Parexel analysis of 12 novel cell and gene therapies (CAGTs) approved in 18 indications by FDA, 2017-2022

CAGTs uniformly qualified for orphan drug and breakthrough therapy designations, targeted heavily pretreated cancers and genetic diseases, and took a median of 6.9 years from Phase 1 trials to FDA approval

Trade Name (generic) **Drug Class** (molecular target)	**FDA Programs for Potentially Expedited Clinical Development**				**FDA Programs for Potentially Expedited Regulatory Review**				**FIH Trial Start or FDA IND Filing Date**	**FDA Approval Date**	**Development Time (Years)**	**First Approved In the U.S.**	**FDA-Approved Indication**
	FT	**OD**	**AA**	**BTD**	**PR**	**1st Cycle Review**	**Other Regulatory Programs**	**RPDPRV**					
Kymriah (tisagenlecleucel) **CAR T-cell therapy - Autologous** (CD19)		✓		✓	✓	✓	ODAC Meeting	✓	04/2012	**08/2017**	5.4	✓	patients 3-25 years with B-cell precursor acute lymphoblastic leukemia (B-ALL) r/r after 2 lines
sBLA #1		✓		✓	✓	✓			–	*05/2018*	–		*adults with LBCL, including DLBCL, r/r after 2 lines*
sBLA #2		✓	✓		✓	✓	*Assessment Aid, RMAT*		–	*05/2022*	–		*adults with follicular lymphoma (FL) r/r after 2 lines*
Yescarta (axicabtagene ciloeucel) **CAR T-cell therapy - Autologous** (CD19)		✓		✓	✓	✓	OCE-CBER review		11/2008	**10/2017**	8.9	✓	adults with LBCL including DLBCL r/r after 2 lines
sBLA #1		✓	✓	✓	✓				–	*03/2021*	–		*adults with r/r follicular lymphoma (FL) after 2 lines*
sBLA #2		✓		✓	✓		*Assessment Aid*		–	*04/2022*	–		*adults with LBCL r/r after 1st line chemotherapy*
Luxturna (onasemnogene abeparvovecl) **Gene therapy – AAV2 vector** (hRPE65)		✓		✓	✓	✓		✓	06/2007	**12/2017**	10.5	✓	patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy
Zolgensma (pralsetinib) **Gene therapy – AAV9 vector** (SMN1)	✓	✓		✓	✓	✓		✓	08/2013	**05/2019**	5.8	✓	children under 2 years with spinal muscular atrophy (SMA) with bi-allelic SMN1 mutations
Tecartus (brexucabtagene autoleucel) **CAR T-cell therapy - Autologous** (CD19)		✓	✓	✓	✓				10/2015	**07/2020**	4.8	✓	adult patients with r/r mantle cell lymphoma (MCL)
sBLA #1		✓		✓	✓		*Assessment Aid*		–	*10/2021*	–		*adults with r/r B-ALL*
Breyanzi (lisocabtagene maraleucel)* **CAR T-cell therapy - Autologous** (CD19)		✓		✓		✓	OCE-CBER review, RMAT		05/2015	**02/2021**	5.7	✓	adults with LBCL including DLBCL r/r after 2 lines
sBLA #1		✓		✓	✓		*RMAT*		–	*06/20 22*	–		*adults with LBCL r/r after 1st line chemotherapy or not eligible for HSCT*
Abecma (idecabtagene vicleucel) **CAR T-cell therapy - Autologous** (BCMA)		✓		✓	✓				09/2015	**03/2021**	5.5	✓	adults with r/r multiple myeloma after 4+ lines
Carvykti (ciltacabtagene autoleucel) **CAR T-cell therapy - Autologous** (BCMA)		✓		✓	✓	✓			10/2015	**02/2022**	6.4	✓	adults with r/r multiple myeloma after 4+ lines
Zynteglo (betibeglogene autotemcel) **Gene therapy – LV1 vector** (βA$^{(T87Q)}$-globin)	✓	✓		✓	✓	✓	CTGTAC Meeting	✓	12/2012	**08/2022**	9.7		adult and pediatric patients with beta-thalassemia who require regular red blood cell transfusions
Skysona (elivaldogene autotemcel) **Gene therapy – LV2 vector** (*ABCD1* cDNA)		✓	✓	✓	✓	✓	CTGTAC Meeting	✓	03/2013	**09/2022**	9.5		early active cerebral adrenoleukodystrophy (CALD)
Hemgenix (etranacogene dezaparvovec) **Gene therapy – AAV5 vector** (h-FIX Padua)		✓		✓	✓				06/2015	**11/2022**	7.4	✓	adults with Hemophilia B (congenital Factor IX deficiency)
Adstiladrin (nadofaragene firadenovec) **Gene therapy – AAV vector** (IFNα2b)	✓	✓		✓	✓		*Assessment Aid*		06/2005	**12/2022**	17.5	✓	adults with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive NMI bladder cancer
TOTALS	**3**	**12**	**2**	**12**	**11**	**8**		**5**		*Median:*	**6.9 yrs**	**10**	
% of novel CAGT approvals (n=12)	**25%**	**100%**	**17%**	**100%**	**92%**	**67%**		**42%**		*Mean:*	**8.1 yrs**	**83%**	

(1) LentiGlobin BB305 lentivirus
(2) Lenti-D

§ This chart includes all Biological License Applications (BLAs) approved by the FDA between January 1, 2017, and December 31, 2022, that were classified by the Center for Biologics Evaluation and Research (CBER) as either "autologous T cell immunotherapies" or "gene therapies." It includes original filings and supplemental BLAs (new indications).

Molecular Target Acronyms: *ABCD1* cDNA: adrenoleukodystrophy complementary DNA; βA(T87Q)-globin: beta-globin gene derivative; BCMA: B-cell maturation antigen; CD19: cluster of differentiation 19; h-FIX Padua: hyperactive factor IX variant R338L; hRPE65v2: human retinal pigment epithelium 65 protein; IFNα2b: human interferon alpha-2b; RPE65: human retinal pigment epithelium 65 protein; SMN1 — spinal muscular dystrophy 1 gene.

Sources & Methodology: Parexel compiled this proprietary analysis from primary FDA data sources, including clinical review memos and other review documents obtained from the FDA Biological Approvals by Year website, agency press releases, and other FDA databases, such as the Orphan Drug Designations and Approvals database. To determine the first-in-human (FIH) trial start date for cell and gene therapies that were developed ex-U.S. prior to the FDA IND filing, we relied on medical literature searches via PubMed and FIH clinical trials registered on clinical trials.gov. We also used the Federal Register database to search for "Determination of Regulatory Review Period for Purposes of Patent Extension" documents to confirm U.S. IND dates listed in FDA review documents, whenever possible.

Regulatory Acronyms and Terms: AAV: adeno-associated virus; AA: Accelerated Approval; Assessment Aid; BTD: Breakthrough Therapy Designation; CBER: Center for Biologics Evaluation and Research; CAGT: cell and gene therapy; CTGTAC: Cellular, Tissue, and Gene Therapies Advisory Committee; DLBCL: diffuse large B-cell lymphoma; FIH: first in human; FT: Fast Track; HSCT: hematopoietic stem cell transplant; IND: investigational new drug application; LBCL: large B-cell lymphoma; LV: lentiviral; NMI: non-muscle invasive; OCE: Oncology Center of Excellence; OD: Orphan Drug; ODAC: Oncology Drug Advisory Committee; PR: Priority Review; sBLA: supplementary Biologics License Application; r/r: relapsed or refractory; RMAT: regenerative medicine advanced therapy designation; RPDPRV: rare pediatric disease priority review voucher.