**Areas of Interest**

**High Priority**
- Alzheimer’s disease
- Atherosclerosis
- Cardiovascular disease
- Diabetes
- Novel vaccines
- Obesity
- Oncology
- Pain
- Sleep disorders

**Focused Interest**
- Antibiotics
- Antifungals
- Antivirals (HCV and HIV)
- Asthma
- COPD
- Neurodegeneration
- Ophthalmology
- Osteoporosis
- Schizophrenia
- Stroke

**Technology Platforms** (enabling products and improving research productivity)
- Biologics and Antibodies
- Drug Delivery
- Information Technologies
- In Vivo Imaging
- Molecular Profiling/Molecular Biomarkers
- New Vaccine Technology
- Research Technologies/Drug Discovery Platforms

In addition to the high priority and focused interest areas, Merck will continue to pursue licensing opportunities in other disease areas where clinical proof of concept exists.

Merck will also pursue niche acquisitions and partnerships in diagnostics and devices.
ATHEROSCLEROSIS

Areas of Interest:

• Acute HDL-mimetic (or apoA-I mimetics) therapy for high-risk patients, infused or oral
• Oral compounds, with known mechanism of action, that increase HDL-C or apoA-I levels
• LDL-lowering therapies
  – eg, Cholesterol absorption inhibitors and agents that target PCSK9
• Agents that increase levels or activity of the LDL receptor, apolipoprotein E, or LCAT
• Agents or combination products that target MTP but do not cause fatty liver

Technology/Methods:

• Acute methods to assess cholesterol transport in humans (especially reverse cholesterol transport)
• Methods to assess anti-atherogenic properties of HDL or other lipoproteins
• Acute methods to assess cholesterol absorption in humans

Not Interested in:

• ACAT inhibitors
• Triglyceride-lowering therapies with no other benefit
• Fibrates or other PPAR-alpha agonists
• PPAR-delta agonists
• Fish oil/omega-3 fatty acids
  – Nutraceuticals
VASCULAR WALL/METABOLIC SYNDROME

Areas of Interest:

• Vascular wall agent or target with mechanistic validation; these include
  – Vascular inflammation agent or target
  – A drug target that favorably affects vascular wall elements
• Acute therapy to lower vascular inflammation in high-risk patients (biologic or small molecule)
• Metabolic syndrome target with strong or predicted activity on hypertension, dyslipidemia, or atherosclerosis
  – Must treat at least 2 components of metabolic syndrome and be registerable on at least 1; lack of detrimental effects on weight and/or insulin sensitivity a plus

Technology/Methods:

• Animal models of
  – Two or more components of metabolic syndrome
  – Plaque vulnerability
• Imaging methods that read out plaque composition or vulnerability
• Circulating biomarkers of plaque burden or vulnerability
• Alliances/consortia around vulnerable/high-risk plaque

Not Interested in:

• Acute treatments for MI
• Post-MI therapeutics for myocardial preservation or perfusion-reperfusion injury
HYPERTENSION

Areas of Interest:

• Antihypertensive agents, with at least preclinical proof of concept, superior and/or additive to current therapies
• Diuretics with improved efficacy and/or safety/tolerability as compared to thiazides
• Long-acting vasorelaxants with improved efficacy and/or safety/tolerability as compared to CCB
• Potassium-neutral mineralocorticoid receptor antagonists
• Novel RAAS pathway modulators
• Agents that mediate vascular remodeling
  – Combination agents with added antihypertensive activity
• Agents with additional benefits on other components of metabolic syndrome
• Platform technologies for identifying novel targets for hypertension

Not Interested in:

• Existing classes: ACE inhibitors, ARBs, CCBs, β-blockers
• Nutraceuticals
• Early-stage endothelin antagonists
• Chronic heart failure agents that increase inotropy or only provide symptomatic relief
• Ventricular/atrial antiarrhythmic agents
• Blood substitutes

Opportunistic Late-Stage Agents:

• Antihypertensive agents that target patient populations poorly controlled with current agents
• Late-stage, best-in-market, patent-protected combinations of 2 drugs (ARB/diuretic, ARB/CCB, and CCB/diuretic) or 3 drugs (ARB/CCB/diuretic)
• CHF agents that can be registered on their antihypertensive effectiveness
• ACE-NEP or ECE-NEP inhibitors with extensive safety database
• Peripheral arterial disease agents
THROMBOSIS

Areas of Interest:

• Novel antithrombotic agent in late-stage (Phase III) clinical development
  – Factor Xa inhibitor; direct thrombin inhibitor; other mechanism (novel mechanism with inherent reduced bleeding risk)
  – Oral, once daily preferred
• Novel antiplatelet agent in late-stage (Phase III) development
  – Overcomes the limitation of clopidogrel (rapid onset, limited “resistance,” possibly reversible)
  – Must be oral and preferably have 1 additional route of administration

Technology/Methods:

• Novel technology to assist in bridge along continuum of PK, magnitude of ex vivo effect, reduction in events/risk
• Point-of-care clinical tests only as needed to assess therapeutic effect of novel agent – to identify responder population or to guide clinicians on difficult-to-manage patients

Not Interested in:

• IV-only antithrombotic or antiplatelet agents
• Thrombolytics
• Point-of-care clinical tests, unless as necessary to support clinical development of a novel agent

IMAGING (Shared With NT-RLC), Diagnostics & Clinical Platforms

Areas of Interest:

• Noninvasive and intravascular imaging platforms for plaque composition and vulnerability
• Image-enhancing agents for plaque composition and vulnerability
• Plaque and/or circulating markers of inflammation, plaque stability, oxidation, endothelial function, plaque composition
• Preclinical and clinical assays for soluble and plaque markers
• Access to coronary atheroma, carotid endarterectomy material and necropsy atherosclerosis
  – Technologies for measuring vascular dynamics (eg, flow, shear stress, vascular compliance

Not Interested in:

• Myocardial imaging platforms
• Additional sources of lower extremity atheroma
BIOMARKERS
HDL Function

Areas of Interest:
- Platforms for measuring HDL-mediated reverse cholesterol transport, preclinically and clinically, including imaging and kinetic models
- Platforms for determining protein or lipid composition of HDL

Not Interested in:
- In vitro reverse cholesterol transport assays

Hypertension

Areas of Interest:
- New technology for measuring vascular compliance
- Markers of responder and/or nonresponder HTN populations
- Markers that link HTN to other metabolic syndrome phenotypes and/or atherosclerosis
- Markers for renal sequelae of HTN, including renal perfusion
- Markers for metabolic effects of diuretics
- Case/control cohorts for hypertension

Not Interested in:
- Markers of CHF

Identification of Responder Populations

Areas of Interest:
- Case/control cohorts for coronary artery disease to test
- Proprietary information on genetic variants associated with CAD, which may define responder populations

Not Interested in:
- Markers and cohorts for areas outside of CVD franchise scope

ANIMAL MODELS

Areas of Interest:
- Preclinical models of atherosclerosis, hypertension, or plaque rupture
- Assays for protein readouts in animals
- Molecular imaging for atherosclerosis
- Cell-based screens for new target identification

Not Interested in:
- Animal models for indications outside of CVD franchise scope
BONE AND ENDOCRINE

Areas of Interest:

• Osteoanabolic agents
  – Novel mechanisms that upregulate LRP5/wnt signaling with pharmacological preclinical POC
  – Novel mechanisms with preclinical POC (increased BFR)
• Non-bone mechanisms for reducing falls or effects of falls
  – Myoanabolic agents
    • Myostatin pathway
  – Novel mechanisms that improve skeletal muscle function
• Fixed-dose combinations with Merck osteoporosis compounds
• Biomarkers
  – Surrogate biomarkers of bone strength
  – More sensitive and faster biomarkers of bone anabolism
  – Selective markers of skeletal muscle turnover
• Diagnostics (at home/clinic) for BMD

Not Interested in:

• Growth hormone or derivatives by any route
• ER alpha agents
• Classic “antiresorptive agents,” including bisphosphonates with improved formulations that allow less frequent dosing or better tolerability
• Testosterone preparations
• Bisphosphonates
**DIABETES**

**Areas of Interest:**

**Oral therapies**
- Novel targets/Preclinical candidates
- Non-PPAR insulin sensitizers, GDIS agents, beta-cell protection
- Treatments for comorbidities

**Non-Oral therapies**
- Improved GLP-1 agonists — less frequent than daily injections; less nausea or potential for greater efficacy; potential for glycemic control and weight loss
- MOA that target glucose and weight loss
- Protein therapeutics – novel MOA; will consider a strategic alliance
- Breakthrough insulins

**Transforming technologies**
- Imaging, oral delivery of peptides, RNAi

**OBESITY**

**Areas of Interest:**

- Novel mechanisms for weight loss or both weight loss and prevention of weight gain
  - Product profile advantageous over CB1 class
  - Includes mechanisms acting on central or peripheral suppression of appetite or enhancement of satiety or metabolic rate
- Weight loss/prevention of weight regain with positive effects on cardiometabolic risk factors
- Mechanisms that are additive or synergistic as combination therapy with CB1 class and other potential classes
- Early-stage opportunities with robust animal proof of concept and preclinical safety data
- New target identification platform technologies to complement existing efforts
- Strategic alliances
- Pharmacogenomics for subphenotyping obesity and prediction of drug response

**Not Interested in:**

- Nutraceuticals
- Lipase inhibitors
- 5HT2 agonists
- Anti-ghrelin vaccine
- Beta3 agonists
- Thyroid receptor beta agonists

**Microvascular complication treatments with Phase Ia data**
- Agents that halt/reverse diabetic nephropathy, neuropathy, and retinopathy

**Pharmacogenetics for prediction of future diabetes, subphenotyping and prediction of drug response**

**Not Interested in:**

- Nutraceuticals
- FBPase inhibitors
- Glycogen phosphorylase inhibitors
- Non–glucose-dependent insulin secretagogues
- Aldose reductase inhibitors
- Agents for only type 1 diabetes
- Compounds with no molecular target*
- SGLT inhibitors* *re-examine if clinical POC
RESPIRATORY

Areas of Interest:

- Compounds for asthma
  - Antiinflammatory agent with novel mechanism with preclinical in vivo proof of concept
  - Mucoregulator with defined mechanism and proof of concept in in vitro and/or in vivo preclinical models of asthma
  - Injury/repair agent with proof of concept in in vitro and/or in vivo preclinical models of asthma
  - Novel bronchodilator mechanisms (non-LABA; non-cholinergic)

- Antitussive with defined mechanism and proof of concept in preclinical models of cough

- Compounds for COPD with clinical proof of concept

- Technologies
  - Inhalation approaches
  - Biomarkers
  - Predictive animal models of asthma pathophysiology

Not Interested in:

- Acute lung injury
- Sinusitis
- ß-agonist bronchodilators
EMBRACING PARTNERSHIPS

Immunology

ARTHRTIS

Areas of Interest:

• Disease-modifying antirheumatic drugs
  – Biologics superior to TNF sequestrants
  – Novel proinflammatory cytokine inhibitors
  – Leukocyte trafficking modulators
  – Selective glucocorticoid modulators
• Disease-modifying osteoarthritis drugs with clinical proof of concept
• Cartilage/joint imaging technologies
• Novel regulators of cartilage metabolism

Not Interested in:

• Broadly immunosuppressant mechanisms
• Injectables for osteoarthritis, unless each dose could last longer than 3 months
• TNF sequestrants
• Calcineurin inhibitors
ANTIBACTERIALS

Areas of Interest:

Bacterial Infections

• Moderate to severe infections treated in the community, where resistance is developing
  – Broad-spectrum oral antibacterial agent for community-acquired respiratory tract infections (RTI) and complicated and uncomplicated skin and soft tissue infections (SSTI) covering multidrug-resistant bacteria with distinctive efficacy and/or safety advantages over current standards of care
  • Oral and IV preferred
  • Preclinical through Phase III; will consider earlier opportunity with completed preclinical safety assessment

• Severe infections in hospitalized patients where resistance is an increasing problem (in order of increasingly narrow spectrum)
  1) Broad-spectrum agent (BSA) with high degree of activity against MRSA (VRE a plus), multidrug-resistant gram-negative enterics (fermenters) as well as nonfermenters (Pseudomonas and Acinetobacter)
    • Preclinical through Phase III; IV (oral step down a plus)
  2) BSA with high degree of activity against MRSA (VRE a plus) and multidrug-resistant gram-negative enterics (fermenters, eg, E coli, Klebsiella spp, etc)
    • Preclinical through Phase III; IV (oral step down a plus)
  3) Agents with high degree of activity against gram-positive resistant infections - MRSA (VRE a plus)
    • Preclinical through Phase III; IV (oral step down a plus)
  4) BSA with high degree of activity against multidrug-resistant gram-negative enterics (fermenters) as well as nonfermenters (Pseudomonas and Acinetobacter)
    • Preclinical through Phase III; IV (oral a plus)
  5) Synergistic combination opportunities:
    • Potentiators: efflux pump inhibitors (EPI) and beta-lactamase inhibitors (BLI) targeting highly resistant gram-negative infections (non-fermenters) eg, PRIMAXIN™ plus; IV
    • Hybrid molecules with distinct mechanisms
    • Preclinical molecules with distinct mechanisms
    • Preclinical through Phase III; IV (oral step down a plus)

Not Interested in:

• Peptide-based agents unless they address liabilities upfront with strong (clinical) data to address
  – Metabolic lability
  – Selectivity
  – Administration issues
  – Manufacturing issues
• Virulence targets for chemical entities (but not for antibody opportunities)
• Topical antibacterials
• Opportunities targeting the following diseases:
  – Bioterrorism targets, malaria, tuberculosis, rare and orphan pathogens, Helicobacter pylori
• Antibacterials for animal health
• Laboratory diagnostics
• Point-of-care diagnostics, unless they support ongoing targeted pathogen opportunities
• In vitro screening assays, in vivo screening assays restricted to gram-positive bacteria
  – Would consider target-based in vitro screens only for gram-negative bacteria
ANTIBACTERIALS (continued)

Areas of Interest:

Targeted (Pathogen) Focus
- MRSA (GISA), *Pseudomonas*, *Acinetobacter*, potentially *C. difficile* and VRE
- Treatment:
  - Chemical agents with high degree of selective activity against medically important species-specific targets
    - Preclinical through Phase III
    - IV (oral a plus)
- Antibodies for therapeutic use
  - Pathogen-targeted antibody opportunities as adjunctive therapy (improved outcome relative to standard Rx)
  - If broadly effective against targeted species, need for diagnostic less important
  - Short term: requirement for rapid diagnostic not as critical, particularly if initial evaluation is salvage therapy
  - Pathogen-targeted antibody opportunities as monotherapy
    - Long term: requires rapid, specific diagnosis, particularly for primary therapy
      - Phase of development for consideration: preclinical through Phase III
      - Route of administration: IV
- Potential for prophylaxis/prevention

Point-of-care diagnostics supporting targeted-pathogen opportunities
- Only to complement ongoing opportunities
- Clinical diagnostics for direct patient testing
  - Identification and susceptibility testing
  - No tests requiring cultivation (agar, etc)
- If broadly effective against targeted species, need for diagnostic less important

Not Interested in:

- Peptide-based agents unless they address liabilities upfront with strong (clinical) data to address
  - Metabolic lability
  - Selectivity
  - Administration issues
  - Manufacturing issues
- Virulence targets for chemical entities (but not for antibody opportunities)
- Topical antibacterials
- Opportunities targeting the following diseases:
  - Bioterrorism targets, malaria, tuberculosis, rare and orphan pathogens, *Helicobacter pylori*
- Antibacterials for animal health
- Laboratory diagnostics
- Point-of-care diagnostics, unless they support ongoing targeted-pathogen opportunities
- In vitro screening assays, in vivo screening assays restricted to gram-positive bacteria
  - Would consider target-based in vitro screens only for gram-negative bacteria
ANTIFUNGALS

Areas of Interest:

• Severe life-threatening fungal infections treated in the hospital
• Broad-spectrum empiric agents
  – Broad-spectrum antifungal agent with improved activity against Candida, Aspergillus, dermatophytes and rare moulds
  • Preclinical through Phase III; IV or oral
• Targeted (pathogen) focus
  – Agents with high degree of selective activity against medically important species (medical need for Aspergillus > Candida)
  – Pathogen-targeted antibody opportunities as adjunctive therapy
  – Pathogen-targeted antibody opportunities as monotherapy or primary therapy
  • Preclinical through Phase III; IV or oral
• Point-of-care diagnostics supporting targeted pathogen opportunities for severe life-threatening fungal infections treated in the hospital
• If broadly effective against targeted species, need for diagnostic less important
• Only to complement ongoing opportunities
• Clinical diagnostics for direct patient testing
  – Identification and susceptibility testing
  – No tests requiring cultivation (agar, etc)
• Moderate to severe fungal infections treated in the community
  – Oral agents for community use with potent activity against Candida and dermatophytes, including azole- resistant strains
  – Preclinical through Phase III; oral/IV acceptable (not IV only)
• Mild to moderate fungal infections treated in the community
  – Agents for onychomycosis with equivalent efficacy and better safety than terbinafine (Lamisil®)
  – Preclinical through Phase III; oral or topical

Not Interested in:

• Peptide-based agents, unless they address liabilities upfront with strong (clinical) data to address
  – Metabolic lability
  – Selectivity
  – Administration issues
  – Manufacturing issues
• Virulence targets for chemical entities, but not for antibody opportunities
• Laboratory diagnostics
• Point-of-care diagnostics, unless they support ongoing targeted pathogen opportunities
ANTIVIRALS – HIV

Areas of Interest:

• Nucleoside analog reverse transcriptase inhibitors
  – Phase II or beyond preferred
  – With differentiating features, particularly activity against resistant virus
• Nonnucleoside reverse transcriptase inhibitors
  – Phase II or beyond preferred
  – With differentiating features, particularly activity against resistant virus
• Protease inhibitors that do not require ritonavir boosting
  – Phase II or beyond preferred
  – q.d. dosing preferred, but will consider b.i.d. dosing
• Integrase inhibitors
  – Phase I or beyond preferred
• RNase H inhibitors
• Inhibitors of viral budding
• Inhibitors of viral maturation
• Other new mechanisms, eg, host targets (NOT chemokine receptors)

Not Interested in:

• Agents administered by injection
• Chemokine receptor (CCR5, CXCR4) antagonists
• PK enhancers

ANTIVIRALS – HCV

Areas of Interest:

• Novel mechanism agents
• Protease inhibitors
• Nucleoside inhibitors
• Nonnucleoside inhibitors in Phase I/II
• Small-molecule inhibitors of HCV helicase
• NS5A inhibitors
• HCV viral entry inhibitors

Not Interested in:

• Enhanced interferons (unless oral)
• Non-oral TLR analogs
• Antivirals – all other
  – HBV
  – RSV
  – Influenza
VACCINES
Areas of Interest:

- Novel technologies for antigen selection, discovery, and identification
- Viral, bacterial, fungal vaccine candidates in areas of high medical need/high incidence, including but not limited to nosocomial infections and chlamydia
  - Preclinical efficacy or clinical proof of concept achieved, an advantage but not required
- Others
  - Influenza
    - Novel approaches to a universal influenza vaccine
    - Seasonal vaccines with efficacy superior to marketed products
  - HIV
    - Novel immunogens that elicit broadly cross-neutralizing immunity
- Novel adjuvants and immunomodulators
  - Highly desirable if preclinical efficacy or clinical proof of concept achieved, but not necessarily required
- Novel viral vector approaches
- Novel delivery mechanisms of vaccine target antigens
- Multiplexed clinical assay platforms
- Novel approaches to production of virus-like particles
- Improvements on existing Merck vaccines, which would allow for reduced dosing or increased cross-strain protection

Not Interested in:

- Biodefense targets
- Products containing thimerosal or unmodified animal/human components
- Traveler’s vaccines
- Seasonal vaccines, unless superior efficacy to marketed product (eg, influenza)
- DNA-based vaccines for infectious diseases
- Viral vectors based on pox viruses, retroviruses, and adeno-associated viruses
ALZHEIMER’S DISEASE

Areas of Interest:

• Agents in late Phase I, entry-ready Phase II with potential disease-modifying activity
  – Specific interest in BACE inhibitors and gamma secretase modulators
• Agents with the potential to modulate the formation of toxic Tau species
  – Includes Tau kinase inhibitors, Tau aggregation inhibitors, microtubule stabilizing agents
  – Excluding GSK3β inhibitors
• Novel-mechanism symptomatic improvement agents with enhanced characteristics over existing approved medications
  – Examples include AMPA or cholinergic receptor agonists or modulators
• Novel-mechanism biologics approaches to disease modification or neuroprotection
  – Preference for non-Aβ mechanisms
  – Would consider advanced (Phase II) Aβ mechanism with proven advantage over existing agents
• Fluid- or imaging-based biomarkers
  – Disease pathology, patient sub-populations, target engagement

Areas of Some Interest:

• Approaches to the manipulation of Aβ degrading enzymes, preferably with in vivo validation
  – Examples include insulin-degrading enzyme, IDE
• Agents with the potential to influence brain cholesterol homeostasis
  – Examples include LXR agonists
• Novel animal models of neurodegeneration for target evaluation
  – Should be non-APP transgene driven with broad applicability and clear IP status
• Novel genetic/RNA-based approaches to target validation or therapeutics
• Collaborative collection of matched sets of control and MCI/AD samples from significantly large (>100s) cohorts
  – CSF, DNA
  – Longitudinal CSF samples

Not Interested in:

• Acetylcholinesterase inhibitors
• The following agents if only at the preclinical stage of development, or with no in vivo validation
  – Aβ-based vaccines
  – Aβ-directed monoclonal antibodies
  – Antioxidants
  – Metal chelators
• Transgenic rodent models incorporating already patented FAD mutations
**PAIN**

**Areas of Interest:**
- Neuropathic pain therapies in Phase I or II
- Inflammatory pain therapies in Phase II or III
- Migraine prevention therapies in Phase II or III
- Acute migraine therapies in Phase II or III
- NGF antagonists and antibody approaches
- ASIC3 blockers
- Biomarkers and genetic markers for chronic pain

**Some Interest in:**
- Subtype selective sodium channel blockers
- Anticonvulsant MOA for pain
- Agents targeting the opioid pathway
- Antidepressant MOA
- P2X antagonists
- K-channel modulators
- New models for chronic pain
- Biologic approaches
- Nerve regeneration approaches
- Novel proprietary targets for neuropathic and OA pain
  - Includes collaborations with KOLs
- Cannabinoid agonists and pathway modulators
  - But no interest in CB1 or CB2

**Not Interested in:**
- Triptans
- New formulations of marketed drugs
- NSAIDs and COX-2 inhibitors
- iNOS inhibitors

**SLEEP**

**Areas of Interest:**
- Any novel mechanism for wake/sleep modification
- Circadian rhythm modulators with novel mechanism of action
- Any wake-promoting compound that does not show abuse potential
- Sleep/wake compounds that have improvements in cognitive/depressive markers
- Non-melatonin-related circadian modulators
- Pharmacological sleep apnea treatments
- Compounds that reduce sleep drive/sleep debt in sleep-deprived patients

**Not Interested in:**
- Histamine H₁ receptor antagonists
- Melatonin modulators
- Agents that promote only sleep onset or total sleep duration without novel mechanism/benefit over current products
- Insomnia compounds with a mechanism likely to result in Scheduling in the US

**SCHIZOPHRENIA**

**Areas of Interest:**
- Add-on therapies that can be combined with existing antipsychotics
- Atypical antipsychotics with cognitive-enhancing activity and improved AE profiles
  - No QT or DDI issues
- New mechanism antipsychotic agents that address both negative and positive symptoms associated with disease
- PDE2 modulators
- COMT inhibitor/modulators
- mGluR2 agonists/potentiators
- Nicotinic alpha7 modulators
- D₁ agonists

**Not Interested in:**
- Atypicals with no unique benefits
**DEPRESSION/ANXIETY**

**Areas of Interest:**

- Novel mechanism antidepressants or anxiolytics (with Phase II/III proof of concept)
- NCEs with incremental improvement on existing MOA conferring satisfactory market value (Phase II/III proof of concept)

**Not Interested in:**

- SSRIs and add-on therapies
- Gene profiling/target identification

**OPHTHALMOLOGY**

**Areas of Interest:**

- Glaucoma – neuroprotection (with IOP lowering especially desirable [≥ preclinical POC])
- Glaucoma – IOP lowering
  - Any MOA with efficacy ≥ Xalatan™ (Phase IIb/III)
  - Trabecular outflow enhancers (≥ Phase I)
  - Non-topical delivery formulations (≥ Phase I)
- Glaucoma – biomarkers and imaging tools
- Atrophic AMD
  - Visual cycle inhibitors (≥ preclinical POC)
  - Neuroprotective therapies, eg, locally delivered photoreceptor trophic factors (≥ preclinical POC)
  - Antiinflammatory agents, eg, complement inhibitors (≥ preclinical)
- Retinal microvascular disease (wet AMD & DR)
  - Locally delivered VEGF inhibitor (≥ 6-month dosing if intravitreal)
  - Angiostatic – non-VEGF (≥ preclinical POC)
  - Antiedema – non-VEGF pathway (≥ preclinical POC)
  - Early diabetic retinopathy therapies, eg, RAGE inhibitors (≥ preclinical POC)
- Retinal delivery systems
  - Retinal drug delivery device with greater than 6-month dosing (≥ preclinical POC)
  - Gene therapy/viral vectors for retinal delivery of siRNAs and trophic factors (≥ preclinical POC)

**Not Interested in:**

- Specific atrophic AMD therapies
- Supplementation of macular pigments
- Antioxidants
- Specific glaucoma therapies
- Antioxidants
- Preclinical IOP-lowering drugs regardless of MOA
- Specific retinal microvascular disease therapies
  - Additional siRNA therapeutics
  - Oral VEGFR2 (KDR) kinase inhibitors
  - SSTR2 agonists
- Nutraceuticals
- Cataracts
- Ocular allergy, infection, and inflammation therapies without indication of superiority to marketed compounds
- Retinal delivery systems – Iontophoresis
- Dry eye — efficacy ≥ Restasis™

**STROKE (Including Neurodegeneration and Movement Disorders)**

**Areas of Interest:**

- New chemical entities that reduce infarct volume at 6 hours or more post-ischemia
- PARP inhibitors
- JNK/p38 inhibitors
- Novel agents for stroke recovery
- Noninvasive markers that reflect infarct evolution in preclinical stroke models and stroke patients
- Markers that distinguish hemorrhagic from ischemic stroke
- EPO analogs or mimetics
- Agents that enhance mitochondrial function
- Compounds that promote axonal protection, remyelination, axonal recovery
- Animal models of progressive neurodegeneration
- Inhibitors of microglial activation

**Not Interested in:**

- Inhibitors of stroke edema
- Non-dopaminergic palliative therapies for PD
- LRRK2 inhibitors

- Thrombolytics, antiplatelets, anticoagulants specifically for stroke
- Any NOS inhibitor
- Acid sphingomyelinase inhibitors
- Bioavailable metal chelators
- Orally active antioxidants
ONCOLOGY
Areas of Interest:

Early Stage (through clinical POC)
- Cell signal transduction and proliferation/survival
- Tumor selective targeted cytotoxics
- Tumor selective chemosensitizing agents
- Developmental pathways/cancer stem cells

Biologics/Technologies
- Therapeutic antibodies
- Antibody-directed therapy
- RNAi
- Immunomodulators
- Vaccines

Late-Stage Clinical (after POC) or Marketed
- Supportive care
- Global or regional deals (US, Europe, and/or Japan)
- Complements internal pipeline and marketed products
- Novel patent-protected formulations of existing products
- Rx-Dx opportunities (as a package)
- Hormonal agents
- Cytokines
- Regulation of energy production/utilization

Not Interested in:

Early Stage (before clinical POC)
- Preventive care
- Personalized immunotherapy/autologous therapies
- Gene therapy

Late-Stage Clinical (after POC) or Marketed
- Hormonal agents
- Cytokines
- Regulation of energy production/utilization in tumors
- Preventative therapies
- Supportive care
EMBRACING PARTNERSHIPS

Research Technologies

MOLECULAR PROFILING

Molecular Biomarker Platforms
- Methods to collect and preserve samples in the clinical setting
- Fractionation technologies for serum (plasma), urine, and CSF
- miRNAs and DNA methylation profiling technologies
- SNP genotyping and long DNA sequencing technologies
- Technologies for location analysis (ChIP-on-chip)
- Technologies to profile transcriptome, including ncRNAs, microRNAs
- Kinase, protein phosphorylation, and metabolite profiling technologies

In Vivo Models
- Technologies for genetic approaches to characterize targets, efficacy, ADME, and safety in model organisms
- Technologies for mammalian mutagenesis and genome engineering
- Non-mammalian platforms for target validation and identification
- Technologies for in vivo target modulation by nongenetic intervention
- In vivo RNAi approaches to phenocopy genetics and pharmacology
- Viral and nonviral delivery technologies to somatic tissues and animals
- Inducible systems for regulating RNAi
- In vivo approaches for GEM and RNAi pathway mapping and/or biomarker identification
- Technologies that complement RNAi for interrogating gene function and pathway mining
- In vivo technology platforms for target advancement and preclinical proof of concept and safety assessment
- Technologies that integrate in vivo platforms (eg, GEMs) for target identification and biomarker discovery and validation (RNA, protein, imaging)

DRUG DELIVERY

Areas of Interest:
- Back-of-the-eye delivery systems
  - Retinal delivery systems – Clinically proven gene tx vectors – retinal delivery of siRNA and trophic factors
  - Retinal delivery systems – Retinal drug delivery device with greater than 3-month dosing
- Inhalation and nasal delivery systems for protein/peptide
- Novel formulations to extend product franchises
- Novel protein and peptide oral and IV delivery systems
- siRNA delivery systems
- Controlled release technologies for IV and sub-Q applications (drugs, peptides, and siRNA)
- Novel technologies for delivery of high concentration antibody formulations
- Novel antibody delivery platform
- Novel technologies for formulation and delivery of adenovirus and DNA
- Novel vaccine and adjuvant delivery technologies
- Technologies for delivery of water insoluble compounds, particularly for IV and oral applications

Not Interested in:
- Transdermal for small molecule delivery
- Needle-free injection
- Iontophoresis for retinal delivery

MERCK & CO., INC.
Whitehouse Station, N.J., U.S.A.
DRUG DISCOVERY PLATFORMS

In Vivo Imaging
• Novel PET, SPECT, CT, MR, and U/S radiotracers and contrast agents with particular interest in oncology, cardiovascular, neuroscience, and diabetes applications
• Optical imaging tools and reporters
• Imaging agents or genetic constructs that report on cellular pathways and processes such as apoptosis, proliferation, cell cycle, angiogenesis
• Image analysis tools to reduce cycle time

Chemical Technologies
• Chemical and biological strategies for inhibiting protein/protein interactions
• Microfluidic and miniaturization methods for organic synthesis
• Novel materials and methods for rapid chiral compound separation and analysis
• Improved and miniaturized cell culture, protein expression, and purification systems for crystal structure generation
• Knowledge-based systems involving published chemistry, SAR, and patent data

Screening and Assay Technologies
• Novel pluripotent human and other disease-relevant cell lines
• Label-free assay technologies
• Voltage and ligand-gated ion channel screening technologies
• GPCR deorphanization technologies
• Whole cell assay technologies
• Technologies for automated siRNA and cDNA screening
• Quantum dot imaging
• Novel GFP and non-GFP labels
• Imaging-based tools to measure biomechanical changes in cells
• Flow-based imaging for screening stem cells
• 3D-imaging tools and analysis software
• Cellular image analysis software
• Improved automated cell culture technologies
• High throughput Western blot technology

Informatics
• Knowledge extraction and representation technologies from structured and unstructured databases and information sources
• Biological pathway content for biomarker identification
• Imaging data analysis, management, and integration
• Biological process modeling technologies
• Natural language text mining technologies
• Advancements in infrastructure networking capabilities or virtualization capabilities to facilitate high-content data movement and access in a global scientific environment

Other
• Biomolecular detection and separation technologies with improved sensitivity and stability (quantum dots and magnetic nanobeads)
• Implantable sensors for real-time nonsacrificial physiological data collection (eg, glucose monitoring)
RNA THERAPEUTICS

Assays for siRNA Intracellular Functions
- Assays for siRNA endosomal escape
- Biochemical assays for strand selection, RISC incorporation, catalytic efficiency

siRNA Sequence, Structure, and Modification
- Novel chemistries for improving resistance to enzymatic degradation
- Novel chemistries for reducing immunostimulation
- Long-term chemical stability
- Improved target specificity

siRNA Encapsulation for Systemic Administration
- Novel polymers and lipids for encapsulation
- Encapsulation agents that improve endosomal escape
- Must be capable of reducing mRNA and protein levels in animals
- Low toxicity and biodegradable
- Amenable to molecular targeting strategies
- Long-term storage stability

Approaches to Molecular Targeting Encapsulated siRNA
- Targeting approaches suitable for nanoparticle or liposome delivery
- Specific for disease-relevant cell types
- Targeting using antibodies, peptides, or small molecules

Validated siRNA Targets
- Demonstrated reduction in mRNA and protein levels in animals
- Reductions have expected effect on disease phenotype

RNA Manufacturing
- Advancements in large-scale production of modified siRNA
- Improved processes for increased quality, efficiency, and reduced COG
- Novel chemistries

Information Technology
- Registration and tracking of information related to complex multi-component biologics

BIOLOGIC PLATFORMS

Areas of Interest:
- Platforms for the identification, generation, and modification of monoclonal antibodies (mAbs, Fabs, scFvs), aptamers, and engineered proteins displaying pharmaceutical properties
- Technologies that:
  – Address/overcome the blood brain barrier
  – Improve/extend half-life
  – Address and provide for multi-specificity
- Non-antibody scaffolds
- Effector functionality in antibodies
- Technologies that enhance expression and production of proteins, and novel delivery systems
- Technologies enabling siRNA therapeutics, including siRNA delivery technologies
- Immunomodulators/immunostimulators

Not Interested in:
- Transgenic animal-based or plant-based production systems for therapeutics