with 3 or more lines of chemotherapy 2	for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy.	Earlier line
Blincyto (blinatumomab)	Philadelphia chromosome negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia	for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.	Broadened-not earlier line
Keytruda (pembrolizumab)	Unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor	patients with unresectable or metastatic melanoma	Earlier line
Zykadia (ceritinib)	ALK-positive metastatic NSCLC that progressed on or is intolerant to crizotinib	for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.	Earlier line
Imbruvica (ibrutinib)	Chronic lymphocytic leukemia after at least one prior therapy	for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy.	Same
Tafinlar (dabrafenib)	In combination with trametinib for unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test	indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test	Same
Mekinist (trametinib)	In combination with dabrafenib for unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test	indicated, in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test	Same
Perjeta (pertuzumab)	In combination with trastuzumab and docetaxel for neoadjuvant treatment of HER2-positive locally-advanced inflammatory or early-stage breast cancer (either greater than 2 cm in diameter or node-positive) as part of a complete treatment regimen for early breast cancer	For use in combination with trastuzumab and chemotherapy: as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence, and neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer	Broadened-not earlier line
Pomalyst (pomalidomide)	Multiple myeloma after at least 2 prior therapies including lenalidomide and bortezomib	for patients with multiple myeloma who have received at least two prior therapies includ-	Same

	and disease progression on or within 60 days of completion of the last therapy	ing lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.	
Blincyto (blinatumomab)	Treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children 1	for the treatment of adults and pediatric patients with CD19-positive B-cell precursor acute lymphoblastic leukemia (B-ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%,	Same
Alimta (pemetrexed disodium)	In combination with pembrolizumab and carboplatin for first-line treatment of metastatic non-squamous NSCLC	in combination with pembrolizumab and platinum chemotherapy for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.	Narrowed
Keytruda (pembrolizumab)	Treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS >/=1) as determined by an FDA approved test	in combination with chemotherapy, with or without bevacizumab, for patients with persistent, recurrent or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1), as determined by an FDA-approved test and as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.	Broadened-not earlier line
Keytruda (pembrolizumab)	Adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma, or who have relapsed after 2 or more prior lines of therapy	adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) and pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.	Earlier line
Lorbrena (lorlatinib)	ALK-positive metastatic NSCLC that has progressed on: • Crizotinib and at least one other ALK inhibitor for metastatic disease; or • Alectinib as the first ALK inhibitor therapy for metastatic disease; or • Ceritinib as the first ALK inhibitor therapy for metastatic disease	patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive, detected by an FDA-approved test.	Earlier line
Venclexta (venetoclax)	In combination with azacitidine or decitabine or low-dose cytarabine for newly-diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy	in combination with azacitidine, decitabine, or low-dose cytarabine (LDAC) for newly-diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities precluding intensive induction chemotherapy.	Same
Polivy (polatuzumab vedotin-piiq)	In combination with bendamustine and a rituximab product for adult patients with	with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for	Earlier line

	relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies.	adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index (IPI) score of 2 or greater	
Xpovio (selinexor)	In combination with dexamethasone for adults with relapsed/refractory multiple myeloma after at least 4 prior therapies and refractory to at least 2 proteasome inhibitors, 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody	in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.	Earlier line
Keytruda (pembrolizumab)	In combination with lenvatinib for advanced endometrial carcinoma not MSI-H or dMMR, with progression following systemic therapy and not candidates for curative surgery or radiation	combination with lenvatinib (Lenvima, Eisai) for patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.	Same
Lenvima (lenvatinib)	In combination with pembrolizumab for advanced endometrial carcinoma not MSI-H or dMMR, with progression following systemic therapy and not candidates for curative surgery or radiation	combination with pembrolizumab for patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.	Same
Padcev (enfortumab vedotin-ejfv)	Adults with locally-advanced or metastatic urothelial cancer who received a PD-1 or PD-L1 inhibitor and a platinum-containing chemotherapy in the neoadjuvant, locally-advanced, or metastatic setting	for adult patients with locally-advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.	Broadened-not earlier line
Enhertu (Fam-trastuzumab deruxtecan-nxki)	Adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting	for adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy.	Earlier line

Trodelvy (sacituzumab govitecan-hziy)	Adults with metastatic TNBC following at least 2 prior therapies for metastatic disease	for patients with unresectable locally-advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.	Earlier line
Tabrecta (capmatinib)	Adult patients with mNSCLC whose tumors have a mutation that leads to MET exon 14 skipping as detected by an FDA-approved test	for adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation leading to mesenchymal-epithelial transition (MET) exon 14 skipping, as detected by an FDA-approved test.	Same
Retevmo (selpercatinib)	Adult patients with metastatic RET fusion-positive Non-Small Cell Lung Cancer (NSCLC)	Adult patients with locally advanced or metastatic non-small cell lung cancer with a RET gene fusion, as detected by an FDA-approved test	Broadened-not earlier line
Keytruda (pembrolizumab)	In combination with chemotherapy for locally recurrent unresectable or metastatic TNBC expressing PD L1 [CPS =10] as determined by an FDA-approved test	for high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.	Earlier line
Libtayo (cemiplimab-rwlc)	Patients with metastatic basal cell carcinoma (mBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate	for the treatment of patients with metastatic basal cell carcinoma who previously received a hedgehog inhibitor (HHI) or for whom a HHI is not appropriate	Same
Jemperli (dostarlimab-gxly)	Adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer (EC), as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen.	For adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following a prior platinum-containing regimen in any setting and are not candidates for curative surgery or radiation.	Narrowed – excludes patients who are candidates for curative surgery or radiation
Scemblix (asciminib)	Adult patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with 2 or more tyrosine kinase inhibitors (TKIs)	Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs)	Same

eTable 4. Oncology drugs converted to regular approval on the basis of response rate or response rate plus duration of response.

Generic drug name	Regular approval indication	Endpoint(s) used for regular approval
Bosutinib	Newly-diagnosed chronic phase Philadelphia chromosome-positive chronic myelogenous leukemia	Major molecular response and complete cytogenetic response (both measured at 12 months)
Asciminib	Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase, previously treated with two or more tyrosine kinase inhibitors	Major molecular response and complete cytogenetic response (both measured at 24 and 96 weeks)
Selpercatinib	Locally advanced or metastatic solid tumors with a rearranged during transfection (RET) gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options	Overall response rate and duration of response
Dostarlimab-gxly	Mismatch repair deficient recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following a prior platinum-containing regimen in any setting and are not candidates for curative surgery or radiation	Overall response rate and duration of response
Pembrolizumab	Unresectable or metastatic microsatellite instability-high or mismatch repair deficient solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options	Overall response rate and duration of response
Capmatinib	Metastatic non-small cell lung cancer whose tumors have a mutation leading to mesenchymal-epithelial transition (MET) exon 14 skipping, as detected by an FDA-approved test	Overall response rate and duration of response
Cemiplimab-rwlc	Metastatic basal cell carcinoma who previously received a hedgehog inhibitor or for whom a hedgehog inhibitor is not appropriate	Overall response rate and duration of response

eTable 5. FDA-required post-marketing commitments for oncology drugs converted to regular approval since 2021 on the basis of response rate or response rate plus duration of response.

Drug	Required under	Description	Status	Explanation of Status
Bosutinib		No post-marketing commitments found.		
Asciminib	Accelerated Approval	PMR 4161-1: Conduct clinical study CABL001A2301 (ASCEMBL), A Phase 3, Multicenter, Open-label, Randomized Study of Oral ABL001 Versus Bosutinib in Patients with Chronic Myelogenous Leukemia in Chronic Phase (CMLCP), Previously Treated With 2 or More Tyrosine Kinase Inhibitors and provide the interim report with at least 24 months (96 weeks) follow-up of all patients to describe and confirm the clinical benefit of asciminib.	Fulfilled	Per FDA letter dated 10/12/2022, this PMR has been fulfilled.
	N/A	PMC 4348-1: Complete Study ASCEMBL to obtain data on long-term efficacy and safety of asciminib in patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs). Provide data at the end of treatment period on safety and efficacy, and at the end of the 5-year follow up period (overall survival and progression-free survival).	Ongoing	
Selpercatinib	Accelerated Approval	PMR 3829-1: Submit the final report including datasets from a multi-center, randomized trial comparing selpercatinib to physician's choice of approved therapies in patients with kinase inhibitor-naïve, progressive, advanced or metastatic RET-mutant medullary thyroid cancer to confirm clinical benefit of selpercatinib with progression-free survival as a key secondary end point as assessed by blinded independent central review.	Ongoing	The trial has been initiated.
	Accelerated Approval	PMR 3829-3: Submit a final report including datasets, to verify and further characterize the clinical benefit of selpercatinib for the treatment of patients with RET fusion-positive thyroid cancer who have received radioactive iodine (if appropriate for their tumor histology) to provide a more precise estimation of the BICR-assessed overall response rate and duration of response in at least 50 patients after all responding patients have been followed for 12 months following onset of response or until disease progression, whichever comes first.	Ongoing	The trial has been initiated.
	Accelerated Approval	PMR 4342-1: Complete clinical trial(s) to obtain data on the clinical efficacy of selpercatinib through more precise estimation of the overall response rate and mature response duration per independent review assessment, in at least 60 patients with locally advanced or metastatic RET-fusion positive solid tumors other than non-small cell lung cancer and thyroid cancer, who have progressed on prior systemic treatment or have no satisfactory alternative treatment options. A sufficient number of patients with tumor types for which responses require additional characterization (e.g., colorectal cancer, esophagogastric cancer, and glioma) will be evaluated. Overall response rate and duration of response will be assessed by independent central review and all responding patients will be followed for at least 12 months following the onset of response or until disease progression or death or early treatment discontinuation, whichever comes first. Include available data regarding RET fusion	Pending	The study has not been initiated, but it does not meet the criterion for delayed.

		partners and cooccurring genetic alterations for all patients.		
Dostarlimab-gxly	Accelerated Approval	PMR 3909-1: Submit the final report and datasets from a clinical trial evaluating overall response rate, and duration of response, to verify and describe the clinical benefit of dostarlimab in patients with mismatch repair deficient (dMMR), recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen, in a sufficient number of patients. In order to characterize response rate and duration of response, patients will be followed for at least 12 months from the onset of response. Alternatively, submit the final report and datasets from a randomized, phase 3 clinical trial that verifies and describes the clinical benefit of dostarlimab in patients with recurrent or primary advanced endometrial cancer. Patients should be randomized to receive chemotherapy with or without dostarlimab. The primary endpoint should be progression-free survival, with secondary endpoints that include overall survival and objective response rate	Fulfilled	Per FDA letter dated 02/09/2023, this PMR has been fulfilled
	Accelerated Approval	PMR 4124-1: Conduct a clinical trial evaluating overall response rate, and duration of response, to verify and describe the clinical benefit of Jemperli in patients with mismatch repair deficient (dMMR), recurrent or advanced solid tumors, including at least 300 patients across all tumor types, and including a sufficient number of patients and representation of tumor types (other than endometrial and gastrointestinal tumors). In order to characterize response rate and duration of response, patients should be followed for at least 12 months from the onset of response. Submit the datasets with final report.	Delayed	The applicant requested revised milestones because additional time is needed to enroll at least 100 patients with non-endometrial cancer/non-gastrointestinal tumors, as requested by FDA. Revised milestones were acknowledged in a letter dated 10/28/2022.
	N/A	PMC 4481-1: Complete the ongoing clinical trial, RUBY Part 1, titled “A Phase 3, Randomized, Double-blind, Multicenter Study of Dostarlimab (TSR-042) plus Carboplatin-paclitaxel versus Placebo plus Carboplatin-paclitaxel in Patients with Recurrent or Primary Advanced Endometrial Cancer (RUBY)”, to provide the pre-specified interim and final overall survival (OS) analyses.	Ongoing	
	Accelerated Approval	PMR 4124-1: Conduct a clinical trial evaluating overall response rate, and duration of response, to verify and describe the clinical benefit of Jemperli in patients with mismatch repair deficient (dMMR), recurrent or advanced solid tumors, including at least 300 patients across all tumor types, and including a sufficient number of patients and representation of tumor types (other than endometrial and gastrointestinal tumors). In order to characterize response rate and duration of response, patients should be followed for at least 12 months from the onset of response. Submit the datasets with final report.	Delayed	The applicant requested revised milestones because additional time is needed to enroll at least 100 patients with non-endometrial cancer/non-gastrointestinal tumors, as requested by FDA. Revised milestones were acknowledged in a letter dated 10/28/2022.
	N/A	PMC 4124-2: Commitment to establish and support the availability of a nucleic acid based in vitro	Ongoing	

		diagnostic device that is essential to support the safe and effective use of Jemperli for patients with tumors that are microsatellite instability high (MSI-H) through an appropriate analytical and clinical validation study using clinical trial data. Summarize the study results in the final report submission.		
Pembrolizumab	Accelerated Approval	PMR 3213-1: Submit the final report, including datasets, from trials conducted to verify and describe the clinical benefit of pembrolizumab 200 mg intravenously every three weeks in patients with microsatellite instability high or mismatch repair deficient tumors including at least 124 patients with colorectal cancer enrolled in Merck initiated trials; at least 300 patients with non-colorectal cancer, including a sufficient number of patients with prostate cancer, thyroid cancer, small cell lung cancer; and ovarian cancer; and 25 children. In order to characterize response rate and duration, patients will be followed for at least 12 months from the onset of response.	Fulfilled	Per FDA letter dated 03/28/2023, this PMR has been fulfilled.
	Accelerated Approval	PMR 3871-1: Submit the final report and datasets from clinical trials evaluating overall response rate and duration of response, to verify and describe the clinical benefit of pembrolizumab in adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [=10 mutations/megabase (mut/Mb)] solid tumors (as determined by an FDA-approved test) that have progressed following prior treatment and who have no satisfactory alternative treatment options. A sufficient number of patients and representation of tumor types (other than lung cancers, MSIH or dMMR cancers, or melanoma; and including CNS tumors that were determined to be TMB-H based on testing of tissue obtained prior to initiation of temozolomide chemotherapy), and with cancers having a TMB of 10 to <13 mut/Mb, will be evaluated to characterize response and duration of response. A minimum of 20 pediatric patients will be studied. Overall response rate and duration of response will be assessed by independent central review for patients with cancers having a TMB of =10 mut/Mb, =10 mut/Mb to <13 mut/Mb, and =13 mut/Mb. All responding patients will be followed for at least 12 months from the onset of response.	Ongoing	The trial has been initiated.
Capmatinib		No postmarketing commitments found.		
Cemiplimab	Accelerated Approval	PMR 4012-1: Submit the report and datasets for the 53 patients with metastatic basal cell carcinoma (mBCC) from clinical study R2810 ONC 1620 evaluating objective response rate and duration of response, to verify and describe the clinical benefit of cemiplimab in patients with mBCC who experienced progression of disease on hedgehog pathway inhibitor therapy or were intolerant of prior hedgehog pathway inhibitor therapy. To further characterize the magnitude and durability of responses in patients with mBCC, all patients will have the opportunity for 57 weeks of follow-up following completion of cemiplimab-rwlc.	Fulfilled	Per FDA letter dated 04/28/2023, this PMR has been fulfilled
	N/A	PMC 4012-2: Submit the final analysis of objective response rate and duration of response for the 53 patients with metastatic basal cell carcinoma (mBCC) from clinical study R2810 ONC 1620, in order to further characterize the durability of response in this cohort. For the analysis, all patients will have the	Ongoing	

		opportunity for at least 1.5 years of follow-up following completion of cemiplimab-rwlc treatment. The study results may inform product labeling.		