Gene Therapy Pipeline

Delivery Platform	Expressed Product	Indication	Abstract	Patents	Inventor
rAAV	miR-SOD1	Amyolateral Sclerosis (ALS; Lou Gehrig's Diseases)	AAV10 vector-based gene therapy for treating ALS with enhanced tropism for neuronal cells. Administration of rAAV encoding inhibitory RNA for superoxide dismutase 1 (SOD1) distributes widely throughout CNS with low toxicity. Long-term inhibition of mutant SOD1 improves lifespan in the animal models. **more info…**	Reference#: UMMS10-36 Patent#: 9,102,949	Guangping Gao Zhushang Xu
rAAV	miR-122 Antagonist	Dyslipidimia, Familial hypercholesterolemia (FH)	Novel therapeutic to treat cholesterol-related disorders by recombinant adeno-associated (rAAV)-based gene therapy. Introduction of miR122-inhibitor transgene in the liver significantly reduces cholesterol levels up to 50% for at least 14 weeks in mice. **more info…**	Reference#: UMMS10-37 Patent#: **9,272,053**	Guangping Gao Phillip Zamore
rAAV	Multiple inserts coding for RNAi/protein	Neurodegenerative Disorders, Canavan Disease	New effective and safe gene therapy approach that allows gene delivery across the blood brain barrier (BBB) upon intravascular administration. Designed to minimize off-target effects by incorporation of non-CNS-tissue specific miRNA binding site into the transgene expression cassette. **more info…**	Reference#: UMMS10-38 Patent#: 9,102,949	Guangping Gao Zhushang Xu
rAAV	rAAV9 variant	Application of new AAV for gene therapy	Novel method to isolate and characterize natural variants of AAV9. This new information allows for designing caspids with higher efficiency in packaging and tissue specificity. **more info…**	Reference#: UMMS10-39 Patent#: Pending	Guangping Gao Terence Flotte
rAAV	shRNA	Application of new expression construct for gene therapy	Newly designed multicistronic expression construct with efficient shRNA delivery. Hairpin RNAi expression cassette shown to specifically improve replication and packaging efficiency. **more info…**	Reference#: UMMS10-40 Patent#: Pending	Guangping Gao

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rAAV/ Small molecules	Aspartoacylase (ASPA)	N-acetyl-asparate (NAA) metabolism in Cavagan and neurodegenerative disease	Newly discovered phenomenon in which changes in brain energy metabolism is observed when N-Acetylaspartate (NAA) levels are perturbed. Altered NAA levels are associated with Cavagan and neurodegenerative diseases where there is increased preference for utilization of fatty acids over glucose, leading to white matter loss. **more info…**	Reference#: UMMS16-17 Patent#: Pending	Guangping Gao
rAAV/ Small molecules	Aspartoacylase (ASPA)	N-acetyl-asparate (NAA) effects on glucose metabolism	Newly discovered relationship between N-Acetylaspartate (NAA) metabolite levels and glucose metabolism. Introduction of ASPA gene can reverse metabolic changes that occur with decreased levels of NAA. Monitoring and adjusting the NAA levels may have implication for wide range of diseases that display changes in bioenergetics metabolism. **more info…**	Reference#: UMMS16-17 Patent#: Pending	Guangping Gao
rAAV	anti-SOD1 miRs	ALS	New miRNA delivered by rAAV for silencing SOD1 & C9orf72 SODl genes, which are associated with ALS. This method enables effective therapy at low doses with the persistence of rAAV episomes that continually expresses the nucleic acids, thus rendering re-treatment unnecessary. This method also minimizes rAAV exposure to non-CNS peripheral tissue. **more info…**	Reference#: UMMS13-19 Patent#: Pending	Robert Brown Christian Mueller
rAAV	Multiple inserts with optimized promoters	Reduce adverse effects of AAV gene therapy for multiple diseases e.g. lysosomal disorders	New AAV vectors that enable transgene expression at therapeutic levels for treatment of lysosomal and other disorders. These levels are achieved without the adverse events that arises due to secondary effects of AAV-mediated product delivery. This newly engineered regulatory element can apply broadly to circumvent adverse effects of AAV therapy. **more info…**	Reference#: UMMS15-19 Patent#: Pending	Miguel Sena Esteves
rAAV	sFasL	glaucoma	New AAV therapy facilitates long-term production of sFasLin the retina by intra-vitreal injection with no detrimental effect observed in normal animals. Glaucoma-prone mice were injected either before or after disease onset and both animals were found to have preserved retinal ganglion cells with their axons, which normally results in death with onset of the disease. **more info…**	Reference#: UMMS16-64 Patent#: Pending	Ann Marshak-Rothstein Bruce Ksander
rAAV	Multiple inserts coding for RNAi/protein	Application of new AAV for high-efficiency of gene therapy in the CNS	New AAV technology with an insertion of 19-amino acid “alanine string” that has dramatically increased CNS tropism compared to that of AAV9, the natural variant with the currently highest known CNS transduction efficiency. This technology shows increased CNS transduction without changing transduction efficiency of peripheral tissues. **more info…**	Reference#: UMMS14-58 Patent#: Pending	Miguel Sena Esteves

Delivery Platform	Expressed Product	Indication	Abstract	Patent	Inventor
rAAV	Multiple inserts coding for RNAi/protein	Application of new AAV for high-efficiency of gene therapy in multiple diseases	Newly designed recombinant AAV capsids with greater efficiency for CNS delivery than AAV9, the natural variant with the currently highest known CNS transduction efficiency. These new AAV capsids, B1-B4, show considerably lower off-target effects in the liver when compared to AAV9. Additionally, each of these AAV capsids show selectively higher efficiency for specific peripheral tissues (e.g. pancreas, sk. muscle, heart, adipocyte). **more info…**	Reference#: UMMS14-59 Patent#: Pending	Miguel Sena Esteves
rAAV	Multiple inserts coding for RNAi/protein	Dual Vector Platform anti trypsin deficiency and other diseases	This invention uses a dual-specificity AAV vectors to correct Alpha 1-Antitrypsin (AAT) deficiency. This dual vector carries: 1) miRNAs that target and inhibit the expression of the mutant endogenous protein (AAT), and 2) gene for modified and functional AAT protein that is not targeted by the aforementioned miRNA. **more info…**	Reference#: UMMS11-45 Patent#: 9,226,976	Terence Flotte Christian Mueller Phillip Zamore
rAVV/ AON	Antisense oligonucleotide (AON)	Dysferlinopathies	This technology originates from identification of a deep intronic mutation in Dyferlin (DYSF) that alters mRNA splicing to include a mutant peptide fragment within a key DYSF domain. This new antisense oligo nucleotide(AON-)mediated exon-skipping to restore production of normal, full-length DYSF in patients' cells *in vitro*, offering therapeutic solution for patient with Dyferlin-associated maladies. **more info…**	Reference#: UMMS14-41 Patent#: Pending	Robert H Brown Janice Dominov
rAAV	micro-RNA	Platform/vector engineering	The technology utilizes methods of implementing viral vectors harboring a transgene(s) in combination with tissue specific anti-miRNA sequences to minimize off-target effects. In addition, this method allows for production of somatic transgenic animal models by targeted destruction of specific cell types. **more info…**	Reference#: UMMS08-55 Patent#: 9,217,155	Guangping Gao Phillip Zamore
rAAV	Ovalbumin with 3'UTR immune associated miRNA binding sites	Application of new AAV vector that increase potency of therapeutic protein levels of interest	This new AAV technology involves co-delivery of a transgene that minimizes immune responses against the transgene product of interest. Specifically, this process involves administering a rAA-harboring a transgene engineered to express an inhibitory RNA transcript that targets one or more immune-associated miRNA. This interaction lowers the immune response and consequently increases the potency of the therapeutic protein and its effects. **more info…**	Reference#: UMMS14-22 Patent#: Pending	Guangping Gao Phillip Zamore

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rAAV	Multiple inserts coding for RNAi/protein	Application of new AAV vector for tissue specificity	New rAAV vector technology desirable for gene therapy applications addressing muscular and lung disorders. A novel AAV9 capsid mutant produces local tissue-restricted expression and genome persistence, delivered by intravascular (IV), intramuscular (IM) and intranasal (IN) route. The therapy is effective while producing low levels of expression in liver. **more info…**	Reference#: UMMS12-73 Patent#: Pending	Guangping Gao Li Zhong
CRISPR	Cas9 nuclease-DNA targeting unit chimera	Improved Cas9 nuclease for genome engineering	New Cas9 technology with improved activity, precision, and sequence targeting range. This new Cas9 nuclease-DNA targeting unit chimera utilizes programmable DNA binding domain for editing specificity. The chimeric nuclease complex allows for conjugation of other Cas9 variants to reduce off-target and undesired editing of the genome. This improved Cas9 technology will have application for future human gene therapy. **more info…**	Reference#: UMMS14-68 UMMS16-26 Patent#: Pending	Scott Wolfe Erik Sontheimer
CRISPR	NmeCas9 inhibitor Acr proteins	Cas9 “off-switch” for prevention of off target genome editing in CRISPR technology	This novel “off-switch” for Cas9 is important for preventing off target editing effects from CRISPR technology. This technology consists of proteins that have the ability to inhibit NmeCas9 nuclease. This invention has great potential for application in genome editing with CRISPR in human application. **more info…**	Reference#: UMMS16-39 Patent#: Pending	Erik Sontheimer Alan Davidson
CRISPR	NmeCas9	Programmable RNA-guided DNase H	This new technology capitalizes on the discovery of DNase H activity in NmeCas9 that could serve as a novel programmable RNA-guided "restriction enzyme" that cleaves ssDNA, with no sequence constraints. Compared to RNase H that degrades the RNA strand of a RNA-DNA hybrid (with little or no sequence preference), NmeCas9's DNase activity makes specific cuts and has the opposite nucleic acid specificity, i.e. cleaving the DNA strand of the hybrid duplex. **more info…**	Reference#: UMMS16-05 Patent#: Pending	Erik Sontheimer

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