APPENDIX A – CIRM TRANSLATIONAL PORTFOLIO

CANCER: HEMATOLOGIC MALIGNANCY				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01430	Disease Team I	IND	AML, CML, ALL, CLL	Existing candidate molecules (3 small molecule, 3 mAbs) targeting leukemic stem cells (LSC) by blocking survival and self-renewal pathways that function preferentially in human LSC compared to normal HSC
DR1-01485	Disease Team I	IND	AML	Monoclonal antibody against CD47 – "Don't eat me" antigen that is expressed on leukemia stem cells and inhibits their phagocytosis by macrophages
TR2-01789	Early Translation II	DC	CML	Small molecule pan BCL-2 inhibitor targeting cancer stem cells
TR2-01816	Early Translation II	DC	AML, ALL	Small molecule inhibitor of BCL6 targeting cancer stem cells
CANCER: SOLID TUMORS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01477	Disease Team I	IND	Colon, ovarian cancers, glioblastoma	Small molecules specific for each of two drug targets in cancer stem cells
DR1-01421	Disease Team I	IND	Glioblastoma	Allogeneic hNSC line to target tumor, engineered *ex vivo* to deliver carboxylesterase to locally convert CPT-11 to more potent SN-38
DR1-01426	Disease Team I	IND	Glioblastoma	Allogeneic hNSC, either of two lines, or hMSC to target tumor, engineered *ex vivo* to deliver a tumorcidal gene product, TRAIL or cytosine deaminase, and a suicide gene
TR2-01791	Early Translation II	DC	Glioblastoma	Tumor homing by hMSC genetically engineered to produce replication competent retrovirus encoding a suicide gene

NEUROLOGIC DISORDERS: INJURY

AWARD #	PROGRAM	GOAL*	DISEASE/ INJURY	APPROACH
CT1-05168	Targeted Clinical Development	Ph I	Spinal Cord Injury (thoracic, cervical)	hESC-derived oligodendrocyte progenitor cells
TR2-01785	Early Translation II	DCF	Spinal Cord Injury (conus medullaris, cauda equina)	hESC-derived motor and autonomic precursor neurons
TR2-01767	Early Translation II	DCF	Traumatic brain Injury	Allogeneic hESC-derived NSC
DR1-01480	Disease Team I	IND	Stroke	Allogeneic hESC-derived NSC line alone or in combination with matrix

NEUROLOGIC DISORDERS: NEURODEGENERATIVE DISEASE

AWARD #	PROGRAM	GOAL*	DISEASE/ INJURY	APPROACH
DR1-01471	Disease Team I	IND	ALS	Allogeneic hESC-derived astrocyte precursors delivered into spinal cord (delivery device)
TR1-01245	Early Translation I	DC	Alzheimer's Disease	Allogeneic hESC-derived NSC or hESC-derived NSC genetically modified with a beta-amyloid degrading enzyme or a transcription factor that promotes neuronal differentiation for transplantation
TR1-01257	Early Translation I	DC	Huntington's Disease	Allogeneic hMSC engineered *ex vivo* to express siRNA targeting mutant huntingtin mRNA. Injected intracranially
TR2-01841	Early Translation II	DC	Huntington's Disease	Allogeneic hESC-derived neural stem or progenitor cells for transplantation
TR1-01267	Early Translation I	DC	Parkinson's Disease	The best of either hNSC derived from tissue, ESC, or iPSC or hVM (ventral mesencephalon) precursors derived from ESC, NSC or tissue
TR2-01856	Early Translation II	DC	Parkinson's Disease	Allogeneic hPSC-derived dopaminergic neurons
TR2-01778	Early Translation II	DCF	Parkinson's Disease	Small molecule modulator of neuroinflammation identified by screening on astrocytes/microglial from patient derived iPSC

NEUROLOGICDISORDERS: NEURODEGENERATIVE DISEASE, PEDIATRIC				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
TR2-01832	Early Translation II	DCF	Canavan Disease	Autologous iPSC-derived neural or oligodendrocyte progenitors, genetically modified to correct mutant aspartoacylase (ASPA) gene
TR2-01844	Early Translation II	DC	Spinal Muscular Atrophy	Small molecule that increases SMN1 gene product in patient iPSC-derived motor neurons
NEUROLOGIC DISORDERS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
TR2-01814	Early Translation II	DCF	Autism Spectrum Disorder (ASD)	Neurons from ASD (and control) iPSC for phenotype screening, assay development and validation, drug screening and biomarker identification
TR2-01749	Early Translation II	DCF	Refractory epilepsy	hESC-derived progenitors of GABAergic inhibitory neurons analogous to those in medial ganglionic eminence
EYE DISEASE				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01444	Disease Team I	IND	Age-related macular degeneration (dry form)	Allogeneic functionally polarized hESC-derived RPE monolayers on synthetic substrate implanted sub-retinally
TR1-01219	Early Translation I	DC	Age-related macular degeneration (dry form)	Autologous iPSC-derived RPE (generated without integrating vectors)
TR1-01272	Early Translation I	DC	Age-related macular degeneration (dry form)	Autologous adult SC (CMZ) or iPSC-derived RPE +/- *ex vivo* engineering to express negative regulators of complement cascade
TR2-01794	Early Translation II	DC	Retinitis Pigmentosa	Allogeneic retinal progenitor cells
TR2-01768	Early Translation II	DCF	Corneal Injury	Ex vivo expansion of corneal epithelial stem/progenitor cells, also known as limbal stem cells

HIV/AIDS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01431	Disease Team I	IND	AIDS Lymphoma	Autologous HSC transduced *ex vivo* with a lentiviral vector engineered to express an shRNA against CCR5 & a fusion inhibitor. IV administration after myeloablation
DR1-01490	Disease Team I	IND	AIDS Lymphoma	Autologous HSC transduced *ex vivo* with non-integrating vector engineered to express a zinc finger nuclease targeting CCR5. IV administration after myeloablation
TR2-01771	Early Translation II	DC	AIDS Lymphoma	Autologous HSC genetically modified with multiple anti-HIV resistance genes and a drug resistance gene
DIABETES & COMPLICATIONS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01423	Disease Team I	IND	Diabetes: Type 1	Allogeneic hESC-derived pancreatic cell progenitors in a device implanted subcutaneously that matures *in vivo* to beta cells that secrete insulin in response to glucose. Transient immunosuppression
TR2-01787	Early Translation II	DC	Chronic Diabetic foot ulcers	Allogeneic hMSC on a dermal regeneration scaffold
BLOOD DISORDERS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01452	Disease Team I	IND	Sickle Cell Disease	Autologous HSC, genetically corrected *ex vivo* by lentiviral vector mediated addition of a hemoglobin gene that blocks sickling. IV administration after myeloablation
TR1-01273	Early Translation I	DC	Fanconi Anemia, XSCID	Autologous iPSC-derived HSC genetically corrected by homologous recombination

BONE DISORDERS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
TR2-01821	Early Translation II	DC	Spinal fusion	Autologous adult perivascular stem cells and an osteoinductive protein on a FDA-approved acellular scaffold
TR2-01780	Early Translation II	DCF	Osteoporosis-related vertebral compression fractures	MSC in combination with PTH (parathyroid hormone)
CARTILAGE DISORDERS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
TR1-01216	Early Translation I	DC	Focal cartilage defect, osteoarthritis	iPSC- or ESC-derived chondrocyte progenitors implanted into chondral defect or injected into OA joint
TR2-01829	Early Translation II	DC	Osteoarthritis	Optimized small molecule of lead molecule PRO1 that induces chondrocyte differentiation of resident hMSC
OTHER DISORDERS				
AWARD #	**PROGRAM**	**GOAL***	**DISEASE/ INJURY**	**APPROACH**
DR1-01461	Disease Team I	IND	Heart Disease: Advanced ischemic cardiomyopathy	Autologous cardiac derived cells, 'cardiospheres', expanded and delivered by direct catheter injection into heart muscle
DR1-01454	Disease Team I	IND	Skin Disease: Epidermolysis bullosa	Epidermal sheets from expanded autologous genetically corrected (to express wild type COL7A1) iPSC-derived keratinocytes
TR1-01249	Early Translation I	DC	Multiple: Bone fractures, wound healing, heart disease, stroke	Recombinant Wnt in a sustained release formulation to stimulate endogenous stem cells to repair tissue

TR2-01857	Early Translation II	DC	Liver Disease (acute liver failure and as a bridge following large liver resections)	Allogeneic genetically modified hESC-derived hepatocytes
TR2-01756	Early Translation II	DCF	Skeletal Muscle Disorders: Duchenne muscular dystrophy	Autologous skeletal muscle precursor cells derived from human iPSC genetically modified to correct the dystrophin gene

* The Project Goals are:

IND - file an approvable IND with the FDA

DC - achieve a development candidate ready for IND-enabling preclinical development

DCF - show feasibility of a potential development candidate by achieving initial proof of concept