Recent RMAT Designations w/ Basis for Designations

parexel

Company/Product	Indication	Date of RMAT	Clinical Phase/Response Rates
UniQure's AMT-130 (single administration gene therapy)	Huntington's disease	6/3/2024	Based on 24-month interim data from P1/2 study (n=39 active cohort; 39 in nonconcurrent criteria-matched natural cohort): • Showing therapy resulted in 0.39-point difference on composite Unified Disease Rating Scale (cUHDRS) at 30 months and a 1.24-point difference at 18 months for the low- and high-dose groups, respectively (baseline values: LD 14.1; HD 14.9). • Therapy demonstrated 0.95-point difference on Total Functional Capacity (TFC) at 30 months in LD group and 0.49-point difference at 18 months in HD (baseline: LD 11.9; HD 12.2). • Active therapy group showed 2.80-point difference in Total Motor Score at 30 months at LD and 1.70 points at 18 months at HD (baseline: LD 13.3; HD 12.1).
Bluerock's bemdaneprocel (cell therapy—dopaminergic neuron precursors derived from embryonic stem cells)	Parkinson's	5/29/2024	Based on P1 study (n=12 Parkinson's patients) showing treatment well tolerated over 18 months and an observed F-DOPA PET imaging signal after stopping immune suppression therapy at 12 months, demonstrating that transplanted cells survive and engraft in the brain.
TScan's TSC-100 and TSC-101 (T cell receptor-engineered T cell therapies)	Patients w/ AML, ALL and MDS undergoing HCT w/ reduced intensity conditioning	5/29/2024	Based on "initial data" from P1 study (n=16) findings at median follow-up of >10 months: • All 8 patients treated with either TSC-100 (HA-1 positive patients) or TSC-101 (HA-2 positive patients) "remained relapse free with no detectable disease." • In contrast, 2 of 8 control-arm patients relapsed ~6 months post transplant and 1 died 3 months later. A third required clinical intervention due to impending relapse concerns, and a fourth died post transplant.
Cartesian's Descartes-08 (autologous mRNA CAR-T directed against BCMA	Myasthenia Gravis (MG)	5/22/2024	In ongoing P2b study (topline data expected mid-2024). In January 2024, Cartesian disclosed 1-year follow-up data for its P1b/2a study (n=14) in generalized MG patients who rec'd 1x weekly infusion for 6 weeks: • At Month 12, 5 of 7 patients on therapy maintained "clinically meaningful improvement in 4 validated MG disease scoring systems (MG Composite, MG Activities of Daily Living, Quantitative MG Scores and QoL 15-revised (at Month 9, 7/7 did). Two patients lost clinical effect at Month 12 and were eligible for retreatment. • All 3 patients with detectable AChR antibody levels at baseline saw "marked reductions" by Month 6, which deepened by Month 9, and were maintained at Month 12.
Pacira BioSciences' PCRX-201 (intra-articular helper-dependent adenovirus gene therapy coding for interleukin-1 receptor antagonist (IL-1Ra)	Knee osteoarthritis	3/13/2024	Supported by "preliminary safety and efficacy findings from P1 (n=72) open-label, single ascending dose study. • Efficacy observed in all 3 dose cohorts through at least 52 weeks, with highest efficacy achieved w/ co-administered steroid group that showed greater % of patients w/ at least 50% improvement in WOMAC pain and stiffness scores plus a meaningful improvement in KOOS functional assessment. • Company will present 52-week data in April 2024.
4D Molecular Therapeutics' 4D-150 (AAV gene therapy)	Intravitreal treatment of wet AMD (1st RMAT or BTD in wet AMD)	12/21/2023	Company stated RMAT "follows" interim P1 PRISM trial data demonstrating encouraging safety, tolerability and clinical activity. In July 2023, 4DMT announced: • Highest tested dose of 3E10 Vg/eye associated with a 100% reduction (4 of 4 evaluable patients) supplemental anti-VEGF injections at 36 weeks • Clinically meaningful reduction in mean central subfield thickness (CST) at 36 weeks in patients w/ a high anti-VEGF need • High-dose cohort also showed durable reduction in supplemental anti-VEGF injections beyond 36 weeks, w/ 3 of 4 evaluable participants remaining injection-free beyond 1 year and 1 patient remaining injection free during a maximum follow-up of 80 weeks.
Ocugen's OCU400 (gene therapy)	Retinitis pigmentosa assoc. w/ RHO mutations	12/19/2023	Appears based on "preliminary" data from P1/2 OCU400-101 study (n-18) in RP and Leber congenital amaurosis. Release states that "latest clinical study update" found that 86% (6/7) of RHO mutation subjects experienced either stabilization or improvement in Multi-Luminance Mobility Test (MLMT) scores from baseline, among which 29% (2/7) demonstrated 2 Lux luminance level improvement.
Atsena's ATSN-101 (gene therapy)	Leber congenital amaurosis (inherited retinal disease) caused by biallelic mutations in GUCY2D (LCA1)	11/14/2023	Based on positive 6-month efficacy data from ongoing P1/2 study (n=15), with 3 adult cohorts in ascending doses, plus 6 additional patients receiving high dose in dose-expansion phase: • Among 9 patients receiving high dose, mean change from baseline in retinal sensitivity by dark-adapted full-field stimulus testing was significantly greater in treated vs. untreated eyes. • 2 high-dose patients demonstrated best corrected visual acuity improvement greater than 0.3 logMAR and none had decrease in BCVA. • Of 5 high-dose patients tested w/ Multi-Luminance Mobility Test (MLMT), 4 demonstrated either a maximum MLMT score of 6 or at least a 2-level improvement compared to baseline when available or to untreated fellow eye.
Immatics' ACTengine IMA203 TRC-T Monotherapy (TCR-T cell therapy comprising autologous modified T cells)	For multiple relapsed and/or refractory HLA-A*02:01-positive and PRAME-expressing cancers (including cutaneous melanoma, uveal melanoma, endometrial carcinoma, synovial sarcoma, and ovarian cancer)*	10/24/2023	Appears based on ongoing P1 study. On 11/8/2023, company reported update on P1a dose escalation (n=27) and P1b (n=18): Phase 1a in 26 solid cancers: • 48% (13/27) ORR • 19% (5/27) confirmed ORR Phase 1b (Cohort A at RP2D) (n=18) in 18 solid cancers: • 50% (9/18) ORR • 47% (8/17) confirmed ORR
Editas' EDIT-301 (gene editing)	Severe sickle cell disease	10/16/2023	Appears based on RUBY, a single-arm, open-label P1/2 study (n=11). On 12/11/2023, company announced: • All patients free of vaso-occlusive events post infusion • All RUBY patients w/ at least 5 months follow-up had achieved a normal hemoglobin level and fetal hemoglobin level of >40% (N=6; range 5-18 months follow-up) • All treated patients w/ >1 months of follow-up followed similar trajectory of total hemoglobin and fetal hemoglobin increases (n=10)
Regenexbio's RGX-121 (gene therapy)	Hunter Syndrome (MPSII)	5/24/2023	Appears based on positive interim biomarker data from P1/2 portion (n=15 patients) of P1/2/3 trial showing dose-dependent reductions of glycosaminoglycans (GAG)** in cerebral spinal fluid (CSF). • At Week 48, median reduction of CSF heparin sulfate (HS) from baseline was 33.5%, 48.9%, and 64.7% in Cohorts 1, 2, and 3, respectively.
Rocket's RP-L301 (gene therapy)	Pyruvate kinase deficiency (rare blood disorder)	5/23/2023	Based on data from ongoing P1 study (n=2) showing "robust efficacy in both adult patients for up to 30 months: • Normalized hemoglobin (from baseline levels in the 7.0-7.5g/dL range), improved hemolysis parameters and red blood cell transfusion independence. • First pediatric patient infusion suggests similar efficacy to both adults (hemoglobin normalized 6 wks post-infusion and measured 13.4 g/dL at 8 wks, from a median baseline of 7.9 g/dL).
Humacyte's human accelular vessel (HAV)	For urgent arterial repair following extremity vascular trauma	5/4/2023	Based on P2/3 study in 66 patients, with 49 patients comprising primary endpoint population, showing improved HAV patency (presence of blood vessels) vs. historic benchmarks (literature). BLA planned later in 2023. In 9/2023, Humacyte released top-line P2/3 study results: • 30-day secondary patency – 90.2% for extremity patients vs. 81.1% historically for synthetic grafts • Primary patency for extremity patients was 84.3% (no comparison) • Secondary comparison of amputation rates: HAV 9.8% rate vs. 20.6% for synthetic grafts historically • Infection rates: 2.0% for extremity patients (HAV) vs 8.9% historically for synthetic grafts
Intellia's NTLA-2002 (1-time in vivo CRISPR therapy to inactivate target gene KLKB1)	Hereditary angioedema (HEA)	3/21/2023	Based on interim results from P1 open-label portion of P1/2 study (n=10) showing deep, dose-related reductions in plasma kallikrein*** across 3 doses, ranging from 64% (25 mg) to 92% (75 mg), with mean HAE attack rate reductions of 91%/89% (Week 1-16/Week 5-16) at 25 mg dose (n=3) and 78%/89% (Week 1-16/Week 5-16) at 75 mg dose (n=3).
IASO's equecabtagene Autoleucel (CAR T-cell therapy)	Relapsed/refractory MM	2/12/2023 (announced w/ FT grant) (US IND cleared 12/22)	Single-arm P1/2 study (n=79 patients receiving recommended P2 dose) in China, showing ORR of 94.9% at median follow-up of 9 months w/ median response time of only 16 days. 73 (92.4%) of patients achieved at least one negative minimal residual disease status after cell infusion.
Mesoblast's rexlemestrocel-L in comb w/ hyaluronic acid as delivery agent (allogeneic cell therapy)	Chronic lower back pain (CLBP) assoc w/ disc regeneration	2/8/2023	Based on P3 randomized study (n=404) finding significant pain reduction vs. saline control at 12/24 mos across all subjects. Reduction in LBP substantially enhanced in pre-specified CLBP group (n=194).
Rocket's RP-A501 (AAV-based gene therapy)	Danon disease (characterized by cardiomyopathy (most common), myopathy,and intellectual disability)	2/7/2023	Based on P1 study (n=6).**** In 2 peds patients w/ up to 9 mos follow-up: • vacuole clearance and marked reduction in brain natriuretic peptide and troponin. • improvement in NYHA class and early improvement in KC cardiomyopathy questionnaire In 4 adults w/ up to 36 mos follow-up: • biomarker, clinical, and functional parameters trend toward improvement in initial months post-therapy appear durable for 2-3 mos post-therapy.
DiscGenics' rebonuputemcel (allogeneic discogenic progenitor cell therapy)	Symptomatic lumbar degenerative disk disease	1/26/2023	In randomized, placebo-controlled FIH study (N=60), statistically significant improvement in back pain scores (100 mm VAS) of >30% at 52 weeks. Statistically significant improvements in disc volume also seen in high-dose group at week 52.

*Immatics understands this to be first RMAT for an oncology drug for more than 2 solid tumor types

** RegenexBio: "Patients receiving the pivotal program dose level continued to demonstrate the largest reductions in CSF GAGs, including Heparin Sulfate (HS) and HS D2S6, which approached normal levels at 48 weeks. CSF GAGs have the potential to be considered a surrogate biomarker that is reasonably likely to predict clinical benefit in MPS II disease under the accelerated approval pathway, as buildup of GAGs in the CSF of MPS II patients correlates with clinical manifestations, including neurodevelopmental deficits. In addition, improvements in neurodevelopmental and daily activity skill acquisition were observed up to three years after RGX-121 administration."

***elevated plasma kallikrein activity triggers the release of bradykinin. Increased bradykinin levels cause blood vessels to release fluid and result in the localized swelling and pain of an HAE attack.

****company noted that "five out of five currently enrolled pediatric and adult patients with a closely monitored immunomodulatory regimen showed improvement in NYHA Class (from II to I) with a follow-up of 6-36 months. Simply put, these data indicate that these patients are no longer affected with cardiac disease symptoms during regular activity or cardiac-related limitations in physical activities."