

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
10/15/20	GEM223	Regulation of cellular phosphate handling and intracellular energy status	Hyperphosphatemia in chronic kidney disease (CKD) Chemotherapy-induced hyperphosphatemia (Tumor Lysis Syndrome, TLS)	Oral Intravenous	Small molecule	Oncology: Supportive care Renal disease	Pre-IND	First-in-class drug with a new MOA that is completely different from those of existing drugs for the treatment of hyperphosphatemia in CKD and TLS, a serious complication in cancer patients. - A unique and highly effective mechanism to reduce blood phosphate levels in mammals - Once-daily dosing potential - No gastrointestinal side-effects - Mechanism-based kidney protective effects - IND-enabling 4-week toxicological studies have been finished
09/18/20	GEM222	Anti-Podoplanin Antibody	Osteosarcoma, Lung squamous cell carcinoma, Soft tissue sarcoma, thrombosis	Injection	Antibody	Cardiology Oncology: Solid cancer	Preclinical	- First-in-Class humanized Anti-Podoplanin Antibody - Podoplanin is a transmembrane protein. It is found to induce platelet aggregation and express in various malignant tumor cells, and involve in proliferation of these tumor cells. - GEM222 suppressed tumor growth and metastasis in human osteosarcoma and human lung squamous cell carcinomas xenografted in immunodeficient mouse. - No side effect was observed in preliminary monkey study.
09/08/20	GEM221	Anti-Globo H ADC	Cancer	i.v.	Antibody	Oncology: Solid cancer	Preclinical	High affinity, fast internalization, good in vitro cytotoxicity - Showed great tumor growth inhibition (>90%, 3 mg/kg) in HCC-1428 animal models without any body weight loss - Can be prepared reproducibly at gram scale.
09/08/20	GEM220	Anti-Globo H Antibody	Breast Cancer	i.v.	Antibody	Oncology: Solid cancer	*Preclinical **Discovery	* Anti-Globo H monolonal antibody - Higher patient population in breast cancer (61%). - Anti-cancer efficacy demonstrated in breast cancer animal model through ADCC and CDC. **Anti-Globo H bispecific antibody - High correct pairing (>95%) -Target cell-dependent T cell activation (Better safety profile). - Anti-cancer efficacy demonstrated in breast cancer animal model through T cell-mediated cytotoxicity.
09/08/20	GEM219	Anti-TIM-3 antibody	Cancer	i.v.	Antibody	Oncology: Solid cancer	Preclinical	GEM219 is a fully human anti-TIM-3 antibody with high affinity in vitro and cell-based binding assay. - The anti-TIM-3 antibodies are also highly functional in cellbased bioassay. - Some anti-TIM-3 antibodies have cross-species recognition ability to mouse TIM-3. - Animal efficacy studies are in progress
09/08/20	GEM218	Anti- Human PD-L1 antibodies	Cancer	i.v.	Antibody	Oncology: Solid cancer	Preclinical	GEM218 is a novel monoclonal antibody that specifically binds to PD-L1 with high affinity and effectively blocks PD-1/PD-L1 interaction. - Can be well detected by the PD-1/PD-L1 Blockade Assay. - Novel binding epitopes. - Good potential for a companion diagnosis. - The efficacy and toxicity are studied in various in vitro and in vivo models
09/08/20	GEM217	AXL Kinase Inhibitor	Cancer with high AXL expression	Oral	Small molecule	Oncology: Solid cancer	Preclinical	GEM217 is a selective AXL kinase inhibitor. - The chemical structure of GEM217 is distinguished from known AXL inhibitors. - Superior antitumor activity to reference compound BGB324, which is currently in phase II clinical trial for treating lung cancer. - Acceptable PK property and orally antitumor activity.
09/08/20	GEM216	Orally Active Hedgehog Inhibitor	Cancer: basal cell carcinoma and cholangiocarcinoma	Oral	Small molecule	Oncology: Solid cancer	Preclinical	Overcome the marketed drug resistant issue - Inhibit both tumor cells and cancer stem cells - Low CYP inhibition potential - GLP tox completed with acceptable safety profile

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
09/08/20	GEM215	Globo H-Specific CAR-T Cells	Solid Tumor: breast cancer, gastric cancer and lung cancer	i.v.	Cell therapy	Oncology: Solid cancer	Discovery	Potential cell therapy for Globo H+ solid tumor. -Combination with anti-PD-L1 Ab overcomes PD-L1-mediated immune suppression on CAR-T cells in tumor microenvironment. -Anti PD-L1 Ab is able to induce bystander effect during Globo H CAR-T cell treatment.
09/08/20	GEM214	Anti-K. pneumoniae (KP) Antibodies	Multiple Drug Resistant (MDR) Klebsiella pneumoniae (KP) infection	i.v.	Antibody	Infection	Preclinical	GEM214 is an anti-MDR therapeutic antibody against Klebsiella pneumoniae Infection. -A fully human mAb, has longer half-life and low immunogenicity. -Antibody Antibiotics Conjugate (AAC) of GEM214 shows dose dependent intracellularly bactericidal potency.
09/08/20	GEM213	Anti-CSF-1R antibody	Cancer, PVNS (pigmented villonodular synovitis)	i.v.	Antibody	Immunology/Inflammation Oncology: Solid cancer	Preclinical	GEM213 is an antibody with high affinity and neutralizing ability. - GEM213 can potently inhibit Colony Stimulating Factor Receptor 1 (CSF-1R) in cellular contexts and has the potential to induce a therapeutic effect on macrophages. - GEM213 has unique CDR sequences and epitopes. - GEM213 is a promising new agent with potential to combine with immune checkpoint inhibitors to relief macrophage-dependent immune suppression and would yield clinical benefit.
09/03/20	GEM-CDV07	CK2 inhibitor	COVID-19	Oral	small molecule	Infection	IND#	- A promising therapeutic compound due to its dual impact on COVID-19 *Block stress granule disaggregation required for active viral replication *Reduce cytokine storm - GEM-CDV07 demonstrates potent anti-SARS-CoV-2 activity. - In process of filing for emergency IND (eIND) to U.S. FDA to test ten patients. #Phase 2 clinical trial is ongoing for other indication.
08/26/20	GEM212	Antivirulent approach targeting antimicrobial resistance of <i>Staphylococcus aureus</i> infections	<i>S. aureus</i> and MRSA	Oral	Small molecule	Infection	Near completion of IND stage	An antivirulent, non-bactericidal small molecule drug candidate for <i>S. aureus</i> infections, including MRSA, in a first-in-class oral form. Potentially reduces the risk of <i>S. aureus</i> resistance. A new mechanism to enhance the killing action of neutrophils. Phase II clinical trials are planned across multiple indications; bacteremia, pneumonia, endocarditis, bone and joint infections
08/26/20	GEM211	Antiviral	Influenza A	Oral	Small molecule	Infection	Lead optimization stage	An antiviral with a more upstream target than Tamiflu, shown to be more effective <i>in vivo</i> . A small molecule, nucleozin, which targets viral nucleoprotein (NP), triggering the aggregation of NP and inhibiting its nuclear accumulation. This impedes viral replication <i>in vivo</i> .
08/26/20	GEM210	TFEB activation	Alzheimer's and Parkinson's disease	Oral	Small molecule	CNS	Lead optimization stage	A new mechanism of action (and first-in-class oral form) to accelerate the degradation of neurotoxic proteins by autophagy. mTOR independent autophagy targets the removal of multiple misfolded proteins (e.g. beta-amyloid, tau) In several neurodegenerative diseases, mTOR/Transcriptional factor EB (TFEB) and therefore autophagy is dysfunctional. GEM210 increases TFEB translocation to the nucleus and enhances autophagy.
08/26/20	GEM209	A3 adenosine receptor (A3AR) allosteric modulator	Erectile dysfunction	Oral	Small molecule	Immunology/Inflammation Urology	Preclinical	<ul style="list-style-type: none"> <li>• Specific agonists of A3AR induce modulation of key signaling proteins, such as PI3K, GSK-3<math>\beta</math>, PKA, PKB/Akt, IKK, and NF-<math>\kappa</math>B, and show anti-inflammatory effects.</li> <li>• Very good safety profile.</li> <li>• GEM209 increased eNOS and VEGF in the cavernosal endothelial cells.</li> <li>• A single dose showed a full recovery in function of in an erectile dysfunction rat model.</li> </ul>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
08/26/20	GEM208	A3 adenosine receptor (A3AR) agonist	Liver cancer* NAFLD**	Oral	Small molecule	Metabolic disease Oncology: Solid cancer Rare disease	Phase 3 in preparation*  Phase 2 completed**	<ul style="list-style-type: none"> <li>• A3AR is highly expressed in inflammatory and cancer cells. Specific agonists of A3AR induce apoptosis of cancer cells but not normal cells.</li> <li>• Very good safety profile.</li> <li>• An orphan drug status for hepatocellular carcinoma (HCC).</li> <li>• In phase-2 study in HCC patients, it did not meet the primary endpoint (OS) but subgroup analysis of Child Pugh B patients showed a positive signal of efficacy for OS.</li> <li>• In phase-2 study (vs placebo) in NAFLD/NASH, it met primary endpoint (liver enzyme) and reduced liver fat, fibrosis and steatosis.</li> </ul>
08/26/20	GEM207	A3 adenosine receptor (A3AR) agonist	Rheumatoid arthritis (RA), Psoriasis	Oral	Small molecule	Dermatosis Immunology/Inflammation Orthopedic Rheumatology	Phase 3	<ul style="list-style-type: none"> <li>• A3AR is highly expressed in inflammatory and cancer cells. Specific agonists of A3AR induce apoptosis of inflammatory cells but not normal cells.</li> <li>• Very good safety profile as 1st line therapy.</li> <li>• In the phase-2b study (monotherapy vs placebo) for 12 weeks in naive RA patients, the endpoint was achieved.</li> <li>• In the phase-2/3 study (monotherapy vs placebo) in moderate to severe psoriasis patients, it did not meet the primary endpoint at 12 weeks, but at 32 weeks the improvement of PASI score was significant vs at 16 weeks.</li> <li>• A phase-3 study (vs MTX) in moderate to severe RA and a phase-3 study (vs apremilast) are ongoing.</li> </ul>
08/24/20	GEM206	FLT3 Kinase Inhibitor	Acute myeloblastic leukemia (AML)	Oral	Small molecule	Oncology: Hematological cancer	Preclinical	<ul style="list-style-type: none"> <li>- Novel chemical structure distinguished from known FLT3 inhibitors</li> <li>- Highly potent against FLT3 and FLT3 mutants (overcome FLT3-TKD mutation mediated drug resistant)</li> <li>- Highly selective</li> <li>- Monotherapy &amp; orally active</li> <li>- Well-tolerance in preclinical tox study</li> <li>- GLP tox study is in progress.</li> </ul>
08/24/20	GEM205	Anti-Mesothelin (MSLN) Antibody-Drug Conjugate (ADC)	Cancer (Pancreatic Cancer, Ovarian Cancer etc.)	Injection	Antibody	Oncology: Solid cancer	Preclinical	<ul style="list-style-type: none"> <li>- Mesothelin is a differentiation antigen overexpressed in many solid tumors</li> <li>- GEM205 showed great tumor growth inhibition (&gt;90%) in animal model without body weight loss.</li> <li>- GEM205 also showed great efficacy in large tumor model (&gt;500 mm<sup>3</sup>).</li> <li>- Self-owned I4 technology was applied in GEM205.</li> <li>- GEM205 showed uniform DAR (4), high affinity, good cytotoxicity.</li> </ul>
08/24/20	GEM192	Selective PI3K $\alpha$ inhibitor	Slow-flow vascular malformations	Oral	Small molecule	Rare disease	Phase 1	<p>Slow-flow vascular malformations including venous malformation, lymphatic malformation, Klippel-Trenaunay syndrome is abnormal clustering of blood vessels that occurs in children or young adults and are caused by PI3K pathway GOF mutation. By selectively inhibiting PI3K<math>\alpha</math> isoform, GEM192 inhibits angiogenesis, but not immune function resulting in better therapeutic effects and lower infectious risk. Phase 1/2 data for another indication demonstrate a favorable tolerability profile. Clinical development to be pursued with new pediatric formulation</p>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
08/24/20	GEM185	GLP-1/GIP dual agonist	Obesity, diabetes	s.c.	Peptide	Metabolic disease	Phase 1	GEM185 is an injectable (QD) dual agonist for GLP-1R and GIPR. Preclinical studies have shown that GEM185 is more effective in improving diabetes and obesity than GLP-1R agonism only. In addition, GEM185 has been shown to improve liver parameters in diabetic and obesity conditions in preclinical research. Hence, GEM185 may be superior to the GLP-1R agonist in improving diabetes, obesity, and non-alcoholic steatohepatitis (NASH). In a preclinical study, GEM185 showed better efficacy in improving glycemic control and an almost same efficacy in decreasing body weight compared to tirzepatide, a Lilly's Ph3 program. A long-acting formulation, which is likely to maximize its therapeutic efficacy, are under development. A phase 1 study (first-in-human study), starting in 2020, is being organized in the UK.
08/12/20	GEM204	Multi-molecular targeting including the Wnt/ $\beta$ -catenin pathway	Hair loss, Androgenetic Alopecia, Telogen effluvium, Senescent Alopecia	Topical and/or oral	Plant extracts	Dermatosis	Commercial	GEM204 is a comprehensive solution for the treatment of hair loss, targeting more than 21 hair regulating molecular pathways to promote hair growth and inhibit hair loss. Market approval and full scientific dossier available with clinical trials in women and men of all hair loss patterns, hair types and skin types.
08/10/20	GEM203	FXR agonist and 5-HTR2A antagonist	NAFLD, Type 2 diabetes, obesity, dyslipidemia and hypertension	Oral	Small molecule	Cardiovascular Metabolic disease	Preclinical	First in class single molecule having both FXR agonistic and 5-HTR2A antagonistic actions.  In DIO mice, GEM203 reduced hyperglycemia, hyperinsulinemia, insulin resistance and liver lipid contents to similar or greater extent vs metformin. GEM203 reduced the body excess weight while metformin did not. In NASH model mice, GEM203 reduced liver excess weight, TG and TC contents, plasma ALT and AST, inflammation and collagen gene expression in the liver.  Strong IP portfolio with long expiry dates granted in major markets.
08/05/20	GEM202	Somatostatin receptor subtype 5 (SSTR5) antagonist	Type 2 diabetes, Gallstone, Primary sclerosing cholangitis (PSC), Inflammatory bowel disease (IBD), short bowel syndrome (SBS)	Oral	Small molecule	Endocrinology Gastroenterology Metabolic disease	IND ready	SSTR5 is primarily expressed in pancreatic $\beta$ -cells and enteroendocrine cells, and its ligand, somatostatin, negatively regulates the secretion of insulin and gut hormones (GLP-1, GLP-2, PYY, etc.). GEM202 is a selective SSTR5 antagonist and is unique owing to its dual action of elevating these hormone secretions and increasing insulin sensitivity, thereby improves glycemic control in obese and diabetic mice. In addition, GEM202 is effective in stimulating gallbladder motility and increasing bile flow, accounting for its therapeutic effects in animal models of gallstones and PSC. Thus, an additional potential application involves treatment of hepatobiliary diseases. Patents have been filed globally.
08/01/20	GEM201	mRNA Vaccine Platform technology. Production of S-Proteins with Immune-modulators in one construct.	Coronavirus (COVID-19); Broader Vaccine Platform	i.v.	Drug Delivery, Cell therapy	Infection Vaccine	Preclinical	GEM201 utilizes TGEM055 technology loaded with antigenic proteins as a mRNA Vaccine Platform - Produce functional antigenic proteins in Lymphatic organs - Localized antigen induction at high intracellular amounts where antigen presenting cells aggregate. Co-delivery of potent Immune-modulators (GM-CSF, IL-12, etc) simultaneously - GEM201 is a vaccine platform - GEM201 is critical for vaccination of elderly and immune suppressed population

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
07/22/20	GEM200	Physically damage bacterial membranes	Multidrug-resistant bacteria	i.v.	Peptide	Infection	Preclinical	<p>A bioengineered peptide that is effective against Gram(-) bacteria and works regardless of any underlying resistance the bacteria may have against other antibiotic drugs. GEM200 is highly efficient against Multi Drug Resistant Acinetobacter baumannii in hospital acquired infections and its unique MoA lowers the probability for development of future resistance or tolerance. GEM200 is Effective where the Standard of Care drugs fail.</p> <p>Advantages:</p> <ul style="list-style-type: none"> <li>- High efficacy in systemic IV administration</li> <li>- Rapid bactericidal MOA that avoids resistance</li> <li>- Targets bacteria only – Non-toxic to human cells</li> <li>- Stable peptides with T1/2=~8 hours in human plasma</li> </ul>
07/08/20	GEM199	A fixed dose combination of Minoxidil, resveratrol and melatonin.	Alopecia / Hair Loss	Topical	Small molecule	Dermatosis	Pre registration	<p>Minoxidil is a potassium channel blocker that prevents hair loss by improving blood flow to the hair follicle. It also suppresses androgen receptor function and stimulates the production of prostaglandins. Resveratrol stimulates hair growth by decreasing prostaglandin D2 (PGD2) and increasing prostaglandin E2 (PGE2). Melatonin is a neurohormone involved in multiple physiological processes underlying circadian rhythm. Due to its antioxidant properties, melatonin has remarkable protective effects on cells and anti-apoptotic properties. Hence the association between melatonin and hair growth. The effect of melatonin on hair growth may be moderated by an interaction with androgens and estrogens and their receptors. Results from a clinical study demonstrated that GEM199 was more effective at stopping hair loss than Minoxidil. US patent issued, and international patents have been filed.</p>
07/08/20	GEM198	A fixed dose combination of melatonin and resveratrol.	Alopecia / Hair Loss	Topical	Small molecule	Dermatosis	Pre registration	<p>Resveratrol stimulates hair growth by decreasing prostaglandin D2 (PGD2) and increasing prostaglandin E2 (PGE2). Melatonin is a neurohormone involved in multiple physiological processes underlying circadian rhythm. Due to its antioxidant properties, melatonin has remarkable protective effects on cells and anti-apoptotic properties. Hence the association between melatonin and hair growth. The effect of melatonin on hair growth may be moderated by an interaction with androgens and estrogens and their receptors. Results from a clinical study demonstrated that GEM198 was more effective at stopping hair loss than Minoxidil. US patent issued, and international patents have been filed.</p>
07/08/20	GEM197	A fixed dose combination of minoxidil, finasteride and latanoprost.	Androgenetic alopecia	Topical	Small molecule	Dermatosis	Phase 3	<p>Minoxidil is a potassium channel blocker that prevents hair loss by improving blood flow to the hair follicle. It also suppresses androgen receptor function and stimulates the production of prostaglandins. Finasteride is a 5 alpha reductase inhibitor that reduces the conversion of testosterone to dihydrotestosterone (DHT), which in turn reduces the binding of DHT to the androgen receptor, thereby reducing the miniaturization of the hair follicle. Finasteride also upregulates SULT1A1, which activates the pro-drug of minoxidil into its active form - minoxidil sulfate. Latanoprost is a prostaglandin analogue that has a positive stimulatory effect on the hair follicle and induces the conversion from telogen to anagen phase in the hair growth cycle. Results from a completed phase 2 study have demonstrated that GEM197 is a well-tolerated, once a day, topical fixed dose triple combination therapy that stimulates new hair growth and prevents further hair loss for the treatment of androgenetic alopecia in men 24-65 years old. The FDA has given a roadmap to start a Phase 3 clinical trial under 505(b)(2). International patents have been issued.</p>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
06/26/20	GEM196	Potassium-Competitive Acid Blocker (P-CAB)	Peptic ulcer	Oral	Small molecule	Infection	Phase 2 completed	Phase 3 is ongoing. P-CABs are the best treatment with better and faster efficacy for gastric acid-related gastrointestinal diseases such as gastric and duodenal ulcer, GERD, NERD, ZES and etc. GEM196 is a potentially best-in-class P-CAB - Faster clinical benefit in phase 2 study compared with Lansoprazole for duodenal ulcer treatment. - Rapid and high absorption, oral bioavailability in clinical study. - Lower toxicity and better PK, PD than TAK-438. - Acid stability- exempt acid protection - Longer lasting-higher concentration on target site - Less individual differences- isoenzyme CYP2C19 metabolism tiny dependence.
06/18/20	GEM-CDV06	A potent DNA-immunotherapy against SARS-CoV-2	COVID-19	Intravenous Injection	In vivo CAR-T	Infection	Preclinical	DNA vector with Anti-CoV-2 Receptors inserted into our original platform (TGEM052) and delivered through liposomes into lymph nodes. The plasmid moves into the nucleus of normal T-cells and converted to CAR. Anti-CoV-2 CAR T-cells attack the virus and diseased cells and destroy them.
06/18/20	GEM195	A potent DNA-immunotherapy for MAGE A	Triple Negative Breast Cancer (TNBC)	Intramuscular Injection	DNA Plasmid	Oncology: Solid cancer	Preclinical	DNA vector with MAGE A inserted into our original platform (TGEM052) and delivered into muscle cells using intramuscular injections followed by electroporation. The plasmid moves into nucleus of muscle cells and starts to over-express MAGE A, eliciting an immune response that can target MAGE A on cancer cells and destroy them.
06/18/20	GEM194	PDE4 inhibitor	Autoimmune dermal disorders (bullous pemphigoid, psoriatic arthritis)	Oral	Small molecule	Dermatosis Immunology/Inflammation	Phase 1	GEM194 is the best-in-class PDE4 inhibitor having potentially a wider therapeutic index compared to clinically efficacious and marketed PDE4 inhibitors such as apremilast and roflumilast. Bullous pemphigoid (BP) is chronic autoimmune skin disorder resulting in generalized, pruritic, bullous lesions in elderly patients currently treated with corticosteroids and multiple antibacterial agents. Anti-inflammatory profile of PDE4 inhibition associated with multiple immune- and inflammatory cells is anticipated to taper doses of systemic corticosteroid. Opportunities exist to extend clinical development for other inflammatory dermal indications such as psoriatic arthritis.
06/18/20	GEM193	PDE4 inhibitor	NASH	Oral	Small molecule	Gastroenterology Immunology/Inflammation Metabolic disease	Phase 1	GEM193 was efficacious in reducing plasma ALT levels, hepatic fibrosis area, TG levels in an animal model of NASH. In addition, GEM193 exhibited anti-obesity and anti-diabetic properties in vivo. PDE4 enzyme is expressed not only in disease-relevant cell population, but also in ubiquitously whole body and its inhibition results in anti-inflammatory, anti-fibrotic and anti-metabolic effects that fit favorable profile as a monotherapy for NASH.
06/18/20	GEM191	Potential of detrusor contraction	Underactive bladder	Oral	Small molecule	Urology	Phase 1	Detrusor underactivity is a main cause of underactive bladder, which causes multiple lower urinary tract symptoms such as residual urine and urinary tract infection. GEM191 potentiates detrusor contraction and shows no impact on bladder storage function or urethral function. Stratified analysis clearly indicates efficacy to reduce residual urine in patients with detrusor underactivity.
06/15/20	GEM190	Lipase inhibition, $\alpha$ -amylase inhibition, aldehyde dehydrogenase (ALDH) activation and anti-oxidant capacity increase	Overweight and obesity Alcohol and tobacco smoke toxicity	Oral	Natural product	Metabolic disease	Clinical	GEM190 is a combination of two purified plant extracts in a form of oral liquid food supplement developed for appetite and weight control. Also, it reduces alcohol and tobacco smoke toxicity by activation of aldehyde dehydrogenase (ALDH) and increasing anti-oxidant capacity. In overweight and obese patients, GEM190 showed significant suppression of appetite and reduction of body weight and body fat as well as it had a beneficial effect on fluid distribution during weight loss, as observed in 12-week treatment. Increased ALDH activity in PBMC was observed already after 24 hours after initiation of GEM190 administration. GEM190 may provide a salvage solution in populations known to be particularly susceptible to a build-up of excess acetaldehyde, such as having a ALDH2*2 genetic mutation. GEM190 claims are under two PCT applications.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
06/05/20	GEM-CVD05	Immune-modulate and slow down the hyperactive active immune system from attacking lung cells (and other solid organs)	Prevention of Respiratory Failure by Treating Acute Respiratory Disease Syndrome Resulting from COVID-19 and other viral pandemics	Refer to Note*	Protein**	Immunology/ Inflammation Infection Respiratory	Phase 3 ready***	1. Treatment of blood/MSCs, Tregs, NK cells with GEM-CVD05 to improve their homing to patients' lungs, thereby enabling those cells to slow down the hyperactive immune attack on the lungs to help prevent deaths from respiratory failure. 2. Treatment of cells such as stem cells enabling them to home/engraft more effectively to the bone marrow and accelerating immune reconstitution with 'younger' immune cells for improved viral infected cell killing. *Infusion with blood, or MSCs, Tregs, NK cells to improve efficacy, safety and cost of care outcomes **Used to treat MSCs, Blood, Tregs, NK cells, Stem Cells to Prevent deaths from respiratory failure ***Phase 2 study for other indication has been completed.
06/05/20	GEM189	Nanoliposome-encapsulated Radionucleotide	*Recurrent Glioblastoma, **Multiple tumor	Intratumoral	Radionucleotide	Oncology: Solid cancer	*Phase 1, **Preclinical	Radionucleotide in GEM189 is ideal one for the treatment of solid Tumors. It delivers a high dose of radiation directly to the tumor while sparing normal, healthy brain tissue, stays at the tumor for several days and Effect lasts for several days and then dissipates. No serious adverse events observed to date. Key advantages over External Beam Radiation Therapy: -At least 500 Gy, -Single 4-day hospitalization -Able to more effectively treat tumor margins - Limited toxicity -Able to verify successful delivery with SPECT scan
06/05/20	GEM188	Dual inhibitor of ROCK and new target kinase	Glaucoma; ocular hypertension	Small molecule	Topical eye drop	Ophthalmology	Preclinical	GEM188, a dual ROCK/new target kinases inhibitor, had shown more effective in intraocular pressure lowering than competitor netarsudil in magnetic bead-induced and hypertonic saline-induced ocular hypertensive models. Moreover, GEM188 also showed lower eye irritation than netarsudil in New Zealand White rabbit. The plasma exposure by eye drops dosing was less than that by iv dosed with NOAEL. The preclinical studies including GMP-compliance production, GLP toxicology, etc., is ongoing in 2020.
05/30/20	GEM187	Mesenchymal stem cell	Rheumatoid Arthritis (RA), Inflammatory Bowel Disease (IBD), COVID-19	Implant (allogenic)	Cell	Gastroenterology Immunology/Inflammation Infection Regenerative medicine Rheumatology	IND	GEM187 is a fresh (non-frozen) human allogenic umbilical cord tissue derived mesenchymal stem cells (hUC-MSC) product. - Proprietary manufacturing process with no risk of contamination. - "Youngest" adult MSC with robust proliferation capacity. - Highly scalable to achieve enough cells. - Superior biological functions: optimal cell viability and biological functions maintained for therapeutic use.
05/29/20	GEM186	Innate Immune System Activator	Solid tumor	i.t.	Microbial	Oncology: Solid cancer	Phase 1	Co-activation of multiple innate immune pathways in tumor dendritic cells. Dose dependent anti-tumor activities in allogenic models. Low systemic risk
05/12/20	GEM184	GPR40 full agonist	Obesity, diabetes, NAFLD/NASH	Oral	Small molecule	Metabolic disease	Phase 1	A first-in-class GPR40 full agonist stimulating multiple islet (insulin, glucagon) and gut hormones (GLP-1, GIP, and PYY). GEM184 is much more effective in improving glucose control than DPP-4 inhibitors and in preclinical models. In addition to glucose-lowering effects, GEM184 effectively decreases body weight in overweight condition via stimulating gut hormones. By binding to a site independent of the fasiglifam binding site, GEM184 induces a similar therapeutic efficacy with much lower exposure (~1/270) compared to fasiglifam in diabetic models. A lower plasma exposure mitigates the risk of side effects including liver toxicities reported with fasiglifam. In addition, glucagon an GLP-1 stimulation by GEM184 induces therapeutic benefits on NAFLD/NASH conditions, in which DPP4 inhibitor and SGLT2 inhibitor were almost ineffective.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
05/12/20	GEM183	Direct renin inhibitor (DRI)	Blood pressure control and/or prevention of heart failure in patients with chronic hemodialysis	i.v.	Small molecule	Cardiology Renal disease	Preclinical	Injectable formulation of GEM182 (oral formulation in phase-2b), is also being developed for potential use for better blood pressure control and/or prevention of heart failure by chronic intravenous treatment three times per week via vascular access established in patients with chronic hemodialysis. Renin inhibitor may be suitable for such patients who often exhibit hyperreninemia potentially due to residual function of juxtaglomerular apparatus as well as reduced renal blood flow after start of the hemodialysis. Although dialysis patients are mostly unavoidable from hypertension, no optimal treatment has been available yet. GEM183 can fulfill such such rapid growing huge unmet medical needs. Licensing discussion is available except for China.
05/12/20	GEM182	Direct renin inhibitor (DRI)	Hypertension (HP), diabetic nephropathy (DKD), chronic hemodialysis, heart failure	Oral	Small molecule	Cardiology Renal disease	HP : Phase 2 ready, DKD: Phase 3 ready	A 2nd generation DRI with better renoprotective effects than ACEi/ARB. Better hypotensive effects than aliskiren is expected due to higher BA, less variability and no food effect following oral treatment. Prolonged renal localization, blood pressure independent renoprotection and positive effect on renal blood flow are evidenced by DRIs. In clinical trials of GEM182 in T2DM patients with microalbuminuria, dose-dependent UACR reduction and increases in remission rate from albuminuria were also seen. This compound have been developed as mono-therapy (not combined with ACEi/ARB). Therefore, GEM182 has no safety issues seen in aliskiren's ALTITUDE trial due to RAS dual blockade. Injectable formulation is also developed (ref. GEM183). Licensing discussion is available except for China.
05/11/20	GEM181	Selective HDAC8 inhibitor	Solid tumor	Oral	Small molecule	Oncology: Solid cancer	Phase 1	Through several mechanisms exhibited tumor inhibitory activity against many cancers, especially with high HDAC8 protein expression. Advantages of GEM181 - Able to pass the BBB - Suppresses angiogenesis - Side effects less than those of curretly marketed drugs - Simple synthetic method
05/08/20	GEM180	Contrasting	MRI Contrasting	i.v.	Nano particle	Diagnosis	Phase 2	GEM180 is a MRI contrast medium which can detect more small liver lesion, compared to marketed product, because of the better contrast. Biopsy confirmed the number of small nodules by GEM180. GEM180 has better imaging results (higher percent signal intensity loss (PSIL) and better consistency) from CT001. So far no obvious severe adverse events seen. Comprehensive patent portfolio exist globally.
05/08/20	GEM179	Iron supply	Iron deficient anemia	i.v.	Nano particle	Hematology	Phase 2	GEM179 is a PEGylated Iron oxide nano particle (IOP) with high macrophage uptake efficiency. GEM179 provide higher efficacy and better safety profiles (serum iron, ROS, hypersensitivity, iFGF23). Comprehensive patent portfolio exist globally.
05/07/20	GEM178	Anti-VEGF and antibacterial activities	Acne, hypertrophic scar, dermatitis	Topical skin	Small molecule	Dermatosis	Preclinical	- The first topical drug for treating skin redness by inhibiting VEGF. - Skin redness originates from the neovascularization. Redness of human acne was rapidly removed in a few days with no irritation nor discomfort. - Strongly inhibited P. acne with an effectiveness >100X clindamycin. - A 505(b)2 path available. - US Patent granted.



## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
05/01/20	GEM-CVD04	- Antiviral - Immunomodulatory - Anticoagulant - Cytokine release control	Pre-Exposure and Post Exposure Prophylaxis for COVID-19	Oromucosal (dissolves in the mouth)	Small molecules	Infection	Phase 1*	- Multi-targeted action - Systemic absorption and topical exposure to upper respiratory tract. colonized by COVID-19 virus. - *Entering Phase 2 for other indication (USA). - Available for a large clinical trial (GMP). - Excellent safety profile - Worldwide patents
04/27/20	GEM-CVD03	Fast response oral vaccine	COVID-19	Oral	Vaccine	Infection Vaccine	Phase-1/2	First-in-class COVID-19 immunotherapy to be used as an oral vaccine. This company has a track record to manufacture oral vaccine against highly pathogenic avian flu virus H5N1 on one week time. Oral vaccine will be easier to distribute to a large number of potentially virus-exposed people within very short period of time. The company is looking for partner who make the company accessing the virus and finance to manufacture the first batch within one week.
04/27/20	GEM177	BOTOX Biosimilar	Refer to Note	Injection	Protein	CNS Ophthalmology Pain/Neuropathy Urology Others	Preclinical	Equivalent efficacy and similar safety profile (for biosimilar for Allergan Botox) Manufacturing using plant-derived mediums  Indication - Therapeutic applications: strabismus, cerebral palsy, cervical dystonia, neurogenic bladder, migraine, facial spasm, blepharo spasm - Aesthetic application: all wrinkles produced due to persistent muscular contractions, square jaw reduction, hyperhidrosis
04/27/20	GEM176	A new anti-angiogenesis drug	Solid tumor* and Retina disorder **	Injection	Protein	Oncology: Solid cancer Ophthalmology	Preclinical	Best-in-class product against anti-VEGF agents The fusion protein of the second domains from VEGF receptor-1 and the Fc portion of human IgG1. Higher avidity for VEGF/PLGF and low immunogenicity and side effect. *More complete blockade of Tumor growth. (pancreatic cancer, liver cancer, gastric cancer, non-small cell lung cancer) **Longer duration of action (wet AMD, Diabetic macular edema, retinal vein occlusion, diabetic retinopathy)
04/24/20	GEM175	Elevates RPE phagocytic function to clear retinal drusen (lipoprotein deposits) and reduce oxidative stress	Intermediate AMD	Oral	Small molecule	Ophthalmology	Phase 2 ready	Novel high-dose reformulation of statin previously marketed as a lipid lowering drug, now developed for the new use of treating intermediate AMD. POC clinical trial showed a marked clearance of drusen and a 75% reduction in progression to late AMD (CNV/GA). Abbreviated 505(b)(2) pathway. Patent applications have been made globally.
04/24/20	GEM174	Invadopodia-Targeted siRNA	Advanced and/or highly metastatic cancers*	i.v.	Nucleic acid	Oncology: Solid cancer	Pre-IND	Invadopodia mediates cancer cell invasion, intravasation and extravasation. Master Invadopodial Regulators (MIRs) are the driver genes of cancer invasiveness and metastasis and are rarely expressed by normal cells. MIR-1 is also a cardinal regulator of Wnt activity and tumor growth. GEM174 is a lipid nanoparticles-formulated siRNA specifically targeting MIR-1. GEM174 suppressed many tumor growth and extended survival time in xenograft model. *hepatocellular carcinoma, triple-negative breast cancer, and gastric adenocarcinoma
04/22/20	GEM173	Anti-fibrotic effects	Anti-Fibrotic-Treatment of patients after Aortic-Valve-Implantation	Oral	Small molecule	Cardiology	Phase 1	Combination of marketed small molecule drugs to exert anti-fibrotic effects. A novel anti-fibrotic therapy is supposed to reduce progression of fibrosis and stabilize heart functioning. Myocardial fibrosis was found to independently predict cardiovascular mortality after AVI. Patent application has been made globally. Discussions are available for Japanese companies and Chinese companies.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
04/22/20	GEM172	Activation of multiple sulfatase	Multiple Sulfatase Deficiency	Oral / or injection	Small molecule	CNS Metabolic disease Orthopedic Rare disease	Preclinical – Phase 1 study in preparation	No effective treatment for the rare disease MSD is available. Combination of marketed drugs increase the activity of multiple sulfatases and significantly reduce toxic glycosaminoglycans in MSD fibroblast cell lines. Priority patent, which lead to global application, has been filed. Discussions are available for Japanese companies and Chinese companies.
04/22/20	GEM171	ARNT regulation	Fibrosis in kidney, heart and liver	Oral / or gene therapy	Small molecule or morpholinos	Cardiology Metabolic disease Urology	Discovery – Preclinical	No effective therapy for fibrosis is available yet. ARNT homodimerization attenuates fibrosis progression and induces regenerative cellular responses. Several mechanisms of action and potential drugs were identified, which show inhibition of ARNT degradation or activation of ARNT expression. PCT patent application filed. Discussions are available for Japanese companies and Chinese companies.
04/22/20	GEM170	Improved PCR	Diagnostic for detection of Paratuberculosis in animals and potentially Crohn's disease in humans	in vitro	Others	Diganosis Gastroenterology Infection	POC obtained in animals	New and improved PCR diagnostic test for fast and early detection of Mycobacterium avium subspecies paratuberculosis (MAP). This method shows better performance than current ELISA as well as on current PCR tests. Diagnostic test for early MAP detection in domestic livestock, exotic ruminations and human patients. Discussions are available for Japanese companies and Chinese companies. * Successfully tested in feces, blood, milk, sperm and tissue samples
04/16/20	GEM-CVD02	Immune modulation (reduction of cytokine storm) with anti-viral medicine	COVID-19	Oral	Small molecule	Immunology/ Inflammation Infection	Launch	COVID-19 progressing process is by first infecting from the virus and intriguing immune system modulated pro-inflammation, further proceeding to more serious inflammation, and later evolving to commencement of pro-fibrosis with infected pneumonia. TLR4 signaling pathway is closely associated with inflammation, immunity, and lung diseases. A TLR4 antagonist works well as an immune modulator for applications on pro-inflammatory diseases. GEM-CVD02 is a launched compound that has TLR4 antagonist activity and is expected the efficacy in combination of anti-viral medicine. GMP manufactured and FDA approved CTM capsules of this candidate are ready for clinical trial uses.
04/10/20	GEM-CVD01	SARS-CoV-2 spike protein expression from RNA followed by antibody response	COVID-19	Intramuscular	RNA Vaccine	Infection Vaccine	Preclinical	This program is a rapid COVID-19 vaccine development. This vaccine is developed on the basis of established technologies of RNA delivery and nanostructured lipid carrier formulation. GEM-CVD01 rapidly induces robust immune responses.
04/10/20	GEM169	Novel mechanism of action in anti-viral drug	Herpes zoster*, Genital Herpes** and Herpes Labialis**	Oral	Small molecule	Dermatosis Gynecology Infection Urology	Launch*, Phase 3**	GEM169 is a herpes viral enzyme inhibitor, that exhibits higher in vitro antiviral activity against both VZV and HSV than existing nucleic acid analogs. -Once daily dosing to support adherence -No cross-resistance with existing nucleic acid analogs -Low emergence of GEM169-resistant virus strains -No major safety concerns to date -No need to adjust dosage for renal-impaired patients (Hepatic excretion type drug)
04/10/20	GEM168	Heat-killed mycobacterium vaccae	Tuberculosis (TB)	Oral	Vaccine	Infection Vaccine	Phase 3	First-in-class tuberculosis immunotherapy to be used as an oral adjunct to standard TB drugs. In a 1-month phase 2 trial, the mycobacterial clearance in sputum smears was observed in 72% and 19% of patients on GEM168 and placebo, respectively.
04/08/20	GEM167	Elimination of MADD protein	Solid tumors	i.v., intra-tumoral	Gene therapy	Oncology: Solid cancer	Preclinical	A systemically deliverable oncolytic viral vector to target and eliminate the MADD protein overexpressed in a wide range of human cancer cell lines and involved in resistance. Systemic delivery demonstrated to colon, breast, liver, and ovarian tumors with no liver or kidney damage. Our parental vector infects and replicates only in cancer cells and has undergone extensive distribution and toxicity studies in mice and baboons and was previously approved for human trials. Breast, liver, and anaplastic thyroid cancer using siRNA achieved 41-60% TGI as mono or combo therapy.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
03/31/20	GEM166	Anti-Nodal antibody	Melanoma, Breast cancer, Pancreatic cancer and Hepatocellular carcinoma	i.v.	Antibody	Oncology: Solid cancer	Preclinical	The first anti-Nodal antibody drug targeting cancer stem cells and aggressive tumors. Nodal is a secreted protein in the embryo. The expression is lost in most adult tissues, but is reactivated in aggressive tumor cells. Expression level is highly correlated with invasion, metastasis, drug resistance and cancer prognosis. Combination of anti-Nodal Ab with current therapies is more effective than monotherapy. A companion diagnostic Nodal ELISA kit is also being developed which can be used as a biomarker for patient selection and disease monitoring.
03/25/20	GEM035	An anti-ENO1 antibody	Immune diseases, Various cancers	s.c.	Protein	CNS Gastroenterology Immunology/ Inflammation Infection Oncology: Solid cancer Respiratory Rheumatology	US FDA IND cleared	GEM035 is a humanized antibody against unique ENO1 target. This therapeutic antibody is first-in-class with macrophage-targeting features and showed efficacy in animal model for MS, IPF, and IBD. It also showed efficacy in animal model for liver cancer, pancreatic cancer, and lung cancer. GEM035 has a worldwide patent protection. US IND of GEM035 is approved and active now for treating MS.
03/13/20	GEM165	Intratumoral production of 5-FU and reduction of T-reg in the tumor	Colorectal cancer, Esophageal cancer, Gastric cancer	i.v.	Bacteria	Oncology: Solid cancer	Phase 2 ready	GEM165 is recombinant Bifidobacterium modified to express cytosine deaminase (CD). Bifidobacterium is anaerobic bacteria constituting human intestinal flora. Intravenously administered GEM165 colonizes to hypoxic solid tumor specifically and converts orally administered 5-FC to a high concentration of 5-FU only inside the tumor. The preclinical data of GEM165 in combination with anti-PD-1 antibody demonstrate synergistic anti-tumor efficacy accompanied by drastic Treg reduction.  Note: •First-in-class, patented, strong preclinical data of GEM165 alone and in combination with PD-1 blocker. •Clinical experiences in over 30 patients in the Phase 1 study in the US. •The design of Phase 2 combination therapy with anti-PD-1 antibody has been already consulted with FDA. The study is ready to start after completion of the Phase 1 study.
03/11/20	GEM164	Anthracycline topoisomerase II inhibitor	Breast cancer, Bladder cancer, Kaposi's sarcoma, lymphoma, and Acute lymphocytic leukemia	i.v.	Small molecule	Oncology: Hematological cancer Oncology: Solid cancer	Bioequivalence study completed	Generic pegylated liposomal doxorubicin hydrochloride. Doxorubicin is well known to cause cardiotoxicity and develop congestive heart failure. Cardiotoxicity of GEM164 is expected to be substantially lower than non-liposomal doxorubicin. Bioequivalence with CAELYX has been demonstrated.
03/02/20	GEM163	Reduction of virus-replication and reduction of inflammation	Virus diseases (incl. coronaviruses)**	Oral	Oligo-saccharides	Infection	NDIN** ready	A novel, intestinally absorbable derivative (pat. pend.) of GRAS $\alpha$ CD ( $\alpha$ -cyclodextrin) to reduce virus entry (endocytosis) and replication/assembly of viruses (availability of lyso-phospholipids). $\beta$ CDs have been effective in vitro against many virus infections, incl. coronaviruses, and typically against influenza and HSV2. $\alpha$ CDs avoid the ototoxicity of $\beta$ CDs and were more effective (tested in HIV-1 cells). **New dietary ingredient notification as a nutritional supplement/FSMP
03/02/20	GEM162	Restoration of autophagy and reduction of inflammation	Age-related diseases**	Oral	Oligo-saccharides	Others	NDIN** ready	A novel, intestinally absorbable derivative (pat. pend.) of GRAS $\alpha$ CD ( $\alpha$ -cyclodextrin) as an intermittent fasting mimetic. $\beta$ CDs have been effective in vivo against many age-related diseases, including cancer, AD, and PD. $\alpha$ CDs are more effective against endocytosis than $\beta$ CDs and lack the $\beta$ CDs' ototoxicity. In the EU, oral $\alpha$ CD may claim to "reduce post-prandial glycemic response", but has low and variable bioavailability. **New dietary ingredient notification as a nutritional supplement/FSMP

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
03/02/20	GEM161	Restoration of autophagy and reduction of inflammation	Cardiovascular and Metabolic Diseases	Oral	Oligo-saccharides	Cardiology Metabolic disease	Phase 2b/3 ready	A novel derivative (pat. pend.) of hydroxypropyl- $\alpha$ -cyclodextrin (HP $\alpha$ CD) that down-regulates the PI-system by controlling serum phospholipids and, thereby, reduces endocytosis. $\beta$ CDs have been shown to be effective in vivo against atherosclerosis (AS), NAFLD, but can cause permanent hearing loss (not applicable to $\alpha$ CDs). Oral $\alpha$ CD is clinically effective against metabolic syndrome, but has low and variable bioavailability. 505(b)(2) is applicable.
03/02/20	GEM160	Restoration of autophagy and reduction of inflammation	Neuro-degenerative diseases	Oral, Intra-theal	Oligo-saccharides	CNS	Phase 2b/3 ready	A novel derivative (pat. pend.) of hydroxypropyl- $\alpha$ -cyclodextrin (HP $\alpha$ CD) that down-regulates serum phospholipids and prevents aging cells from accumulating A $\beta$ /tau (AD), $\alpha$ -syn (PD), myelin (MS), mHTT (HD), SOD1 (ALS), ... . $\beta$ CDs were effective in vivo against AD and PD, but development was abandoned (except for NPC) due to the risk of permanent hearing loss (not applicable to $\alpha$ CDs). In the US, $\alpha$ CD is generally recognized as safe (GRAS) for oral use; in the EU, $\alpha$ CDs are approved for oral and parenteral use. 505(b)(2) is applicable.
03/02/20	GEM159	Restoration of autophagy and reduction of inflammation	Breast cancer and other carcinomas*	Oral, intra-venous	Oligo-saccharides	Oncology: Solid cancer	Phase 2b/3 ready	A novel intestinally absorbable derivative (pat. pend.) of hydroxypropyl- $\alpha$ -cyclodextrin (HP $\alpha$ CD) that down-regulates the Phosphoinositide-system by controlling serum phospholipids and, thereby, reduces endocytosis. $\beta$ CDs were effective in vivo against breast, ovarian, lung, and colon cancer, and metastatic melanoma, but need to be infused overnight and can cause permanent hearing loss. $\alpha$ CDs are not ototoxic and were more effective in vivo against growth and metastases of breast cancer. *Mono- or adjuvant treatment. 505(b)(2) is applicable.
02/27/20	GEM158	Anti-mitotic chemotherapy	Small cell lung cancer	i.v.	Small molecule	Oncology: Solid cancer	Phase 1 completed	Proprietary innovative albumin-stabilized pegylated liposomal docetaxel formulation. Elevated exposures of docetaxel compared with free (nonencapsulated) docetaxel were confirmed in animals and humans. Acceptable tolerability and results suggesting anti-tumor efficacy were observed in Phase 1. FDA orphan drug designation was granted and confirmed with FDA that 505(b)(2) NDA pathway appears to be an acceptable approach.
02/21/20	GEM157	Combined adoptive cell therapy (autologous)	Hepatocellular carcinoma (HCC)*	Infusion	Cell therapy	Oncology: Solid cancer	Launch	A combined adoptive cell therapy comprising cytokine-induced killer cells and activated cytotoxic T lymphocytes. In Phase III using patients whose tumors have been removed after curative resection for HCC, RFS was 44 months for the immunotherapy group while that of the control group was 30 months. The HR for tumor recurrence or death in the immunotherapy group vs the control group was 0.63. The mortality rate was reduced by 79% in the immunotherapy group vs the control group. Clinical trials for other solid tumors are ongoing. *: Adjuvant therapy for patients whose tumors have been removed after curative resection for HCC.
02/18/20	GEM156	Chromatin destabilizing	Solid and hematological tumors	Oral, i.v., i.a	Small molecule	Oncology: Hematological cancer Oncology: Solid cancer	Phase 1	A First-In-Class chromatin destabilizing agent that intercalates into DNA, and interferes with histone/DNA binding changing its spatial structure. Consequent functional inactivation of a histone chaperon FACT leads to inhibition of several previously undruggable pro-cancer transcriptional factors, activation of p53 and interferon response. Dose-dependent nonclinical antitumor activity is seen in multiple models of solid and hematological tumors. Oral and i.v. phase 1 studies demonstrated a manageable safety profile and disease control with tumor regressions and protracted stable disease.
02/18/20	GEM155	FPR2-specific ligand	Atopic dermatitis/Psoriasis, Dry eye disease, IBD (Inflammatory bowel disease), Asthma, Rheumatoid arthritis	Topical, Eye drop, s.c.	Peptide	Dermatosis Immunology/ Inflammation Ophthalmology Rheumatology	Preclinical	GEM155 is a small (7mer) lipidated peptide ligand for pro-resolving receptor FPR2 (N-formyl peptide receptor 2) involved in regulation of innate immune system and inhibition of ILC2 function (adaptive immune system). It also has anti-microbial effect for pathogenic bacteria through fusion with functional moiety. Efficacy is seen in animal models for the indications. CMC study is almost done. Toxicity study for topical usage and subcutaneous injection is going-on. Formulation for topical use is almost finished.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
02/18/20	GEM154	Collagen-inducing peptide	Dermal filler, Cosmetics	Topical	Peptide	Dermatosis Others	Preclinical	Laminin-derived peptide. Boosts collagen synthesis at sub-nanomolar concentration (Wrinkle-care) & inhibits melanin synthesis (Whitening). Registered cosmetic ingredient.
02/18/20	GEM153	Angiogenic peptide	Wound-care, Diabetic foot ulcer, Cosmetics	Topical	Peptide	Dermatosis Metabolic disease Others	Preclinical	Increases blood vessel formation (VEGFA/VEGFR1 expression ↑ & cell proliferation/migration ↑). Boosts collagen synthesis at sub-nanomolar concentration (Wrinkle-care) & inhibits melanin synthesis (Whitening). Registered cosmetic ingredient.
02/18/20	GEM152	Fat-adsorption inhibitor	Obesity, Diabetes, Fatty liver	Oral	Natural product	Metabolic disease	Preclinical	Mushroom-derived natural product. Reduces weight gain and obesity, blood glucose and lipid contents in the liver via reduction of lipid absorption in the gut.
02/18/20	GEM151	anti-GM-CSF monoclonal antibody	Rheumatoid arthritis & multiple new indications* (see note)	i.v.	Antibody	Immunology/ Inflammation Rare disease Rheumatology	Preclinical (ready for IND-enabling studies)	GM-CSF is a key player in inflammation and autoimmunity. GEM151 is a fully human monoclonal antibody generated by single B cell cloning and has superior affinity (Kd: 7.3 X 10 <sup>-11</sup> M) compared to competitors. Neutralizing activities were confirmed by four different functional assays. *cytokine release syndrome., GvHD, multiple sclerosis/neuroinflammation, Kawasaki disease
02/12/20	GEM150	Melanocortin 4 & 5 agonist	Obesity	Oral	Peptide	Metabolic disease	Preclinical	A pro-drug of the cyclic peptide (BL3020-1) which is a melanocortin 4 & 5 agonist showing good permeability in the gut and BBB and great reduction in food consumption and body weight gain in mice. The pro-drug did not show aggregation which BL3020-1 did. Currently the pro-drug is being optimized.
01/29/20	GEM149	PKC modulator	Alzheimer disease	Oral, Intranasal	Small molecule	CNS	Phase 1	Up-regulates production of α-secretase which cleaves the amyloid precursor protein, APP, into a harmless soluble form, sAPP-α, which is non-neurotoxic and limits the formation of amyloid plaques.
01/29/20	GEM148	CCR5 inhibition	HIV	i.v.	Nucleic acid	Infection	Preclinical	GEM148 is a nanoencapsulation of proprietary, synthetic CCR5-siRNA targeted to knock-down and eliminate HIV-1 in chronic HIV patients as well as prevent HIV-1 infection in naïve patients and re-infection in acutely-infected patients.
01/29/20	GEM147	Insulin	Diabetes	Oral	Peptide	Metabolic disease	Preclinical	GEM147 is a nanoencapsulation of insulin in biodegradable polymer nanospheres. Nanoencapsulation protects insulin during stomach passage. In vivo, statistically significant reduction in blood glucose was seen in diabetic rats with oral GEM147 within 30 minutes.
01/29/20	GEM146	VD Receptor	Prostate cancer, Autoimmune diseases	i.v.	Small molecule	Immunology/ Inflammation Oncology: Solid cancer	Preclinical	GEM146 is a nanosomal formulation of a nontoxic Vitamin D3 analog. In vivo studies have shown strong anticancer effects of GEM146 against Hormone Refractory Prostate Cancer xenografts in nude mice at doses approximately 6.5 times less than the parent hormone, without significant toxicity.
01/29/20	GEM145	5-HT	Chemotherapy Induced Nausea and Vomiting (CINV)	Oral	Small molecule	Oncology: Supportive care	Phase 2/3	Acute vomiting was blocked effectively by 5-HT3 anti-emetics plus the adjuvant Emend® <u>but no benefits were observed in terms of the incidence of nausea</u> . Phase 2/3 clinical trial on GEM145 as an adjuvant to conventional 5-HT3 anti-emetics was completed (more than 600 cancer patients). All doses of GEM145 significantly reduced acute nausea severity compared to the placebo (p=0.003).
01/29/20	GEM144	PKC modulator plus HDAC inhibitor	HIV Latency	i.v., Oral	Small molecule	Infection	Phase 2a	GEM144 is a nanoencapsulation of PKC modulators plus HDAC inhibitor in targeted, pegylated phospholipid nanosomes for improved therapeutic index. Activates HIV from latent reservoirs so that HIV can be eradicated from the body by antiviral therapy and/or immune system.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
01/29/20	GEM143	CB1, CB2, 5-HT1a	Multiple Sclerosis (MS), Opioid addiction, Chemotherapy induced Peripheral Neuropathic Pain (CIPNP), and Epilepsy	Oral	Small molecule	CNS Immunology/ Inflammation Oncology: Supportive care Pain/Neuropathy Rare disease	Preclinical	GEM143 is a nanoencapsulation of the API in biodegradable polymer nanospheres for improved oral bioavailability. <u>MS</u> : The API has multiple actions on key molecular neuroinflammation and neurodegeneration targets, with highly effective in vitro and in vivo bioactivities. <u>Opioid addiction</u> : The API is not an opioid and has been shown to alleviate cue-induced opioid addiction behaviors and allosterically modulate the $\mu$ and $\delta$ -opioid receptors. <u>CIPNP</u> : Nanoencapsulation is being used to protect the API during the stomach passage. <u>Epilepsy</u> : The API is an effective anti-convulsant with a specificity more comparable to drugs clinically effective in major seizures.
01/20/20	GEM142	Nrf2 Activator	COPD and Diabetic kidney disease	Oral	Small molecule	Metabolic disease Respiratory Urology	Phase 1	A novel Nrf2 activator. Inhibited airway inflammation to a similar degree as roflumilast in a mouse smoke exposure model. Improved urinary albumin/creatinine ratio in STZ-induced rat diabetic model (Type I) and KK-Ay mouse (Type II) and inhibited damage of the renal tissues. Synergistic effects by combination with losartan on urinary albumin/creatinine ratio were noted in KK-Ay mice. No adverse events were seen in multiple dose phase 1 study even at 1000 mg/man/day.
01/16/20	GEM141	Esophageal implant (See note)	Pediatric esophageal atresia and other conditions that affect the esophagus	Implant (autologous)	Cell therapy	Gastroenterology Regenerative medicine	IND ready	Esophageal implant made by combining a novel cell therapy platform (see TGEM38) with a patient's own cells (haematopoietic stem and precursor cells). GEM141 leverages the body's inherent capacity to heal itself as it is a "living tube" that facilitates regeneration of esophageal tissue and triggers a positive host response resulting in a tissue-engineered neo-conduit that restores continuity of the esophagus. These implants have the potential to dramatically improve the quality of life for children and adults
01/08/20	GEM140	Limbal stem cells	Intractable limbal stem cell deficiency	Implantation	Cell therapy	Ophthalmology	Clinical	Establishment and production of limbus-derived epithelial cell plate manufacturing process in GMP facility with excellent economic feasibility. Phase 1 study is currently in progress.
01/08/20	GEM139	<i>Staphylococcus aureus</i> vaccine	<i>Staphylococcus aureus</i> infection	s.c.	Vaccine	Infection Vaccine	Preclinical	The vaccine comprising antigens and toxin is being developed. The candidate antigens to block the immune-evasion pathway by MSCRAMMs and toxin of <i>S.aureus</i> have already been defined.
12/24/19	GEM138	Biosimilar adalimumab	Same indications as adalimumab	i.v.	Antibody	Dermatosis Gastroenterology Immunology/ Inflammation Ophthalmology Rheumatology	Preclinical	Purified GEM138 is highly similar to adalimumab by SDS-PAGE. GEM138 and adalimumab show a similar response in a TNF- $\alpha$ ELISA assay. Plant-based technology (TGEM036) was applied for production of GEM138.
12/24/19	GEM137	Biosimilar ranibizumab	Same indications as ranibizumab	Intra-vitreous	Antibody	Ophthalmology	Preclinical	Peptide mapping by Mass Spectrometry confirms amino acid sequence identity of GEM137 with ranibizumab. Purified GEM137 is highly similar to ranibizumab by SDS-PAGE. Ligand (rVEGF) binding by GEM137 demonstrated to be similar to ranibizumab by ELISA. Plant-based technology (TGEM036) was applied for production of GEM137.
12/24/19	GEM136	Biosimilar trastuzumab	Same indications as trastuzumab	i.v.	Antibody	Oncology: Solid cancer	Preclinical	GEM136 N-terminal sequences are identical to trastuzumab. Levels of contaminating proteins, profiles of breakdown products and inhibitory activity to trastuzumab on in vitro growth of hER2 positive breast cancer cell line are similar between GEM136 and trastuzumab. Plant-based technology (TGEM036) was applied for production of GEM136.
12/20/19	GEM135	Inhibition of proteasome via novel target	Multiple tumors	i.v., i.p. and Oral	Small molecule	Oncology: Hematological cancer Oncology: Solid cancer	Preclinical	Novel target different from that for all the commercially available proteasome inhibitors. Works against many cancer cell lines tested including bortezomib, cisplatin and paclitaxel resistant cell lines. Significant therapeutic window between cancer and normal cells. Favorable toxicity profile. Regressed tumor growth and prolonged survival on syngeneic and xenograft mouse models. Expected to be effective against solid tumors without off target effects and peripheral neuropathy. Two lead compounds are being developed.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
12/06/19	GEM134	Anti-CD147 antibody	Hematological (AML, MM etc) and solid tumors (liver, colon, lung etc)	i.v.	Antibody	Oncology: Hematological cancer Oncology: Solid cancer	Preclinical	Fully human antibody binding to human/ cynomolgus CD147. Has been shown to be very effective in various types of cancers in vivo xenograft mouse model. ADCC activity mainly contributes to the anti-tumor effect.
11/29/19	GEM058	Increase cellular ATP and promote wound healing	Diabetes foot ulcer	Topical	Small molecule	Dermatosis Metabolic disease	Phase 2 completed	Reducing inflammation of endothelial cells of blood vessels. Increasing cellular ATP and speeding up the healing of wounds by promoting the migration of epithelia cells in the skin of wounds. The arrangement of actin which is essential for cell migration is ATP dependent. Applicable to all kind of wound and low cost treatment
11/25/19	GEM133	Myocardial protection by cardiac arrest temporarily	Open heart surgery	Intra-coronary infusion	Others	Cardiology	Launched	GEM133 is a novel warm cardioplegic solution which in mixture with patient's oxygenated blood can produce effective and sustained cardiac arrest by a single dose 400ml. In addition, it has the following advantages; virtually unlimited aortic cross-clamp time, unassisted resumption of the cardiac rhythm, no ischemic and /or reperfusion injury, no need for cardiotoxic support in the immediate postoperative period.
11/15/19	GEM132	Matrix metalloproteinase-13 (MMP-13) inhibitor	Osteoarthritis (OA)	Intraarticular or Oral	Small molecule	Orthopedic	Preclinical	Extremely potent non-hydroxamic acid containing, non-zinc binding inhibitors of MMP-13 have been identified. High selectivity has been shown for this class of inhibitors over other MMPs. Lead inhibitor tested in the monoiodoacetate (MIA) rat model of OA and shown to protect cartilage when injected into the joint. Exhibits good oral bioavailability in the rat.
11/15/19	GEM131	Matrix metalloproteinase-2 (MMP-2) and MMP-9 inhibitor	Neuropathic pain and Amyotrophic Lateral Sclerosis (ALS)	Oral	Small molecule	CNS Pain/Neuropathy Rare disease	Close to IND ready *	Pain: GEM131 can block inflammatory responses at the site of nerve damage and has been shown to be efficacious in 4 different rodent models of neuropathic pain (spinal nerve ligation, chronic constriction injury of the infraorbital nerve, morphine withdrawal and thermal injury). ALS: Elevated levels of MMP-2 and -9 have been found in the skin and blood of people with ALS. Significantly improved larval locomotion in both the TDP-43 and SOD1 larvae models in Drosophila. Exhibits good oral bioavailability. *: Final stages of completion of IND enabling studies for both neuropathic pain & ALS
11/15/19	GEM130	Antiviral	Infections caused by herpes simplex virus in face and lip	Topical	Small molecule	Dermatosis Infection	Launched	<ul style="list-style-type: none"> <li>• First cold sore product on the market that combines the therapeutic benefits of an antiviral with an innovative transparent bioadhesive film.                             <ul style="list-style-type: none"> <li>• When applied to the lesion, generates a transparent film that acts as a bioadhesive sustained matrix release that improves product bioavailability while promotes itching reduction and wound healing.</li> </ul> </li> <li>• Indicated for the topical treatment of symptoms (tingling, burning, discomfort) of recurrent herpes labialis caused by herpes simplex virus (VHS).</li> </ul>
11/15/19	GEM129	Immuno-modulator	Anogenital warts, Actinic keratosis, Basal cell carcinoma	Topical	Small molecule	Dermatosis Infection Oncology: Solid cancer Urology	Phase 2	<ul style="list-style-type: none"> <li>• The first product on the market that combines the therapeutic benefits of a marketed immunomodulator with an innovative transparent bioadhesive film.</li> <li>• When applied to the lesion, generates a transparent bioadhesive film, which acts as a reservoir or matrix release and reduces the local reactions and increases the permanence of the product in the action site.</li> <li>• The results of non-clinical studies demonstrate that GEM129 has a better safety profile with an equivalent efficacy than its reference product. Clinical studies on-going.</li> </ul>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
11/15/19	GEM128	Antibiotic	Primary and secondary skin infection - canine pyoderma	Topical	Small molecule	Others	Clinical for animal	<ul style="list-style-type: none"> <li>The first medicine on the market that combines the therapeutic benefits of a marketed antibiotic with an innovative film-forming, long-lasting delivery technology.</li> <li>When applied to the lesion, generates a transparent film that acts as a bioadhesive sustained release matrix maintaining the optimum concentration of the antibiotic in the skin for a period of 6-8 hours.</li> <li>The bioadhesive film generated reduces product removal from the area due to animal scratching, licking or friction with skin folds which contribute in improving the treatment efficacy. Also, reduces oral antibiotic overusing by improving topical treatment with this innovative technology. *Canine bacterial infections of the skin, including superficial pyoderma</li> </ul>
11/15/19	GEM127	Antibiotic	Primary and secondary skin infection - Impetigo, folliculitis, furunculosis (human use)	Topical	Small molecule	Dermatosis Immunology/ Inflammation Infection	Launched	<ul style="list-style-type: none"> <li>The first product on the market that combines the therapeutic benefits of a marketed antibiotic with an innovative transparent film-forming and bioadhesive delivery technology.</li> <li>When applied to the lesion, generates a film that acts as a bioadhesive sustained release matrix, maintaining the optimum concentration of antibiotic in the skin for a period of 6-8 hours.</li> <li>The bioadhesive film generated prevents the removal of the antibiotic from the lesion and acts as a protective dressing that prevents infection spreading.</li> <li>Both antagonizes and degrades ER alpha in cells to achieve the goal of blocking the estrogen signaling pathway.</li> <li>Favorable oral pharmacokinetics in healthy rats and dogs whereas fulvestrant has a low bioavailability and can only be intramuscularly administrated.</li> <li>Favorable preclinical in vitro and vivo single agent efficacy in inhibiting ER+ breast cancer cell proliferation, in models of tamoxifen-sensitive and tamoxifen-resistant breast cancer.</li> <li>Highly selective, no effect on other kinases and receptors.</li> <li>Can be licensed to global area with some limitation.</li> </ul>
11/5/19	GEM126	Selective estrogen receptor downregulator	ER+ advanced or metastatic breast cancer	Oral	Small molecule	Oncology: Solid cancer	Phase 1	<ul style="list-style-type: none"> <li>Both antagonizes and degrades ER alpha in cells to achieve the goal of blocking the estrogen signaling pathway.</li> <li>Favorable oral pharmacokinetics in healthy rats and dogs whereas fulvestrant has a low bioavailability and can only be intramuscularly administrated.</li> <li>Favorable preclinical in vitro and vivo single agent efficacy in inhibiting ER+ breast cancer cell proliferation, in models of tamoxifen-sensitive and tamoxifen-resistant breast cancer.</li> <li>Highly selective, no effect on other kinases and receptors.</li> <li>Can be licensed to global area with some limitation.</li> </ul>
11/5/19	GEM124	Improves endothelial cell function and cellular fluidity. Antiatherosclerotic, antiinflammatory, anti-fibrotic, fat-targeting composition	1) Atherosclerosis (#) 2) Treatment of NASH (Stage F2-F3) Fibrosis with no worsening of fibrosis.	Oral	Small molecule	Cardiology Immunology/ Inflammation Metabolic disease	Preclinical	<p>1) Developed to target vulnerable, high risk plaques while also reducing LDL cholesterol, increasing HDL cholesterol and reducing Triglycerides. (#) Future indications: primary prevention of Heart Attack, Stroke and Death and Secondary Prevention of Myocardial Infarction in Europe. US Patent to treat Atherosclerosis is valid until 2035.</p> <p>2) Concurrently being developed to treat liver inflammation, fibrosis and fat accumulation while also reducing LDL cholesterol and Triglycerides. *May be used in combination with other drugs, such as Intercept's Ocaliva that increases Triglycerides or Gilead's NASH candidate that increases LDL cholesterol.</p>
10/29/19	GEM123	miRNA targeting cancer stem cells	Colon cancer	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	GEM123 suppressed the stemness of cancer cells by inhibiting KLF5 expression, and provoked apoptosis and cycle arrest through the downregulation of TFDP1 and MDM2 expressions. GEM123 also inhibited tumor growth with no apparent side effect in mouse model.
10/29/19	GEM122	Natural Killer T (NKT) cell-mediated anti-tumor responses	Solid cancer	i.v.	Cell therapy	Oncology: Solid cancer	Phase 1	GEM122 shows its anti-tumor activity by activating endogenous NKT cells. Activated NKT cells strongly enhance both innate and acquired immune systems, induce the long-term immune memory and promote accumulation of TILs (tumor infiltrating lymphocytes) in tumor sites. GEM122 consists of a novel NKT ligand and a novel APC. The novel NKT ligand shows much stronger NKT activity than the previous NKT ligand, $\alpha$ -Galactosylceramide and by using the novel APC, the cellular product can be manufactured efficiently as well.
10/23/19	GEM121	Modified phytic acid	Cancer	Oral	Small molecule	Oncology: Hematological cancer	Preclinical	<ul style="list-style-type: none"> <li>Demonstrated selective anti-cancer effects including apoptosis and inhibition of AKT activation.</li> </ul>
10/23/19	GEM120	Inhibition of membrane binding of Pr55Gag	HIV	i.v.	Small molecule	Infection	Preclinical	<ul style="list-style-type: none"> <li>Inhibited the membrane localization of Pr55Gag and stopped budding of HIV virus.</li> <li>Captures HIV in immune cells and induces apoptosis of the HIV-infected immune cells.</li> </ul>



## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
10/23/19	GEM119	Inactivation of end-product of lipid peroxidation	Cerebral Infarction	i.v.	Small molecule	CNS	Preclinical	<ul style="list-style-type: none"> <li>• Showed more potent 4-hydroxynonenal - quenching activity compared with carnosine or histidine hydrazide (HH) at 30min incubation.</li> <li>• GEM119 (ip administration) rescued the hippocampal CA1 cell death of transient cerebral ischemia model of Mongolian gerbil whereas HH did not.</li> </ul>
10/23/19	GEM118	Suppression of TGF-β/Smad and related signaling	Systemic sclerosis	Oral	Small molecule	Dermatosis Rare disease	Preclinical	<ul style="list-style-type: none"> <li>• Inhibited phosphorylation of Smad3 and expression of Col1a2, FN1 and CTGF stimulated by TGF-β in cultured human dermal fibroblasts.</li> <li>• Ameliorated bleomycin-induced skin fibrosis in both preventative and curative mouse model.</li> </ul>
10/16/19	GEM117	Induction of apoptosis in adipocyte	Liposysis, Non-surgical fat reduction, Diabetesity,	Sub-cutaneous	Small molecule	Metabolic disease	Phase 2a	<ul style="list-style-type: none"> <li>• GEM117 specifically induce apoptosis on local injection site adipocyte</li> <li>• Phase 1 showed great safety without drug related SAE in 40 healthy volunteers</li> <li>• In pre-clinical study</li> <li>- Better efficacy on local fat reduction and less side effects that surpass the current surgical liposuction and other non-surgical products.</li> <li>- Has benefit effects on lipid and glucose metabolism and improves the indicator of diabetes</li> </ul>
10/16/19	GEM116	Increase in lipolysis, fat and energy metabolism	Obesity, Diabetesity, NAFLD/NASH	Oral	Small molecule	Metabolic disease	Phase 2	<ul style="list-style-type: none"> <li>• GEM116 demonstrated the safest profile in its clinical phase 2 study with more than 200 patients without any drug related AE or SAE and potentially lower CVD risk seen by other competitors in the market.</li> <li>• Around 30% of subjects lost at least 5% body weight in 12 weeks, GEM116 shows around 5% body fat lost, lower TC by around 12mg/dL, and lower LDL by around 6 mg/dL</li> <li>• Pre-clinical study shows GEM116 has the potential to treat NAFLD/NASH via reducing liver fibrosis by around 40% .</li> </ul>
10/16/19	GEM115	Trastuzumab biosimilar-ADC	HER2-positive metastatic breast cancer	i.v.	Antibody	Oncology: Solid cancer	Phase 1	<p>Conjugate of trastuzumab biosimilar and DM-1. The profiles of trastuzumab of GEM115 and GEM115 are similar to Herceptin and Kadcyca, respectively, in peptide mapping, receptor binding affinity, inhibition of cell proliferation, ADCC activities, in vivo xenograft mouse model, PK etc.</p> <p>Potential Indication: Early Breast Cancer (adjuvant)</p>
10/16/19	GEM114	Ophthalmic formulation of GEM113	Wet AMD	Intra-vitreol	Antibody	Ophthalmology	Phase 1	<p>GEM114 mainly distributed in retina, vitreous body and aqueous humor after intravitreal injection in animals.</p> <p>Potential Indication: Diabetic Macular Edema; Myopic Choroidal Neovascularization (mCNV); Retinal Vein Occlusion (RVO); Diabetic Retinopathy (DR)</p>
10/16/19	GEM113	Bevacizumab biosimilar	Non-Squamous NSCLC	i.v.	Antibody	Oncology: Solid cancer	Phase 3	<p>The profile of GEM113 is similar to Avastin, in peptide mapping, receptor binding affinity, inhibition of cell proliferation, in vivo xenograft mouse model, PK etc.</p> <p>Potential Indication: Metastatic Colorectal Cancer; Recurrent Glioblastoma; Metastatic Renal Cell Carcinoma; Persistent Recurrent or Metastatic Cervical Cancer; Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer</p>
10/4/19	GEM112	Antibody against <i>H.pylori</i> - derived HSP60	Eradication of <i>H.pylori</i>	i.v.	Protein	Gastroenterology Infection	Preclinical	<p>Antibiotic-resistance <i>H.pylori</i> are getting serious and antibiotic therapy failure rate is over 20%. GEM112 is a highly specific antibody against H.Pylori-derived HSP60 which inhibits T cell proliferation and induces IL-10 and TGF-β1. GEM112 does not bind to human HSP60.</p>
10/4/19	GEM065	Fucosylation of CAR-T cell and TCR-T cells to improve homing to tumors, increased intra-tumor penetration and killing of cancer cells. Potential for enabling CAR-T cell therapies to achieve higher response rates for treatment of blood cancers and also work for treatment of solid tumors	Lymphoma, Leukemia, Melanoma, Lung and breast cancers are initial indications	Infusion	Protein	Oncology: Hematological cancer Oncology: Solid cancer	Preclinical; Human safety and efficacy observed in stem cell transplantation	<p>Ex-vivo fucosylation kit using proprietary recombinant fucosyl-transferase enzymes aimed at improving efficacy, safety and cost of care for T-cell therapy not only for treatment of blood cancers but also importantly, enabling CAR-T cell therapy to work in the treatment of solid tumors . Similar technology as in GEM036 for hematopoietic stem cell therapy, but a different fucosyl-transferase is used. Fucosylation enhances homing and intra-tumor penetration of CAR-T, TCR-T, TIL/CTL cells for improved tumor killing. Fucosylation does not affect healthy tissues.</p>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
9/30/19	GEM111	c-RAF allosteric inhibitor	Multiple cancers (lung, renal, liver etc)	Oral	Small molecule	Oncology: Solid cancer	IND	A second generation (novel salt) of the c-RAF allosteric inhibitor in GEM 110 allowing for a more patient-centric dose profile. The clinical safety profile of GEM110 thus far will be informative and additive to the current clinical program thereby significantly de-risk and accelerate the clinical stage development of GEM111.
9/30/19	GEM110	c-RAF allosteric inhibitor	Multiple cancers (lung, renal, liver etc)	Oral	Small molecule	Oncology: Solid cancer	Phase 1	The product is the combination of GEM110 and sorafenib. The product induces pDA PK and c-Raf to transfer from mitochondria to cytoplasm together with ROS increment resulting tumor cell death and demonstrated 73% and 57% tumor inhibition rate respectively in lung cancer and renal cancer animal xenograft model. FDA approved the clinical protocol to explore subjects by p-DAPK biomarker whose expression could be related with tumor progression.
9/30/19	GEM108	Buccal Epithelial cells for re-epithelization	Urethral strictures	Implantation	Cell therapy	Regenerative medicine Urology	Phase 2b completed	Live cultured buccal epithelial cells indicated for urethral strictures. Excellent safety and efficacy profiles have been established through Phase IIb clinical trials. Potential label extension to rare disease in pediatric population; hypospadias.
9/30/19	GEM107	Chondrocytes for hyaline cartilage regeneration.	Articular cartilage defects	Interventional Implantation	Cell therapy	Orthopedic Regenerative medicine	Launch	Live cultured chondrocytes indicated for hyaline cartilage regeneration in cartilage injuries. Over 600 patients treated with several publications and patent protection.
9/30/19	GEM106	Osteoblasts for bone regeneration	Avascular necrosis/ Osteonecrosis	Interventional Implantation	Cell therapy	Orthopedic Rare disease Regenerative medicine	Launch	Live cultured osteoblasts indicated for bone repair and regeneration that stop progression of avascular necrosis. Over 400 patients treated with GEM106. Potential label extension to different indications. This product has been granted Orphan Designation by the US FDA & EMA
09/24/19	GEM105	Viscosupplementation	Knee osteoarthritis	Intraarticular	Poly-saccharide	Orthopedic	NDA application	Cross-linked sodium hyaluronate hydrogel with sodium hyaluronate fluid. Long lasting and sustainable efficacy due to unique rheology of the cross-linked hydrogel. Injected only once and single injection shows comparable efficacy to a multiple-injection treatment. Phase-III clinical trial has been finished and NDA application has been submitted.
09/12/19	GEM104	Interleukin-1 beta inhibition	Various types of colitis (IBD, immune-related and chemotherapy-induced colitis)	Oral	Small molecule	Gastroenterology	Preclinical	-A known approved drug molecule developed for new therapeutic indications of treating and alleviating symptoms of various types of colitis. -Showed greater pharmacological effects than the reference drug, mesalazine, in reducing inflammatory colon swelling and intestinal ulceration, while restoring damaged intestinal membrane. -One of few products capable of repairing damaged intestine membrane caused by colitis. -Synergistic effect via different mechanism of actions, can provide greater medical benefits to patients suffering from IBD or various types of colitis caused by cancer treatment with chemotherapy or immuno-therapy.
09/03/19	GEM103	Iron chelator	Neurodegenerative and Ophthalmologic diseases including Traumatic brain injury (TBI) and AMD as lead indications. Additional indications in PD and	Oral	Small molecule	CNS Ophthalmology Rare disease	Phase 2 ready for TBI and Phase 1 ready for AMD	Novel oral iron chelator with excellent PK and ability to penetrate the brain and retina. Non-protein bound or "free" iron has been demonstrated to be deeply involved in neurodegenerative and ophthalmologic diseases, yet optimal chelators are not available. GEM103 efficiently removes free iron from the brain and retina. Biomarkers to guide drug development are available for both TBI and AMD. Phase 1 trials have been completed for transfusion-related iron-overload. Chronic toxicology completed.
08/21/19	GEM102	Cyclodextrin derivative	Cancer	i.v.	Small molecule	Oncology: Solid cancer	Preclinical	Modified Methyl- $\beta$ -Cyclodextrin (CyD). Displayed potent antitumor activity in vitro, compared to M- $\beta$ -CyD. Drastically inhibited tumor growth after a single intravenous injection to tumor-bearing mice, compared to doxorubicin and M- $\beta$ -CyD, without any significant change in blood chemistry values.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
08/16/19	GEM101	GABA-A negative allosteric modulator and an inhibitor of $\alpha 2 \delta$ subunit of voltage-gated calcium channels	Depression and PTSD	Intra-nasal	Peptide	CNS	Preclinical	Exhibited both rapid and long-lasting anxiolytic and antidepressant activity in vivo animal models. Stable in vivo and crosses the blood-brain barrier. No adverse effects typical for standard of care drugs (No sedation, No tolerance, No cognitive impairment, No addiction potential).
08/16/19	GEM100	mGluR5 negative allosteric modulator	Depression and movement disorder	Intra-nasal	Peptide	CNS	Preclinical	mGluR5 leader peptide was discovered and in vivo efficacy confirmed. GEM100 specifically increases locomotor activity in rats, with no effects on behavior.
08/16/19	GEM099	TrkB modulator	Depression	Intra-nasal	Peptide	CNS	Preclinical	TrkB peptide modulator discovery was launched.
08/13/19	GEM098	GnRH receptor antagonist	Endometriosis and Uterine fibroids	Oral	Small molecule	Endocrinology Gynecology	Phase 1	In Phase 1b, GEM098 showed dose-dependent suppression of LH, FSH and E2. The suppressive effects on E2 lasted up to 24 hrs and were more excellent when compared with the published phase 1 data of Elagolix in healthy premenopausal women. No serious adverse events were seen and well tolerated up to 320 mg QD.
08/13/19	GEM097	Factor VIIa derivative	Bypassing therapy in hemophilia with inhibitors	i.v.	Protein	Hematology	IND ready	GEM097 is rFVIIa fused to transferrin and has longer half-lives than rFVIIa in rats and monkeys. A cleavable linker between rFVIIa and transferrin of GEM097 allows minimal reduction of FVIIa activity due to fusion. Preclinical (GLP) toxicity studies did not show any toxic evidence in rats or monkeys.
07/31/19	GEM096	Progesterone receptor agonist	Recurrent preterm birth	Oral	Small molecule	Endocrinology Gynecology Rare disease	Phase 2 completed	Potentially the first oral hydroxyprogesterone caproate product candidate indicated for the prevention of recurrent preterm birth and has been granted orphan drug designation by the FDA. An end of Phase 2 meeting was completed with the FDA.
07/31/19	GEM095	Androgen receptor agonist	NASH, Cirrhosis	Oral	Small molecule	Metabolic disease	Phase 1	An oral prodrug of bioidentical testosterone that is being developed as a treatment of cirrhotic non-alcoholic steatohepatitis (NASH).
07/31/19	GEM094	Androgen receptor agonist	NASH, Pre-Cirrhosis	Oral	Small molecule	Metabolic disease	Phase 2 ongoing	An oral prodrug of bioidentical testosterone that is being developed as a treatment of non-alcoholic steatohepatitis (NASH) and is being studied in the LifT Phase 2 clinical study in biopsy confirmed NASH subjects.
07/31/19	GEM093	Androgen receptor agonist	Hypogonadism	Oral (QD)	Small molecule	Endocrinology Urology	Phase 2 completed	A novel next generation oral prodrug of testosterone with potential for once-daily oral dosing that has completed Phase 2 testing.
07/31/19	GEM092	Androgen receptor agonist	Hypogonadism	Oral (BID)	Small molecule	Endocrinology Urology	Phase 3 (a few months before PDUFA date)	A novel oral prodrug of testosterone that is designed to help restore normal testosterone levels in hypogonadal men. GEM092 was well tolerated and met the primary end-points in Phase 3 testing with twice daily dosing. Easy to use for patients and physicians to prescribe due to fixed dosing regimen.
07/16/19	GEM091	Prevention of protein aggregation via increased intracellular ATP and increase of expression of tyrosine hydroxylase (TH)	Parkinson's disease	Oral Nasal	Small molecule	CNS	Preclinical	New treatment for Parkinson's disease. GEM091 increases intracellular ATP level and ATP is reported to boost protein solubility. GEM091 increases TH expression and dopamine production, reverses paraquat induced PD symptoms and improves behavior of 6-OHDA treated mice.
07/16/19	GEM090	Increase cellular ATP and promote wound healing	Epidermolysis bullosa (EB)	Topical	Small molecule	Dermatosis Rare disease	Preclinical	Increasing cellular ATP and speeding up the healing of wounds by promoting the migration of epithelia cells in the skin of wounds. Expected to shorten wound healing time and improve EB patients' QOL with a formulation optimized for EB treatment. Moreover, maybe reduces the risk of squamous cell carcinoma which is highly related to Dystrophic EB patients.
07/12/19	GEM089	Inhibition of pro-cytokines, enhancement of growth factor PDGF	Alzheimer's disease and Vascular dementia	Topical	Botanical	CNS	Phase 2	Small molecules from soybean extract. MOA is different from Tau and Amyloid mechanisms. Effective in $AlCl_3$ induced Alzheimer-like dementia model and bilateral common carotid artery occlusion induced vascular dementia model. In Phase 2 study, MMSE and ADAS-Cog for patients without any dementia medication indicated that 70-85% patients improved at weeks 4 and 12.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
07/12/19	GEM088	SSRI with agonist-antagonistic action on 5-HT receptors	Urinary incontinence	Oral	Small molecule	Urology	Phase 3 ready	<p>Repositioning from another indication and has already a proven record of good safety in more than 300 patients with further 300 treated in phase 2. It has shown therapeutic activity in animal models of both stress and urge urinary incontinence.</p> <p>In phase 2 trials, clinically meaningful effects in mixed incontinence were shown as well as very good tolerability. The compound is ready to enter phase 3.</p>
07/08/19	GEM087	Corticosteroid receptor agonist	Ocular inflammation and Meibomian gland dysfunction (MGD)	Topical (eye drop)	Small molecule	Ophthalmology	Preclinical	<p>New ophthalmic suspension of loteprednol etabonate (LE) with improved ocular bioavailability.</p> <ul style="list-style-type: none"> <li>- Drug exposure in aqueous humor and iris ciliary body are about 6 fold higher than Lotemax® in rabbits.</li> <li>- The new formulation of LE administered twice a day for the treatment of adjuvant induced chronic uveitis model in rabbits showed a similar efficacy with lotemax administered four times a day</li> </ul>
07/08/19	GEM086	VEGF inhibitor	Wet AMD (age-related macular degeneration)	Topical (eye drop)	Small molecule	Ophthalmology	Preclinical	<p>New formulation of axitinib designed to deliver the drug across ocular tissues to choroid and retina.</p> <ul style="list-style-type: none"> <li>- Greatly enhancing aqueous solubility (4000-fold solubility enhancement)</li> <li>- High drug exposure in retina (300-fold of IC50)</li> <li>- Potential for substitution of anti-VEGF Ab treatment via intravitreal injection</li> </ul>
07/08/19	GEM085	Cancers with moderate to high Her2 expression	Cancers with moderate to high Her2 expression	i.v.	Protein	Oncology: Solid cancer	Preclinical	<p>The anti-Her2 ADCs consisting of trastuzumab and novel linker-drugs.</p> <ul style="list-style-type: none"> <li>- 10-100 fold higher potency comparing to Kadcyla®</li> <li>- High therapeutic window (MED ~1-2 mg/kg, MTD ~100 mg/kg in mice)</li> <li>- High tumor growth inhibition rate (90-100%) with high stability in vivo</li> </ul>
07/04/19	GEM084	MRI contrast agent formulation	Diagnosis of bladder cancer	Topical (Intravesical)	Other	Diagnosis	Phase 2 ready	<p>New formulation consisting of iron and gadolinium for intravesical instillation. A pilot trial in humans provided evidence that the MRI contrast agent can be detected in the bladder wall. No treatment-related AEs were observed.</p>
07/04/19	GEM083	Vasoconstriction and anti-inflammatory action	Hemorrhagic cystitis	Topical (Intravesical)	Small molecule	Immunology/ Inflammation Oncology: Supportive care Rare disease Urology	Phase 2	<p>Pre-liposomal lyophilate containing tacrolimus.</p> <p>POC achieved in animal models of both chemo-cystitis and radiation cystitis.</p> <p>POC achieved in first-in-man experience treating severe recurrent hemorrhagic cystitis.</p> <p>Orphan drug designation granted.</p>
06/27/19	GEM082	Modified IL-1 receptor antagonist (IL-1RA)	Osteoarthritis, Gout, Anterior cruciate ligament (ACL) injury	Intra-articular	Protein	Immunology/ Inflammation Orthopedic	Preclinical	<p>Single intra-articular injection of Anakinra (rhIL-1RA) improved OA symptoms vs placebo in clinical Phase-2 but the effect was short-lasting.</p> <p>GEM082 showed prolonged retention in the joint and sustained efficacy. GEM082 targets directly the biology of the inflammasome, involved in acute OA pain flares, without the adverse effects of steroids.</p> <p>Available for licensing outside the USA.</p>
06/12/19	GEM081	Oncolytic virus	Solid tumor (Melanoma, GI cancer etc.)	IM	Virus	Oncology: Solid cancer	Phase 2 ready	<p>Genetically non-modified and non-pathogenic virus with</p> <ul style="list-style-type: none"> <li>- oncolytic, oncotropic and immunomodulating properties</li> <li>- excellent safety profile</li> <li>- various development options</li> </ul> <p>Medicine containing this virus is already approved for treatment for many years in certain countries.</p> <p>This virus has established fully GMP certified API production</p>

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
06/06/19	GEM080	Novel cell surface receptor for insoluble protein involved in Parkinson's/Lewy body diseases	Parkinson's diseases, Lewy body disease	NA	NA	CNS	Preclinical	Cell surface receptors for insoluble protein involved in Parkinson's disease/Lewy body disease which were newly identified by utilizing artificial liposomes embedded with endogenous membrane proteins (see TGEM025 in Technology). Antagonists of the receptors are expected to be effective on Parkinson's/Lewy body diseases.
06/06/19	GEM079	Novel cell surface receptor for angiogenesis regulation	Cancers, Chronic inflammation, Diabetic retinopathy, Myocardial infarction, etc	NA	NA	Cardiology Oncology: Solid cancer Ophthalmology	Preclinical	Cell surface receptor involved in angiogenesis which was newly identified by utilizing artificial liposomes embedded with endogenous membrane proteins (see TGEM025 in Technology). Agonists of the receptor are expected to be effective on diseases where angiogenesis is involved as an aggravating factor.
05/30/19	GEM078	Hyaluronic acid-based nanocarriers of cisplatin	Head and neck cancer, Pancreatic cancer, Melanoma with metastasis	i.v.	Small molecule	Oncology: Solid cancer	Preclinical	CD44 targeting and higher stability lead to enhance lymphatic delivery and inhibit cancer with lymphatic metastasis. Chemodrug encapsulated by nanocarriers minimize systemic toxicities. Convenient dosing by intravenous injection.
05/30/19	GEM077	AMPK activator	Topical fat accumulation	Transdermal or oral	Small molecule	Metabolic disease	Preclinical	A small molecular AMPK activator. It inhibited the growth of adipocytes in vitro and suppressed body weight and fat increases in vivo. Topical used formulation is under testing.
05/30/19	GEM076	Galectin-12 inhibitor	Seborrheic dermatitis; Sebaceous hyperplasia	Transdermal	siRNA	Dermatosis	Preclinical	A modified siRNA for suppressing gene expression of galectin-12 which is a lipid droplet protein and regulates lipid accumulation and lipolysis. The siRNA can reduce the lipid in sebocytes and adipocytes and shows good stability and selectivity to reduce the lipid accumulation through transdermal delivery in vivo.
05/30/19	GEM075	Novel functional excipient	Oral formulation (e.g. direct compression, granulation, solid dispersion)	Oral	Polymer	Others	Preclinical	The synthetic polyvinyl acetate (PVAc)-based polymer of functional excipient is utilized as solubilizer that could increase drug solubility and enhance drug absorption. This novel excipient has better flowability, easy for use and widely application. This excipient will be useful for new drug and insoluble drug development.
05/30/19	GEM074	Dual inhibitor of Topo 1 and Topo 2	Drug resistant cancers	i.v.	Small molecule	Oncology: Solid cancer	Phase 1	1st-in-class combo therapy, covalently conjugated to simultaneously inhibit Topo 1 and 2, w/ EGFR cross-talk and extremely low toxicity for high dosing. Reduced tumor sizes w/ 38% CR and 98% TGI (compared to 0% and 33%, respectively, for imatinib) in CML xenograft models; and 98% TGI in colon cancer models at low doses. Showed immunotherapy enhancement effects with anti-PD-1 Ab and anti-CTLA-4 Ab with 100% CR in ovarian cancer model. No toxicity in rat & monkey models; No SAEs reported in Phase I at high dose 180mg/m2. Excellent PK profile and GI permeability of 9.2 enabling oral formulation.
05/30/19	GEM073	Kinase inhibitor of TGFβ-mediated phospho-SMAD2 signal transduction	COPD, IPF, Lung cancer	Oral	Small molecule	Immunology/ Inflammation Oncology: Solid cancer Respiratory	Phase 1	This kinase is selectively expressed in resident macrophages and airways epithelia of the lung and upregulated in COPD and IPF patients. A highly selective inhibitor showed efficacy across at least 3 different animal models relevant to COPD, IPF and NSCLC. Phase 1 trial has completed with a clean safety and tolerability profile.
05/30/19	GEM072	Orally available somatostatin analogues	Metabolic syndromes, Acromegaly, Hyperprolactinemia etc.*	Oral	Protein	Endocrinology Gynecology Metabolic disease	Preclinical	The technology and "know-how" to synthesize somatostatin analogues which will be more potent, more specific, stable and orally available have been established. A few analogues (at lead generation/optimization stage) with different combination of receptor selectivity and differential hormonal secretion inhibition properties are available. *: Congenital hyperinsulinism, insulinomas, glucagonomas
04/02/19	GEM071	Nanoparticl formulation of 2-deoxy-glucose	Hepatocellular carcinoma, Renal cancer, Colorectal cancer	i.v.	Small molecule	Oncology: Solid cancer	Preclinical	In the xenograft model, the administration of nanoparticle formulation once a week showed superior antitumor effect than daily administration of 2-deoxyglucose alone. No side effects were observed. Enhanced the antitumor effect by combination with existing anticancer drugs. Enhanced T cell infiltration into tumor tissue. The substrate used in the nanoparticle formulation are used in approved medicines (FDA).

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
04/02/19	GEM070	Nanoparticl formulation of $\gamma$ -Oryzanol	Diabetes, Hyperlipidemia, Menopausal disorder, Irritable bowel syndrome, etc.	Oral	Small molecule	Endocrinology Gastroenterology Metabolic disease	Preclinical	Improved intestinal absorption and shows a drug effect in an extremely small amount (1/1000 of normal particles). Reduced preference for high fat diet. Suppressed ER stress enhancement on hypothalamic/pancreatic islet. Improved abnormal glucose metabolism and abnormal lipid metabolism. The substrate used in the nanoparticle formulation are used in approved medicines (FDA).
03/12/19	GEM024	1. Selective inducer of apoptosis through modulation of NF- $\kappa$ B/P53 axis. 2. Eliciting adaptive immune response by recruitment of T Cells to tumors.	Oral squamous cell carcinoma	Oral, pastille based topical delivery	Small molecule	Oncology: Solid cancer	Phase 2 ready	Updated on March 12, 2019  First-in-class, patented, combination therapeutic that simultaneously upregulates a cluster of genes promoting cell death and downregulates a cluster of genes promoting survival of cancer cells. Phase 1 results showed no significant AE, dose-dependent modulation of key biomarkers involved in disease pathogenesis, and T cell recruitment to tumor making it "hot". FDA approved moving to Phase 2.
03/07/19	GEM069	Immuno-modulator (adjuvant)	Vaccine, Cancer immunotherapy etc.	Injection	Other	Immunology/ Inflammation Oncology: Solid cancer Vaccine	Preclinical	<i>E.coli</i> producing monophosphoryl Lipid A whose structure is similar to existing adjuvants such as MPL and GLA. Shows similar efficacy with MPL in vitro and in vivo. Lower cost production through simple fermentation and purification steps.
03/01/19	GEM068	Gene therapy for novel target	Lung and other cancers	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	The expression of this gene is reduced in various cancers. Adenovirus expressing this gene inhibits the HIF-1 $\alpha$ expression and proliferation of various cancer cells. Adenovirus expressing this gene suppresses growth of lung cancer in nude mice.
03/01/19	GEM067	c-Kit inhibitor	Diabetic macular edema & Retinopathy	Oral	Small molecule	Ophthalmology	Phase 2a	Inhibits stem cell factor-induced hyperpermeability Reverses retinal vascular leakage in STZ-induced diabetic rats Improved compliance to administration (oral) than anti-VEGF therapy (intra-vitreous injection) Applicable to non-responders to anti-VEGF therapy Repositioning of a marketed drug
03/01/19	GEM066	Selective STAT3 inhibitor (DNA-based Decoy)	Head and neck squamous cell carcinoma and Non-small cell lung cancer (including exon 20 mutations)	i.v.	Nucleic acid	Oncology: Solid cancer	Pre-IND for systemic administration formulation	1st-in-class STAT3 decoy; Suppresses binding of STAT3 to genomic DNA; Inhibits proliferation and promotes apoptosis of many cancer cells; Suppresses expression of STAT3 target genes and tumor growth in animal models; Shows increased response in combination with cetuximab and also with PD-1; Human Phase 0 study (intratumor injection); Suppresses STAT3 target genes expression with one dose Does not affect normal oral keratinocytes; Exploratory animal toxicology studies show no significant adverse effects
03/01/19	GEM064	Selective inhibitor of Na <sub>v</sub> channels	Pain	Oral	Small molecule	Pain/Neuropathy	Preclinical	Potent and selective inhibitors for Na <sub>v</sub> 1.7/1.8 subtypes Effective in inflammatory & neuropathic pain states Excellent non-clinical ADMET profile No off-target activity, very good in vitro cardiac safety margin, non-mutagenic
02/12/19	GEM063	Novel 24hr ibuprofen patch	Local pain in sprains	Local	Small molecule	Orthopedic Pain/Neuropathy	Phase 1	High payload: Contains 200 mg ibuprofen, Constant delivery over 24 hours, Class-leading adhesion, Water-resistant, Comfortable to wear and remove Pre-clinical safety studies were completed 2017 with no concerns/issues Phase I PK and sensitisation/irritancy studies were successfully completed in 2018 with no concerns/issues

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
01/11/19	GEM009	BET inhibitor	Cancer, RA	Oral	Small molecule	Oncology: Solid cancer Rheumatology	Preclinical	Updated on January 11, 2019  More potent enzyme inhibition and anti-tumor activities compared with competitors (more potent than GSK525762A and comparable to ABBV-075). Superior safety profile than competitors (no inhibition on hERG or CYP3A4) and can be applied to RA. Easier manufacturing due to absence of asymmetric carbon.
01/11/19	GEM003	Selective glucocorticoid receptor agonist	RA/OA, Please refer to Note	Local	Small molecule	Dermatosis Gastroenterology Immunology/ Inflammation Orthopedic Respiratory Rheumatology	Preclinical	Updated on January 11, 2019  Expected to reduce unfavorable responses of glucocorticoids by selectivity of action (transrepression>transactivation) Discontinued development for RA/OA. Available for repositioning. Possible indications: Atopic dermatitis, Psoriasis, Asthma, COPD, Inflammatory bowel disease etc.
01/11/19	GEM002	Kappa-opioid receptor agonist	Pain/Itching, Please refer to Note	Oral	Small molecule	Gastroenterology Pain/Neuropathy	Preclinical	Updated on January 11, 2019  Discontinued development for pain because of company strategy. Available for repositioning. Possible indications: Chronic pains (Back pain, Arthritis pain, Cancer pain, Post-herpetic neuralgia, Trigeminal neuralgia etc), Pruritus, Irritable bowel syndrome
01/11/19	GEM001	TRPV-1 agonist	Rheumatoid Arthritis, Please refer to Note	Oral	Small molecule	Dermatosis Gastroenterology Hematology Infection Metabolic disease Oncology: Hematological cancer Oncology: Solid cancer Pain/Neuropathy Rheumatology	Phase 2a	Updated on January 11, 2019  Potently inhibits TNF- $\alpha$ production by oral administration. Discontinued development for RA. Available for repositioning. Possible indications: Neuropathic pain, Crohn's disease, Systemic lupus erythematosus, Cachexia, Acute infectious disease, Allergy, Pyrexia, Anemia, Diabetes, Diseases related TNF- $\alpha$ (Colitis, Psoriasis etc.)
01/07/19	GEM062	Cannabinoid-releasing topical formulation (sustained release for about 24 hours)	Chronic pain, Sclerosis, Lupus, others	Topical	Small molecule	Dermatosis Pain/Neuropathy	Preclinical	Cannabinoid's utility: nausea and vomiting during chemotherapy, chronic pain, muscle spasms, epilepsy, sclerosis, lupus, schizophrenia etc. This sustained-release topical formulation has significant potential to help treat these disorders. Preclinical efficacy demonstrated in a cutaneous lupus rodent model using AEA.
01/07/19	GEM061	Curcumin-releasing topical formulation (sustained release for about 24 hours)	Please refer to Note	Topical	Small molecule	Cardiology Hematology Immunology/ Inflammation Orthopedic	Preclinical	Indication: Osteoarthritis, CV disease, chronic inflammatory disease, vascular disease (Sickle Cell)  Note: Curcumin's utility: chronic pain, chronic inflammatory conditions such as osteoarthritis, vascular disease such as Sickle Cell and diabetes. This formulation breaks through the limitations of the poor bioavailability of curcumin with oral administration. Preclinical efficacy demonstrated in an rodent arthritis model and a rodent diabetes model.

Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
01/07/19	GEM060	Nitric Oxide-releasing topical formulation (sustained release for over 48 hours)	Please refer to Note	Topical	Small molecule	Dermatosis Otolaryngology	Preclinical	<p>Indication: Acne, Atopic Dermatitis, Fungal diseases, Wound healing, Chronic rhinosinusitis, Diabetic foot ulcers, Raynaud's Phenomenon, Middle-ear infections, Erectile dysfunction, Others</p> <p>Note: NO function: Regulation of the vasculature (vasodilatory), broad spectrum antimicrobial activity, anti-inflammatory, anti-oxidant, wound healing, skin cell maturation and survival etc. Human POC already shown with NO in onychomycosis, genital warts, moscullum contagiosum, pulmonary hypertension, acne, atopic dermatitis (preliminary); animal POC demonstrated in over 20 peer-reviewed papers. This formulation breaks through the limitations of sustained NO (topical) delivery.</p>
12/27/18	GEM059	Recombinant Human Interleukin-1 Receptor Antagonist	Please refer to Note	IM	Protein	Gastroenterology Immunology/ Inflammation Infection Oncology: Supportive care Orthopedic	Phase 1	<p>Indication: 1: Infection, as manifested by febrile neutropenia, in patients with malignancies receiving chemotherapy drugs. 2: Diarrhea in patients with malignancies receiving chemotherapy drugs. 3. Gout arthritis</p> <p>Note: The world's first multiorgan protection agent for tumor chemotherapy. Inhibits cell cycle progression of normal cells and renders them resistance to chemotherapy. No effects on tumor growth and their sensitivity to chemotherapy Phase 1 : No dose limiting toxicity, None of subjects presented grade 3 or above chemotherapy-induced neutropenia or diarrhea. Gout arthritis: Well tolerated and safe for patients who are restricted from NSAID, glucocorticoid, or colchicine.</p>
12/27/18	GEM057	Increase hair follicle ATP and delay senescence of dermal papilla cells	Alopecia	Topical	Small molecule	Dermatosis	Phase 2	<p>Boosts the ATP of human follicle dermal papilla cells, thereby slowing down the aging speed and prolonging hair cycle. No side effects and shorter time to observe efficacy Human trial (Androgenetic Alopecia): significantly improved 37.5% vs 0% (placebo) during 2 months. Phase 2 (Female pattern hair loss) resulted in earlier improvement of hair loss and patient responses than minoxidil.</p>
12/13/18	GEM054	Intracellular superoxide removing agent	Chemotherapy induced Peripheral Neuropathy (CIPN)	i.v.	Small molecule	Oncology: Supportive care Pain/Neuropathy	Phase 2	<p>There is currently no approved drug to prevent or treat CIPN. Completion of Phase 2b study. Global Phase 3 started in US, Currently in preparation for Phase 3 in Japan, South Korea, Taiwan and Hong Kong. Can be licensed to South Korea, Taiwan and Hong Kong.</p>
12/13/18	GEM052	Mitochondria-targeted apoptosis inducer	Relapsed/Refractory Peripheral T-cell Lymphoma (PTCL) and other hematological cancers	i.v.	Small molecule	Oncology: Hematological cancer	Phase 2	<p>No approved drugs for PTCL indication in Europe (3 drugs have been approved in Japan and US). Less toxic compared with competitors approved in Japan and US. US Phase 2a: 5 responders in 11 refractory PTCL and DLBCL patients, and 2 responders in 7 PTCL patients. Applicable to relapsed and refractory PTCL. Phase 2 Pan-Asia pivotal study is ongoing. Can be licensed to US/EU and China (except Beijing, Shanghai and Guangzhou)</p>
12/10/18	GEM051	Protective agents from heat stress	Heatstroke	Oral	Other	Immunology/ Inflammation	Preclinical	<p>Suppression of vascular endothelial cell damage and production and release of inflammatory cytokines from blood cells due to heat stress. Ingredients derived from citrus fruit extract.</p>



Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
11/22/18	GEM050	Curcumin analogue	CML, Pancreatic cancer, Glioblastoma etc.	Oral	Small molecule	Oncology: Hematological cancer Oncology: Solid cancer	Preclinical	Inhibited proliferation of CML and pancreatic cancer cells at the submicromolar level. Unlike imatinib, the inhibitory action is irreversible. Suppressed almost completely human CML cell growth without significant changes in body weight and peripheral white blood cell count in vivo. An increase in ROS/RCS produced by inhibition of their scavenging enzymes is assumed to be involved in anti-tumor action. Induced M phase arrest.
11/15/18	GEM049	Pan-NOX inhibitor	IBD, IPF, Neurodegenerative diseases	Oral	Small molecule	Gastroenterology Immunology/ Inflammation Pain/Neuropathy Respiratory	Preclinical	Highly potent NOX inhibitor : 20~50 times more potent than GKT-137831 Significant effects in DNBS-ulcerative colitis and LPS-induced acute inflammatory animal studies. Also showed positive results in IPF animal model. High oral bioavailability and clean off-targets profile.
10/25/18	GEM047	Lactoferrin complexes	Pain on Peripheral Neuropathy, Cancer	i.v.	Protein	Oncology: Solid cancer Pain/Neuropathy	Preclinical	Improved PK profile over natural lactoferrin. Analgesic effect on periferal neuropathy induced by oxaliplatin. Inhibitory effects on the growth of syngeneic murine lung cancer model Inhibitory effects on the growth of human non-small cell lung cancer cell in vitro. Positive effect of treatment on sepsis mice model.
10/25/18	GEM046	Indirect activator of AMPK	Hyperlipidemia, type 2 diabetes, Cancer	Oral	Small molecule	Metabolic disease Oncology: Hematological cancer	Preclinical	Derivative of fungus product ascochlorin. Good PK profile in rats. Superior effects than metformin on blood glucose and triglyceride level in diabetic mice model. Significant enhancement of the efficacy in combination with metformin on T2D model Significant enhancement of the antitumor activity of anti-PD-1 antibody in mouse model
09/20/18	GEM045	Autotaxin Inhibitor	NASH, Pancreatic cancer	Oral	Small molecule	Immunology/ Inflammation Metabolic disease	Preclinical	Showed antifibrotic efficacy with significant histopathological score reductions in chronic pancreatitis and NASH (Stelic STAM & MCD) in mice. Showed significant anti-inflammatory effects in paw edema animal study.
09/20/18	GEM042	TLR4 antagonist	NAFLD, NASH, AIH, CLD and CD	Oral	Small molecule	Gastroenterology Immunology/ Inflammation Infection Metabolic disease Rare disease	Phase 2	NAFLD (nonalcoholic fatty liver disease): The phase 2 results demonstrated significant improvement on relevant diagnosis and biomarkers. NASH: has recently been approved by US FDA for Phase 2 trial (Feb in 2020) AIH (autoimmune hepatitis; orphan designation): The phase 2 (open label) results will be available soon. CLD(chronic liver disease by HCV infection): A strong trend of improvement of liver function and safety in Phase 2. CD (Crohn's disease): Good efficacy in three Phase 2 POC studies. The drug is safe and tolerable in these trials. Can be licensed to territories except Asia
08/31/18	GEM040	Topical anti-inflammatory	Joint pain, Muscle pain, Gout, Local inflammatory pain	Topical	Small molecule	Orthopedic Pain/Neuropathy	Preclinical	Topical formulations of Ibuprofen, Naproxen, Diclofenac to use in the treatment of inflamatory pain and related conditions Formulation shows 5 to 10X increase human skin permeation coupled Potential for OTC or RX introduction: minimal development timeline
08/31/18	GEM039	Antifungal	Onychomycosis	Topical	Small molecule	Dermatosis Infection	Preclinical	Novel and unique topical formulation of Terbenafine with exceptional permeation (40 fold) across the human nail. Potential for OTC or RX introduction: minimal development timeline
08/31/18	GEM038	Locally acting anti-inflammatory- Trigeminal neuroinflammation	Migraine	Local	Small molecule	Pain/Neuropathy	Phase 2a	Clinical POC in acute migraine therapy in Phase 2a Efficacy comparable to Triptans but with no systemic side effects or restrictions Shortened development timelines (NDA:2021) Product opportunity for use in Temporomandibular Joint Disease and trigeminal neuralgias

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
08/31/18	GEM037	Allosteric modulator of the CCR3 receptor	Asthma, Rhinitis	Oral	Small molecule	Immunology/ Inflammation Otolaryngology Respiratory	Phase 2a	In phase 2a: Highly significant effects on the methacholine provocative response Showed trends to improvement in EAR (Early Phase Allergic Response) Reduced induced sputum eosinophil percentage and increased percent blood eosinophil
08/27/18	GEM036	Hematopoietic stem cell fucosylation	Prevention of infection & GvHD from hematopoietic stem cell transplantation	Infusion	Protein	Immunology/ Inflammation Oncology: Hematological cancer Regenerative medicine	Phase 3 ready with FDA SPA	In Phase 2 study: Statistically significant acceleration of immune system reconstitution (neutrophil/platelet recovery) Significantly reduced infection and GvHD Improved survival Positioned to be best-in-class No reports of adverse event specifically attributable to fucosylation
08/07/18	GEM034	Derivative of neuroprotective protein	Stroke, Huntington chorea, Schizophrenia and PTSD	i.v.	Peptide	CNS	Preclinical	A cell-permeable recombinant peptide. Can cross the blood-brain barrier, is resistant to degradation, and can bind constitutively to its substrates. Significantly reduces brain damage in rodent stroke model. Expected to be treated after stroke without diagnosis of stroke type before dosing.
08/07/18	GEM033	Inhibitors of bacterial resistance mechanisms	Gram-negative MDR bacterial infections, Lung infections in cystic fibrosis (CF) patients	Intravenous, Aerosol, Topical	Small molecule	Infection	Preclinical	Restore effectiveness of shelved antibiotics. Lower the effective dose of antibiotics. Mitigate antibiotic resistance. Disrupt biofilm-based infections. Over 1,000 compounds with lead compounds for each indication identified.
07/20/18	GEM029	A cancer stem cell-associated transcription factor inhibitor	Malignant gliomas including glioblastoma (GBM)	Oral	Small molecule	Oncology: Solid cancer	Phase 1 ready	Directly kills the cancer stem cells. Significantly improves survival in orthotopic GBM PDX models. Inhibits tumor growth in a mouse implanted with GBM cells and the growth inhibition is augmented by combination with temozolomide/radiation. No significant toxicities are identified at therapeutic doses.
07/09/18	GEM028	miRNA targeting refractory colon cancer with mutated K-ras and refractory pancreatic cancer	Pancreatic cancer Colon cancer	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	The miRNA regulates K-ras, Bcl2, survivin, and NF-kB and demonstrate excellent antitumor effect in vitro and in vivo.
07/09/18	GEM027	miRNA targeting refractory colon cancer with mutated K-ras	Colon cancer	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	The miRNA regulates EGFR signaling pathway by directly inhibiting of both KRAS and AKT1 and demonstrate excellent antitumor effect in vitro and in vivo.
07/09/18	GEM026	siRNA suppressing the expression of novel cancer stem cell gene "Gene A"	Cancer	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	Novel cancer stem cell gene "Gene A", which was discovered by single cell analysis of cancer stem cell, shows character as follows. 1. Superior cancer stem cell diagnostic marker than known cancer stem cell marker CD44v9 2. SiRNA targeting Gene A demonstrate excellent antitumor effect with current medicines.
07/09/18	GEM025	miRNA suppressing the expression of a protein characteristic of pancreatic cancer stem cells	Pancreatic cancer	i.v.	Nucleic acid	Oncology: Solid cancer	Preclinical	Excellent antitumor effect was demonstrated in uniquely established pancreatic cancer stem cell model in vitro and in vivo.
07/05/18	GEM021	Opioid and non-opioid analgesics with respiratory stimulant	Pain	Oral	Small molecule	Pain/Neuropathy	Preclinical (close to IND)	Combination of generic opioid/non-opioid analgesics with a generic respiratory stimulant using a regulatory approach known as the 505(b)2 submission. First drug introduction therapeutically equivalent to Vicodin® that prevents overdose death, deters abuse and prevents addiction. Low cost of goods.
06/04/18	GEM020	3rd generation immunotherapy targeting little gastrin	Gastro-intestinal cancer (Pancreatic)	s.c.	Protein	Oncology: Solid cancer	Preclinical	Applied 3rd generation immunotherapy technology to little gastrin. In-vivo POC has been validated in non-human primates.

## Drug Candidates



As of 10/15/20

Date	Candidate	Mechanism of action	Indication	Route	Modality	Disease area	Development stage	Note
06/04/18	GEM019	3rd generation immunotherapy targeting HER2	HER2 overexpressing cancer (Breast)	s.c.	Protein	Oncology: Solid cancer	Preclinical	Applied 3rd generation immunotherapy technology to HER2. Superior efficacy to trastuzumab and pertuzumab. In-vivo PoC has been validated in non-human primates.
06/04/18	GEM018	3rd generation immunotherapy technology	Cancer	s.c.	Protein	Oncology: Hematological cancer Oncology: Solid cancer	Discovery	Unique technology that triggers B and T cells simultaneously while activating all possible natural tumor killing mechanisms available to the immune-system. Tumor-directed specific activation reduces side effects to the minimum. Applicable on a target basis.
04/10/18	GEM008	Selective cMET inhibitor	NSCLC and HCC etc.	Oral	Small molecule	Oncology: Solid cancer	Phase 2	Effective on exon 14 skipping xenograft Development by an originator has been discontinued.