

Partnering with Pfizer Worldwide R&D



## Partnering with Pfizer

Welcome to Pfizer Worldwide Research & Development (WRD), where strategic partnership is at the heart of fulfilling Pfizer's purpose as we work to translate advanced science and technologies into medicines and vaccines that significantly improve patients' lives. As the world's leading biopharmaceutical company, Pfizer is proud to offer you access to our world-class research scientists, our cutting-edge capabilities in medicine and vaccine design, our global network of external collaborations, and our industry-leading manufacturing and commercial capabilities.

We recognize that to continue to expedite the pace of innovation, it is vital to collaborate in new and dynamic ways. To this end, we have detailed the specific areas in which we seek to create a new partnership in this brochure and on our website, www.pfizer.com/wrdpartnering Our External Research & Development Innovation (ERDI) – an externally-focused scientific team of high profile PhDs / MDs, embedded within our research groups – seeks to identify late-breaking science that forms the basis of innovative therapies and drives related collaborations that deliver value to Pfizer, our partners, and patients. ERDI works closely with Pfizer Business Development and Pfizer Venture Investment to form an effective partnering team with a diverse blend of research, clinical, and business expertise.

To discuss opportunities most pertinent to you, please contact the member of our partnering team listed on each page of this brochure. We are confident that you will find Pfizer to be a great partner in advancing your science and bringing high-impact medicines and vaccines to improve human health.



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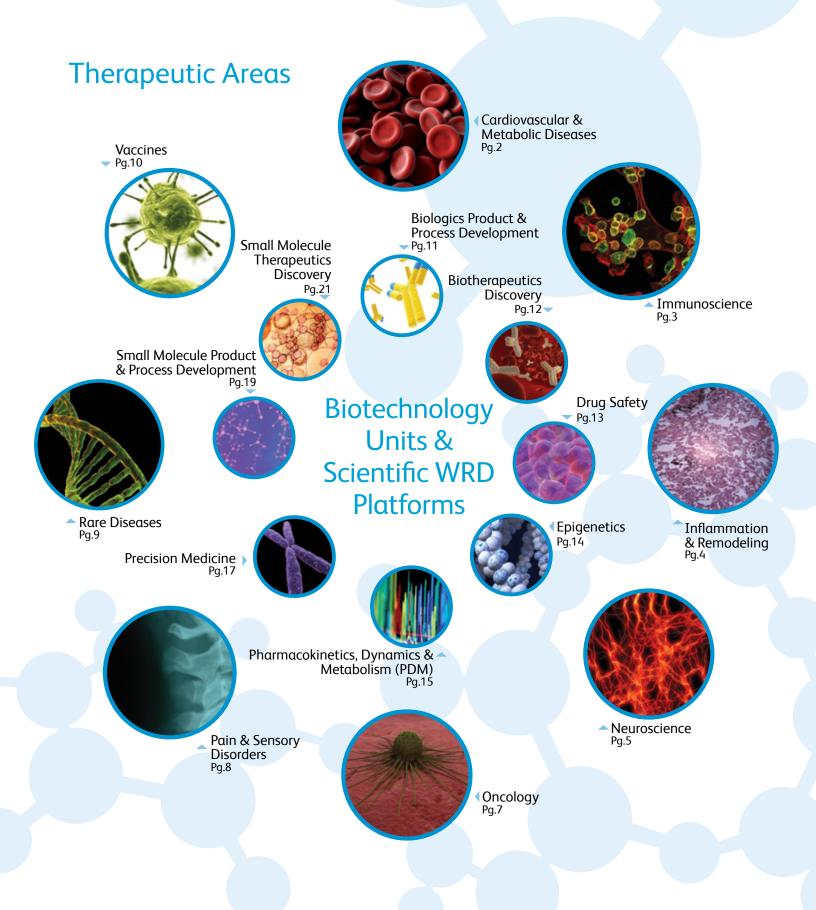


Bob Smith Senior Vice President WRD Business Development



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## WRD Research Focus Areas



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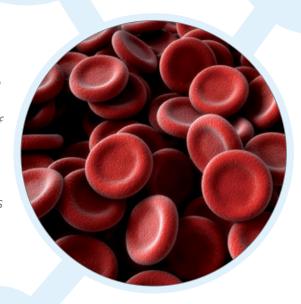
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## Cardiovascular & Metabolic Diseases

Cardiovascular diseases (CVD) remain the leading cause of global mortality, accounting for about 1 in every 2 adult deaths worldwide. Declines over the past few decades in the incidence of CVD in Western populations – mediated in part by development of acute interventions and medicines targeting lipid and blood pressure pathways – have began to plateau, and rates of CVD in developing countries continue to increase at an alarming rate. At the same time, rates of CVD-related morbidity, heart-failure, nephropathy and peripheral vascular disease increase as more patients survive hearts attacks, and the population ages. The global burden of chronic kidney disease and end-stage renal disease, recognized and likely causal risk factors for CVD, is also growing. Contemporary estimates suggest that over 40M people in the US, and over 120M people in China, have impaired renal function. Pfizer scientists are eager to work with world-class partners who share our mission to develop novel and differentiated medicines to improve the lives of patients suffering from cardiovascular and metabolic diseases, including diabetes, renal and co-mordbidities around the world.

## WRD is interested in establishing partnerships to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- CV-risk (ACS, peripheral vascular disease, stroke, atherosclerosis, and heart failure) in nondiabetics and diabetics through improvement in vascular function, protection or repair, reduced vascular inflammation, dyslipidemia, or enhanced cardiac repair and performance
- Blood pressure in difficult to treat hypertensives
- Prevention of renal disease in non-diabetics and diabetics
- Centrally-acting anorectics
- Bariatric surgery mimetics



- Solute transporters and their role in metabolic and in renal disease
- Kidney podocyte architecture
- The progression of co-morbidities related to T2D, specifically peripheral vascular disease and heart failure
- Insulin sensitization with weight loss
- Beta-cell function and survival in obesity and T2D
- Dysregulation of alpha-cell function
- Metabolic adaptations to exercise which protect against or reverse diabetes
- Mechanisms which protect mitochondria under conditions of chronic caloric excess
- Lipid content and the development of liver fibrosis in patients with NASH / NAFLD
- Dysregulation of liver metabolism
- Weight-loss approaches to shift people to negative energy balance, e.g., modulators of beige and brown fat metabolism
- Gut and brain signals that regulate energy homeostasis and metabolism
- The role of sleep and circadian rhythm in regulating endocrine function and metabolism
- 2 External R&D Innovation Contact: Barry Ticho (Barry.Ticho@pfizer.com) or Joachim Fruebis (Joachim.Fruebis@pfizer.com)

## Immunoscience

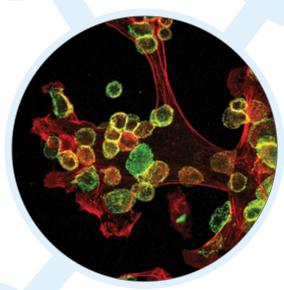
Pfizer is a global leader in developing medicines for patients suffering from chronic immune diseases. Pfizer's commitment to the discovery and development of novel therapeutics to help patients living with chronic autoimmune diseases is evidenced by products such as Xeljanz<sup>®</sup> (tofacitinib citrate), Celebrex<sup>®</sup> (celecoxib capsules), Rapamune<sup>®</sup> (sirolimus), and Enbrel<sup>®</sup> (etanercept) for patients suffering from conditions such as osteoarthritis, solid organ transplant rejection, rheumatoid arthritis, and psoriasis. The Immunoscience Research Unit, led by Johan Lund, Chief Scientific Officer, is focused on evolving the next generation of therapies for immune-mediated diseases. Pfizer is interested in entering into strategic relationships with innovative collaborators to develop increasingly novel and differentiated therapies for autoimmune diseases.

## WRD is interested in establishing alliances to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- Rheumatoid Arthritis
- Systemic Lupus Erythematosus
- Inflammatory Bowel Disease
- Psoriasis
- Multiple Sclerosis and smaller indications with high unmet need that are mechanistically related to those above

## Specific areas of interest include:

- Cytokines and their signaling pathways
- Adaptive Immunity, Lymphocyte biology including Th17 lymphocytes
- Regulatory cells and Tolerance induction
- Host-microbial interactions and microbiome
- Technology platforms and products to help understand patient segmentation in the disease areas of interest and develop precision medicine strategies for innovative portfolio products



### Not actively seeking partnering opportunities in:

- Adequately controlled RA
- TNFα, IL-1β targeting biologics
- B cell depleting biologics
- Corticosteroids

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# Inflammation & Remodeling

The Inflammation & Remodeling Research Unit, led by Christelle Perros-Huguet, Chief Scientific Officer, is focused on discovering and developing novel and differentiated therapeutic options targeting chronic inflammatory diseases. Chronic inflammation can result from sensing and integrating injury or danger signals including for example infectious agents, free radicals and oxidative stress. The unit focuses on three mechanistic themes each defining a distinct intervention point in the cycle of disease chronicity. The three mechanistic areas include: 1) epithelial, endothelial and parenchymal sensors of danger signals and the engagement of the innate immune system; 2) integrators and amplifiers of inflammation including cell signaling, chemotaxis, production of inflammatory mediators by various cell types and disruption of the mucosal/microbiome barrier surface; and 3) targeting tissue remodeling and fibrosis by regulating  $TGF\beta$ signaling, matrix stiffness, and fibroblast proliferation.

## WRD is interested in establishing alliances to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- Diabetic nephropathy
- IgA nephropathy, Lupus nephritis and membranous nephropathy
- Autosomal dominant polycystic kidney disease
- Acute kidney injury
- COPD
- Severe asthma
- Pulmonary hypertension and Idiopathic Pulmonary Fibrosis
- Other pulmonary and skin fibrotic diseases

## Specific areas of interest include:

- Innate immune suppressors
- Oxidative stress modulators
- Anti-fibrotics
- Technology platforms and products to help understand patient segmentation in the disease areas of interest

- Corticosteroids
- ACE / ARB

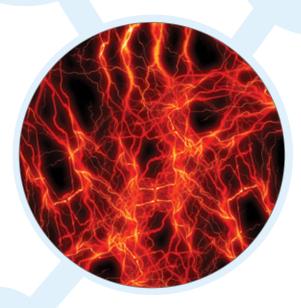
## Neuroscience

In the US today, 7 of the 10 leading causes of disability are neurological and psychiatric disorders. To meet these patient needs, Pfizer is taking a bold leadership approach that spans symptomatic to disease-modifying therapies. As a result, Pfizer is investigating new ways to attack Alzheimer's Disease, Parkinson's Disease, Schizophrenia and other debilitating conditions of the nervous system. In addition, we continue to expand inquiry into alpha-2-delta binding site agents, the mechanism that has already led to the development of Neurontin® (gabapentin) and Lyrica<sup>®</sup> (pregabalin capsules). Pfizer neuroscientists are eager to work with world-class partners and collaborators who share our mission to improve the lives of patients suffering from neurological and psychiatric disorders.

## WRD is interested in establishing alliances to develop therapeutics, expand our disease biology understanding, and to identify biomarkers that impact:

- Alzheimer's Disease (AD)
- Parkinson's Disease (PD)
- Huntington's Disease
- Cerebrovascular Disease
- Hearing Loss
- Schizophrenia: positive, negative and cognitive deficits
- Bipolar Disorder
- Depression
- Addiction
- Autism Spectrum Disorders

Pfizer is also interested in Muscular Disorders, Eating Disorders; Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis, Friedrich's Ataxia,Traumatic Brain Injury and Post Traumatic Stress Disorder (PTSD).



## Specific areas of interest include:

## Neurodegeneration / Neurological Disease:

- Novel potential symptomatic agents for AD or PD (could include L-DOPA-induced dyskinesias)
- Agents affecting microvascular circulation and brain metabolism with validated link to AD
- Imaging agents (e.g., tau, synuclein neurotransmitters, neuroinflammation and gliosis)
- Translational biomarkers preclinical to clinical
- Biological samples (e.g., induced pluripotent stem cells) from well defined AD or PD patient populations
- Agents impacting neuroinflammation
- Conformational antibody that has cross reactivity to all "amyloids" (e.g., tau, Aβ, huntingtin, δ-synuclein)
- Novel delivery of growth factors and other biotherapeutics (e.g., viral delivery or implanted device)

#### Psychiatry / Behavioral Disorders:

- Novel depression treatments with ketaminelike profile (speed of onset / duration) without psychological side effects
- Adjunctive agents for residual symptoms of major depression disorder (e.g., anxiety)
- Adjunctive schizophrenia agents with negative and/or cognitive symptom efficacy (e.g., GlyT1, mGluR2/3, GABA agents)
- PET imaging agent for CNS psychiatry targets
- Novel technologies for monitoring patient behavior, compliance and/or treatment efficacy of any modality
- Biological samples (e.g., induced pluripotent stem cells) from well defined psychiatric disease patient populations
- Improved clinical or animal models of cognitive domains in psychiatry that are amenable to translation
- Quantitative neuropsychological testing methodologies

#### **Enabling Technologies:**

- Remote cognition assessment tools
- Sensor/biosensors that measure motor dysfunction via ocular end points
- Functional imaging studies (FDG, fMRI, MRS) evaluating disease relevant circuitry and processes
- Fast imaging analysis with lower variability
- Acquisition and analysis tools for high throughput processing of electrophysiology/EEG data in rodents, non human primates, and humans
- Computerized/web-based tools for cognitive assessment in humans that have been cross-validated with standard scales but allow for multi-domain assessment
- In vitro blood brain barrier models comprised of rodent, non human primate or human
- In vivo blood brain barrier models
- Mechanisms of trans-blood brain barrier transport with robust improvement in pharmacokinetics and in which the mechanism is well understood

#### Not actively seeking partnering opportunities in:

- Protein "anti-aggregators"
- "Black box" mechanisms
- Aβ lowering agents: small molecules (unless in P1 or later) and/or large molecules
- Large molecule therapeutics with CNS targets absent data for brain penetration

- Anti-oxidants
- D2/5-HT based antipsychotic drugs with low possibility of differentiation
- Stand alone mania treatments
- SSRIs, SNRIs

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## Oncology

Pfizer's Oncology Research Unit (ORU) strives to advance the frontiers of cancer biology and to translate this knowledge into high-impact medicines for cancer patients. The ORU comprises four pillars: Tumor Cell Biology; Bioconjugates Discovery and Development; Precision Medicine; and Integrative Biology and Biochemistry. The Tumor Cell Biology group is focused on oncogenic drivers, tumor metabolism, and epigenetics. The Bioconjugates group seeks to establish industry leadership in the therapeutic applications of 'empowered antibodies', with a major focus on antibody-drug conjugates (ADCs). Precision Medicine represents an integrated cluster of technology platforms and translational science configured to enable patient-tailored, hypothesis-driven experimental medicine approaches. Finally, our Integrative Biology and Biochemistry team supports novel target identification and validation through functional genomics, proteomics, and other "omic" approaches.

## WRD is interested in establishing alliances to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- Lung, colorectal, breast, ovarian, renal, and hematologic cancers
- Cancers prevalent in Asia (e.g., gastric cancer, hepatocellular carcinoma)

## Specific areas of interest include:

- Targets and technologies that enable antibody and ADC approaches
- Oncogenic signaling mechanisms
- Tumor metabolism
- Epigenetics

- Directed tumor cell killing via immune-based mechanisms
- Precision medicine
- Immune checkpoint modulators
- Functional genomics

### Not actively seeking partnering opportunities in:

- Gene therapies
- Antisense / siRNA / shRNA therapeutics

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- Reformulated cytotoxic agents
- Radioconjugates
- Oncolytic Viruses

## Pain & Sensory Disorders

Pfizer is a global leader in pain medicines with products in each of the major classes: Celebrex® (celecoxib; COX2 inhibitor); Lyrica<sup>®</sup> (pregabalin); Neurontin<sup>®</sup> (gabapentin; α2δ); Avinza<sup>®</sup> (morphine sulphate); and Oxecta<sup>®</sup> (oxycodone immediate release, opioid agonists). Additionally, the novel NGF inhibitor antibody, tanezumab, is in late stage clinical trials in high medical need patients. Despite these medicines, large numbers of pain sufferers still experience inadequate relief. We are working to develop novel therapeutics and improved formulations and combinations of existing therapies. Pain is a distinct group of conditions with unique underlying biology, affecting patients in different ways depending on co-morbidities, background genetics and psychology. Pfizer is interested in partnering with innovative collaborators to develop novel and differentiated medicines to address the needs of patients suffering from pain. Neusentis, our research unit, is based in Cambridge, UK and Research Triangle Park, North Carolina, USA. The unit has a particular emphasis on ion channel modulators that can address patient need in pain and sensory disorders. Additionally, regenerative medicine research is carried out at the Cambridge site, both to support pain projects and also to pursue cell therapies for other indications.



WRD is interested in establishing alliances to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- Chronic pain
  - Neuropathic pain
  - Nociceptive pain
- Acute pain
  - Perisurgical pain management, prevention of chronic post-operative pain
- Epigenetic approaches to understanding pre-disposition to pain phenotypes

- Sensory disorders
  - Disorders involving abnormal sensations of clinical relevance (e.g., visual, auditory, vestibular, somatosensory systems)
  - Therapeutic opportunities for sensory disorders should preferably have the potential to be used to treat any of the pain populations listed above

## Specific areas of interest include:

- Ion channels, notably targets where there is a strong human genetic evidence for a role in pain or in mechanistically-related sensory disorders
- Novel targets on pathways with known relevance to pain, e.g., neurotrophins
- Improved opiates with fewer side effects, including novel abuse-resistant formulations and approaches to address over-consumption
- Nociceptor-specific drug delivery
- Technology platforms and products to help understand and segment patients in pain and develop Precision Medicine strategies for our innovative portfolio
- Novel approaches to demonstrate cross-species target engagement of an ion channel-excluding fMRI, microneuography, threshold tracking, capsaicin/cinnamaldehye flare, UVB, etc.

- General anesthetics
- NGF antibodies

## Rare Diseases

Pfizer's Rare Disease Research Unit, led by Chief Scientific Officer Kevin Lee, is adopting an innovative and collaborative approach to the development of new medicines for patients with rare diseases. We have a track record of creating innovative strategic partnerships with academic institutions, patient advocacy groups, and commercial enterprises to accelerate the development of novel therapeutics across the entire spectrum of rare diseases. We are looking to capitalize on recent scientific advances linking diseases to specific genetic defects. As 70% of rare diseases are monogenic in origin, we believe this is an area where scientific knowledge is enabling significant advances in drug development. Our expertise in large molecule therapeutics, small molecule protein chaperones, and transcriptional modulators has resulted in a broad pipeline of potentially transformative medicines across multiple disease areas.

## WRD is interested in establishing alliances to develop therapeutics, expand disease biology understanding, and identify biomarkers that impact:

- Hematology (non-malignant)
  - Hemophilia
    - Coagulation factors with extended duration of activity and/or improved delivery
    - Oral agents to treat hemophilia
    - Immune tolerance
    - Novel approaches (including gene therapy) to treat hemophilia patients
  - Other rare hematologic (non-malignant) indications
    - Sickle cell anemia, & beta-Thalassemia follow on with focus on disease modifying and/or therapies that significantly change disease pathology
    - Hemostasis (systemic and topical)
    - Opportunistic approaches in the field of hematology that promise well differentiated novel medicines
- Neuromuscular Diseases
  - Duchenne/Becker muscular dystrophy and other muscular dystrophies (e.g., DM1, FSHD, LGMD): disease-modifying therapies preferred
  - Spinal Muscular Atrophy
  - Friedreich's ataxia: upregulate frataxin expression
  - Amyotrophic lateral sclerosis: protein misfolding approaches

- Pulmonary Diseases
  - Cystic Fibrosis (in conjunction with the CF Foundation)
  - Pulmonary arterial hypertension and idiopathic pulmonary fibrosis

Disease modifying approaches for other diseases such as transthyretin amyloidosis, myasthenia gravis, Huntington's disease

- General mechanisms of interest
  - Pharmacologic chaperones and other modifiers of protein trafficking, misfolding, or degradation that could apply to multiple diseases (e.g., a small molecule approach that could apply across multiple lysosomal storage disorders)
  - Targeting technologies / platforms (e.g., muscle and CNS targeting)
  - Modifiers of gene transcription via epigenetic approaches
  - Nucleic acid therapy approaches therapies
  - Antibody-drug conjugates
  - Small molecule approaches (oral)

- Undifferentiated approaches in well-served markets
- Medical devices
- Diagnostic tests (in absence of a therapeutic approach)

## Vaccines

Our vision is to become a recognized leader in the development of prophylactic and therapeutic vaccines for unmet medical needs at all stages of life and for all geographies. We focus on prevention of pneumococcal disease; infections in hospitals and healthcare settings; infectious diseases in infants, children, adolescents and older adults; select therapeutic vaccine targets and emerging markets.

## WRD is interested in establishing alliances to pursue development of:

- Vaccines for the prevention and/or treatment of infectious diseases
- Vaccines for the prevention and/or treatment of non-infectious diseases through the active elicitation of disease-modifying immune responses

## WRD is also interested in:

- Adjuvants
- Novel in vitro systems for assessment of vaccine immunogenicity
- Novel animal models for assessment of vaccine effectiveness
- Novel immunomodulators of the adaptive immune response
- Novel vaccine target antigen identification systems
- Novel vaccine delivery platforms
- Novel vaccine administration systems

### Not actively seeking partnering opportunities in:

• Novel vaccines in disease areas for which effective vaccines are already available / licensed (with the exception of novel influenza virus vaccines)

## Biologics Product & Process Development

WRD Pharmaceutical Sciences envisions a network of strategic partnerships integral to its biologics technology initiatives, which include biopharmaceutical and vaccine development and manufacturing and prokaryotic expression to augment core competencies.

## I. WRD is interested in establishing alliances to develop and access:

- Next generation of microbial and mammalian cell protein production systems
- Next generation process and manufacturing technologies

## Specific areas of interest include:

- Systems and Synthetic Biology
  - Technologies to design and influence host cell performance and product quality
  - Novel expression systems with alternative post-translational modifications (e.g. glycosylation)
  - Automated methods for mammalian cell line screening, selection and scale up
  - Next generation cell culture process technologies
  - Next generation purification process technologies
    - Harvesting technologies (e.g., smart polymer, automation)
  - High throughput analytics for product quality attributes
  - Advanced analytics for glycoconjugates and antibody drug conjugates
  - Flexible and adaptive manufacturing technologies for biotherapeutics

II. WRD is interested to ensure commercial and clinical differentiation of products by accessing leading drug delivery technologies.

## Specific areas of interest include:

- Tissue specific delivery
- Alternative routes of delivery (transdermal, transmucosal)
- Analytics (biophysics) to predict stability
- Advanced formulations (improved stability, high dose delivery)

Not actively seeking partnering opportunities in:

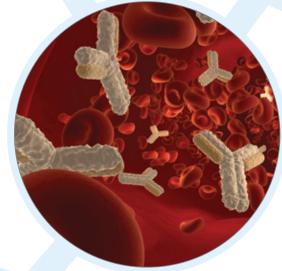
• Transgenic animal-based or plant-based production systems for biologics

## Biotherapeutics Discovery

Pfizer strives to become the leading biotherapeutics company by building on internal expertise and fostering strategic partnerships to access the best technologies with patent protection and technical capabilities that provide a competitive advantage.

## WRD is interested in establishing alliances to develop and access:

- Transformational technologies to design, construct, and optimize biotherapeutics
  - Informed protein design optimizes molecular properties resulting in superior efficacy, pharmacokinetics, pharmacodynamics, safety, manufacturability and differentions
- Antibody drug conjugate technologies
  Novel ADC platforms, novel payloads, linkers, conjugation sites
- Bioconjugation technologies
  - Novel approaches that enhance antibody function or improve site-specific bioconjugation
- Combinatorial biologics such as bi-specific and multi-functional platforms with promising biophysical and manufacturing properties
- Structure-based and computational design of therapeutics
  - Novel technologies to rationally design antibody, protein and peptide therapeutics that display superior pharmaceutical properties (including selectivity, half-life extension, stability, formulatability)
- Technologies that enhance multi-transmembrane protein target expression / presentation for antibody generation and screening



- Technologies and patient sample access for antibody discovery from human antibody responses
- Targeted delivery technologies that address / overcome cell membrane penetration, cross blood brain barrier
- Technologies that can significantly enhance general protein expression, purification, stability for discovery
- Integrated service providers to support early discovery activities for development of therapeutics
- Broadly applicable platforms to enhance speed / quality of antibody generation
- Novel biologics, combination therapies, and "biobetters" that fit Pfizer strategies

- PEGylation for bioconjugation
- Protein scaffold platforms with challenging stability attributes and/or difficult manufacturability

## Drug Safety

Pfizer's Drug Safety R&D group develops and applies the skills, experience and scientific tools necessary for safety assessment and risk management of targets and compounds across the research, development and commercial phases of drug development. We seek to enhance our capabilities for target safety assessment, selection of safer compounds, toxicity risk management and translation of preclinical models.

## WRD is interested in establishing alliances to develop and access:

- Mechanisms, biomarkers, and screening approaches related to target organ toxicity
  - Cardiovascular safety
  - Liver injury
  - Hypersensitivity
  - Nephrotoxicity esp., glomerular
  - Skeletal and cardiac muscle toxicity
  - Ocular safety
  - Screening for abuse potential
- Biotherapeutics-related analytical technologies
  - Immunogenicity and other safety-relevant assays
- Deeper knowledge of targets and pathways
  - Knock-in, knock-out technologies
  - Novel technologies and increased throughput for target localization studies
- Safety biomarker technologies
  - Platforms; multiplex; analytical approaches; validated reagents

- Genetox Screening
- hERG related assays
- *In vitro* screening models without significant validation
- In silico approaches without experimental validation

## Epigenetics

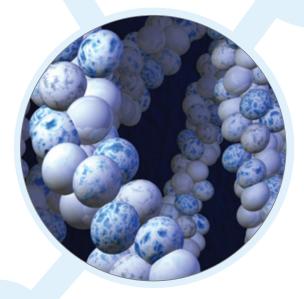
Modification of epigenetic signaling has the potential to serve as a new route in to the treatment of human diseases, including a range of chronic and life-threatening conditions. Epigenomic profiling may form a component of successful Precision Medicine strategies, for conditions with epigenetic and non-epigenetic treatments. Epigenetic modifications are also key mediators of cell fate, with implications for cellular therapies using reprogrammed somatic cells.

## WRD is interested in establishing alliances to develop and access:

- Epigenetic targets with a high degree of biological validation
- Novel compounds with epigenetic mechanisms of action
- Epigenomic biomarkers

## Specific areas of interest include:

- Validated epigenetic targets with strong mechanism of action support in chronic and life-threatening conditions
- Applications for epigenetically targeted compounds in orphan diseases and genetic conditions



- Epigenomic biomarkers for disease stratification, progression or treatment sensitivity
- Novel epigenetically-targeted compounds with known mechanism of action and defined patient populations
- Selective HDAC inhibitors

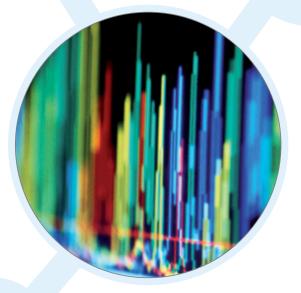
- Pre-clinical DNA methyltransferase inhibitors for oncology
- Pre-clinical pan-HDAC inhibitors
- Non-coding RNAs (microRNAs etc) as systemic therapeutic agents

## Pharmacokinetics, Dynamics & Metabolism (PDM)

PDM is focused on the development of innovative small and large molecule therapies through an improved understanding of targets, pathways and modeling for preclinical efficacy, and discrete toxicity. PDM will pursue collaborations to enhance physiological relevance of prarmacological endpoints, biomarkers / biomeasures, systems pharmacology/PKPD, quantitative bioanalytics, prediction of transporter-mediated disposition, tissue targeting capabilities, optimizing human ADME properties.

## WRD is interested in establishing alliances to develop and access:

- Translational research large and small molecule efforts
  - Translational modeling and simulation approaches, including Systems pharmacology/ PK-PD, integrated with quantitative biomeasures to lead to: deeper knowledge of targets and pathways; and increased confidence in target and drug selection.
  - Systems models of specific areas of toxicity, e.g., cardiovascular toxicity
  - Application of PKPD to safety biomarker technologies
  - Influence of hepatic and renal uptake and clearance on toxicology in these organs – focus on disorders of bile production and bile acid transport
- Quantitative Bioanalytics, Biomarkers, Biomeasures, and Immunogenicity (ADA) Assays – large and small molecule efforts
  - Novel LC-MS/MS large molecule bioanalysis and automation techniques



- Flow cytometry, cellular imaging techniques (Amnis) for biomarkers and biomeasures, and highly multiparametric single cell analysis using mass cytometry (CyTOF)
- Deleopment of a universal platform for cell-based neutralizing antibody assays
- Biosimilars / Biocomparability
- Key vendor development for biotherapeutics bioanalytical capabilities in (a) various platforms (e.g., mass spectrometry-based, ligand-binding assays, flow cytometry) across various modalities, (b) quantitative biomarker capabilities in support of biomarker / biomeasure studies, and (c) regulated toxicology and clinical sample analyses
- Next-generation of advanced intelligent high-throughput automation platforms for bioanalysis

- Disposition of Antibody-Drug Conjugates large and small molecule efforts
  - Cellular and systemic fate of the conjugate and components
  - Quantification and prediction of pharmacokinetics
- Disposition and oral delivery of peptides large and small molecule efforts
  - Novel commercially viable delivery technologies (oral and non-oral)
  - Predictive tools and technologies targeting oral absorption and disposition of peptides
- Targeting, prediction and modeling of transporter-mediated disposition and DDIs – small molecules
  - Quantitation and scaling of transporters for input into physiological PK models of tissue penetration and clearance
  - Determination of intracellular unbound concentrations of transported drugs
  - Prediction and quantification of human transport mediated (e.g., biliary) clearance
- Immunogenicity prediction (in conjunction with efforts in PDM Translational Research and Drug Safety R&D) – large molecules
  - In silico immune epitope prediction
  - In vitro drug-specific immune response (e.g., PBL stimulation; whole protein & epitope mapping; DC-T cell assays, Bcell response assays)
  - *Ex vivo* immune response and immune tolerance biomarkers
  - Nonclinical models for predicting immunogenicity impact of product and treatment-related risk factors
- Physiologically relevant in vitro assays
  - Methods for expanding cell numbers or stabilizing phenotypes of directly isolated primary cells (particularly from patients)
  - Robust, reliable *in vitro* differentiation protocols from human pluripotent stem cells for difficult to obtain cell types

- Non-natural amino acid substitutions in target proteins to create novel screening readouts
- Advances in human genome editing technologies for High Content Analysis cell based assays
- Endogenous gene reporter models in human primary cells and stem cells
- Detection of tagged-protein at physiologically relevant concentration in human cell based assays (targeted reporter gene)
- Visualization of drug interaction with targeted-protein within the cellular environment
- Quantification of cellular environment changes by biosensors
- Advances in high content analysis in 3D culture system
- In vitro Phenotypic Screening:
  - Novel deconvolution advances for *in vitro* phenotypic screening
  - Prediction of *in vitro* cellular phenotypic changes due to patient-derived single point mutation and genetic defects
  - Quantification of electro-physiologic measurement in plate cell based assays
  - Advances in single cell mass cytometry technology for phenotypic screening
- Optimizing Human ADME Properties and PK Prediction Capabilities for Small Molecules
  - Ability to develop SAR for ADME properties utilizing chemical library, high-throughput in vitro assays coupled to LC-MS detection and computational models
  - Ability to conduct a suite of nonclinical studies to develop robust human PK prediction for routine and less common elimination pathways (AO, UGT, GST etc.)
  - Integration of PK understanding and assumptions into PB/PK models to predict human plasma-time profiles
  - Prediction of routine and complex DDI involving CYPs

## Precision Medicine

Precision Medicine is an approach to discovering and developing medicines and vaccines that deliver superior outcomes for patients, by integrating clinical and molecular information to understand the biological basis of disease. This effort leads to better selection of disease targets and identification of patient populations that demonstrate improved clinical outcomes.

## WRD is interested in establishing alliances to develop and access:

- Patient cohorts with high quality longitudinal molecular and phenotypic data and/or DNA and appropriately-consented, IRB-approved tissue samples in diseases of interest to Pfizer for
   clinical trials
  - o clinical triais
    o data mining
  - biomarker studies
  - genetic and pharmaco-genomic studies
- Systems Biology / Pharmacology
  - Databases with high quality treatment and disease outcomes associated with genetic, as well as molecular (metabolomic, proteomic, transcriptomic, epigenetic of clinical chemistry markers) or functional measures in particular imaging data
  - Databases of searchable eQTLs, pQTLs across tissues
  - Disease biology guided combination therapy design platforms
  - Systems biology approaches and proven in silico tools to evaluate pharmacological perturbation and elucidate mechanisms of in vivo toxicity
  - Mining of data for correlation and understanding of causality
- Breakthrough diagnostic technologies that also are highly quantitative, require minimal tissue and can be multiplexed.
- In vivo imaging technologies (including MRI, PET, CT, optical imaging technologies, imaging agents, genetically encoded tags, etc.) with particular interest in
  - Imaging agents for small and large molecule compound distribution studies



- Imaging agents monitoring physiology mechanisms and disease
- Analytical tools and technologies
- Ex vivo Tissue and Cell Analysis
  - Circulating tumor cell and Nucleic Acid quantification and analysis
  - Multiplexed flow cytometry for leukocyte analysis
  - Automated IHC for tissue analysis (cancer, safety)
  - Advanced ADME related genotyping
- Physiological Biomarkers
  - Technologies adding precision to pain management and treatment in pre-clinical and clinical studies
  - EEG-based biomarker for assessment of central pharmacology
- iPS cell resources and technologies to generate iPS cells that may be used to enable Precision Medicine strategies
  - Validated cell differentiation protocols
  - iPS cells derived from sub populations with specific genotypic/phenotypic data
  - Technology to create iPS cells in a rapid and reproducible fashion without insertional approaches

## Rinat

## RINAT

Originally established in 2001 as a private biotech company in South San Francisco, Rinat was acquired by Pfizer in 2006 and is operated as an independent biotechnology unit within Pfizer's Worldwide R&D group. This model allows Rinat to maintain the unique culture and scientific environment of a small company while exploiting the world-class capabilities and resources of the broader Pfizer R&D organization. Rinat is led by Jaume Pons, Chief Scientific Officer, and focuses on antibody-based therapeutics across all disease areas of interest to Pfizer. Rinat researchers couple the latest scientific advancements in human biology with state of the art protein engineering technology platforms to build a premier pipeline. Rinat has also established a group of leading geneticists and computational scientists who leverage novel approaches in genomics to discover and aid in the development of the pipeline. Scientists at Rinat are interested in working with partners who have novel therapeutic approaches or targets, as well as with those who have distinctive technology platforms that can augment Rinat's expertise in converting validated therapeutic targets



into novel protein-based therapeutics. With in-depth expertise across multiple therapeutic and technology disciplines, Rinat's partnering interests are broad and considers a wide variety of asset-based and technology partnering opportunities. In addition, Rinat also leads Pfizer's R&D efforts in Cancer Immunotherapy and is focused on partnering clinical stage oncology and immunology opportunities, with an emphasis on antibody-based therapies that are immunomodulatory, including those that directly engage or impact T-cell function.

## Small Molecule Product & Process Development

WRD Pharmaceutical Sciences envisions a network of partners to enhance active pharmaceutical ingredients (API) and drug product development and manufacturing of small molecules.

## WRD is interested in establishing alliances to develop and access:

- Computational Product and Process Design (CPPD) – Complement and advance our experimentation and manufacturing processes with computational tools, including translating drug molecular structures to material properties in silico. Specific areas of interest include:
  - Computational models for process operations
  - Prediction of oral absorption in humans
  - Computational Chromatography
  - Multi-scale integrated modeling platform technologies for systems-based
     Pharmaceutics predictions and simulations
  - *In-silico* design and screening of API synthetic pathways
- Materials Sciences and Particle Engineering Development of molecular structure-based particle design and engineering tools that allow for the prediction and manipulation of crystal form/ morphology, solid-state stability and material properties. Specific areas of interest include:
  - Computational Materials Science for particle engineering
  - Solid State Chemical Stability Prediction and Control
  - Delivery of API ensuring physical integrity during ensuing process operations
  - Particle engineering through directed assembly
- Portable, Continuous, Miniature and Modular Development and Manufacturing Equipment – Design and development of fit-for-purpose, small footprint, plug-and-play (modular) processing platforms, for drug product and/or API that allow the same equipment to be used for development and commercial manufacturing. Continuous/ semi-continuous operation, rapid deployment, and rapid changeovers between products are cornerstone concepts that are being pursued. Desired state is for processing modules to be capable of manufacturing multiple products at a wide range of manufacturing scales and enable significant reduction in scale-up/tech transfer efforts.

- Innovative and Chemical Synthesis Development of new platform syntheses that include sustainable/"green" chemical technologies and innovative chemical transformations. Specific areas of interest include:
  - Replacement of endangered metal catalysts
  - General methods for catalytic preparation of chiral amines
  - General methods for "direct" amide formation
- Drug Delivery Technologies Advance drug delivery technologies to enable differentiated therapies and the next generation of precision medicine. Specific areas of interest include:
  - Tissue targeting of drugs to improve therapeutic index (e.g., brain delivery, tumor targeting, etc.)
  - Technologies to improve/monitor patient adherence/compliance
  - Differentiated pediatric dosage forms that
    - Neutralize or improve taste without affecting the pharmacokinetics for oral immediate-release products,
    - 2) use a "solids-based" platform (versus conventional liquids), and/or
    - are enabled by use innovative dosing/ administration aids

- Rapid Analytics Innovative analytical platforms to enable real-time process understanding and/or control via on-line or at-line technology for Drug Product and Active Pharmaceutical Ingredients (API). Specific areas of interest include:
  - Rapid, precise, robust, and integrated *in-situ* Process Analytical Technologies (PAT) for routine process monitoring
  - 3-D mapping/imaging of drug products
  - Real-time data integration from disparate sources

## Small Molecule Therapeutics Discovery

Pfizer's Worldwide Medicinal Chemistry core capabilities include small molecule design and associated functions including structural biology and computational chemistry, synthetic innovation and compound safety prediction. Our partnering strategy is designed to maintain and enhance these areas as well as generate new synergistic capabilities.

## WRD is interested in establishing alliances to develop and access:

- High content and *in silico* approaches to predict small molecule toxicity
- Computational methods to integrate, manage, visualize, and mine large-scale compound-centric datasets from published literature and patents
- Technology to expand NCE target space orally bioavailable and cell penetrable peptides, and non-Ro5 compounds
- Next generation natural product screening technology
- Ion channel modulator design and screening technologies
- Membrane protein structural biology technologies and capabilities
- Small molecule computational design platforms
- New high efficiency synthetic transformations and novel flow chemistry approaches
- Systems biology approaches and proven in silico tools to elucidate mechanisms of in vivo toxicity
- Systems / chemical biology technologies enabling mechanism determination for phenotypic screening hits
- Bioinformatic approaches to define target selectivity

- CH activation chemistry
- Novel synthetic methodology to access small conformationally constrained multifunctional templates
- Novel strategies for enhancing the oral bioavailability of peptides
- Novel fragment or compound collections validated for protein-protein interaction targets
- Identification of and access to novel sub-nanomolar cytotoxic agents
- New chemistry to develop disease imaging agents (e.g., plaques / AD, beta cells / T2D, angiogenesis / cancer
- Novel methodology and capabilities to enable <sup>18</sup>F chemistry
- Biophysical techniques to enable rapid state dependent ion channel screening
- Novel tissue targeting strategies

- *De novo in silico* approaches without wet lab experimental validation
- Compound libraries with a limited track record of finding hits

## Innovative Partnering Models

Pfizer has established a number of novel approaches to work with partners in developing new medicines. Moving beyond traditional collaborations and licensing deals, here are a few examples:

## Academic & Start-Up Company Partnerships

Pfizer currently supports numerous collaborative partnerships with researchers at activities with worldclass research institutions such as the University of California, Yale, Penn, the University of Virginia, and Peking University among many others, and is seeking additional opportunities to collaborate in areas of strategic interest to WRD. We are committed to exploratory research and have empowered our External R&D Innovation team to seek opportunities to identify seed-stage investment opportunities to support early-stage technologies as they transition from a pure academic environment into new startup companies that align with our core research interests. These investments complement our Pfizer Venture Investments activities.

## Academic & Start-Up Partnerships Contacts: North & South America, Europe, India:

Ron Newbold (Ron.Newbold@pfizer.com)

Asia/Pacific: Yuan-Hua Ding

(Yuan-Hua.Ding@pfizer.com)



## **Alternative Development / Funding Models**

Pfizer WRD is actively exploring risk and cost sharing approaches to develop WRD as well as external partner programs to enable promising therapies to reach patients. Approaches include partnering WRD assets with pre-defined buy back rights, leveraging non-dilutive funding, and establishing strategic disease area alliances with biopharmaceutical companies and private equity / venture capital groups. Partnerships across the full range of WRD disease areas of interest, which are described in this brochure, will be considered with a focus on clinical stage programs in particular.

## Alternative Development / Funding Models Contact:

Girish Aakalu (Girish.N.Aakalu@pfizer.com)

### **Centers for Therapeutic Innovation**

The Centers for Therapeutic Innovation (CTI) labs were created to establish real-time research partnerships with select academic medical centers. CTI academic research partners work side-by-side with Pfizer scientists in the discovery and development of new therapies for unmet medical needs. Pfizer has opened new CTI labs in San Francisco, New York, Boston and San Diego. These state-of-the-art laboratories are populated with Pfizer scientists and post-docs exploring opportunities to advance novel antibody therapeutics through preclinical development and first-in-human proof of mechanism studies.

Pfizer's Centers for Therapeutic Innovation demonstrates the company's deep commitment to establishing close partnerships with leading academic medical centers to translate ground breaking research into important, new therapies that address key unmet medical needs.

## **CTI Contact:**

Tony Coyle (Anthony.Coyle@pfizer.com)

### **Pfizer Venture Investments**

Pfizer Venture Investments (PVI), the venture capital arm of Pfizer, invests in private companies in traditional venture capital syndicates. PVI also uses equity to support novel business structures such as consortium-based technology development (e.g., Ablexis), product out-licensing (e.g., Clovis Oncology) and business spinouts (e.g., Ziarco). Further, PVI invests in funds that offer geographic reach to provide a view into the development of healthcare and life sciences businesses in developing countries such as Africa, Brazil and China. PVI has an interest in working with others to explore new business models that can create value for all players in the healthcare/lifesciences ecosystem and ensure the continued development of therapeutics, technologies and services for all those whose medical needs are not being met.

Please visit www.pfizerventureinvestments.com

## **PVI Contact:**

Barbara Dalton (Barbara.Dalton@pfizer.com)

#### **ERDI Global Scouting**

The Global Scouting team is composed of skilled scientists with pharmaceutical and biotechnology research experience, all working to support Pfizer's global research interests by scouting for collaborative relationships with both academic and biopharmaceutical partners. These scientists are deployed globally to ensure Pfizer is an active participant in regional scientific discussions and help us work closely with our partners once relationships are established. By working with our 100+ Pfizer country organizations, we have built a strong international scouting network capable of connecting our R&D scientists to innovative opportunities around the world.

This team also directs the investment of a seed fund available to support collaborations with start-up companies founded by experienced entrepreneurs pursuing the commercialization of inventions that benefit patients and which closely align with Pfizer's research interests and portfolio.

#### **Contacts:**

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## Directory of Contacts WRD External R&D Innovation (ERDI)

## SVP & Chief Scientific Officer, ERDI

## **Therapeutic Areas**

Cardiovascular & Metabolic Diseases

Immunoscience Inflammation & Remodeling Neuroscience Oncology Pain & Sensory Disorders Rare Diseases

Vaccines

## Biotechnology Units & Scientific WRD Platforms

Biologics Product & Process Development Biotherapeutics Discovery Drug Safety Drug Delivery Devices Epigenetics Pharmacokinetics, Dynamics & Metabolism (PDM) Precision Medicine Regenerative Medicine Rinat Small Molecule Product & Process Development Small Molecule Therapeutic Discovery

## **Innovative Partnering Models**

Academic & Start-Up Company Partnerships

Alterative Development/Funding Models Centers for Therapeutic Innovation Global Scouting Uwe Schoenbeck

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## Directory of Contacts WRD Business Development

## SVP, WRD Business Development Therapeutic Areas

Cardiovascular & Metabolic Diseases

Inflammation & Remodeling Neuroscience Oncology

Pain & Sensory Disorders Rare Diseases Vaccines

### **Biotechnology Units & Scientific WRD Platforms**

Biologics Product & Process Development Biotherapeutics Discovery Drug Safety Drug Delivery Devices Epigenetics Pharmacokinetics, Dynamics & Metabolism (PDM) Precision Medicine

Regenerative Medicine Rinat Small Molecule Product & Process Development Small Molecule Therapeutic Discovery

## **Innovative Partnering Models**

Academic & Start-up Company Partnerships Alternative Development/Funding Models Centers for Therapeutic Innovation Global Scouting Pfizer Venture Investments Bob Smith

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