Disease area/Organ toxicity	Specific Areas in Critical Need for Biomarker Development	Biomarker Names	Context of Use	Why Is The Biomarker Useful in Drug Development?
Neurodegenerative Diseases	Alzheimer's Disease (AD)	N/A	i) Selecting patients at risk for AD ii) Monitoring patients receiving AD treatments	Monitoring patients receiving AD treatments to shorten clinical trial treatment period.
	Alzheimer's Disease (AD) and other Dementia	Imaging biomarkers (PET and MRI)	More accurate diagnosis, stratification of patients and surrogate endpoint.	Brain imaging such as PET and MRI can assess changes in brain activity and structure comparing specific areas relevant to dementia.
	Alzheimer's Disease (AD)	Cerebrospinal fluid (CSF) levels of neurogranin peptide; Molecular Neuroimaging of Tau protein.	Prognostic or Efficacy	N/A
	Development of drug-target biomarker and therapies for Huntington disease	Measurement of Huntington biomarkers in CSF	i) As a pharmacodynamic biomarker in early clinical trials to demonstrate target engagement and proof of principle (immediate goal). ii) Additionally it could be used to guide dose-escalation.	i) To make clinical assessment of a drug by demonstrating the presence of agent in target organ and the real likelihood of a clinical effect. ii) Biomarkers are helpful to ascertain biological activity.
	Alzheimer's Disease (AD), Parkinson's Disease (PD)	Neuro-imaging and blood tests for neural insulin resistance and p-tau.	i) Screening patients for prodromal Alzheimer's disease. ii) Using biomarkers as a benchmark for efficacy during clinical trials.	N/A

Neuromuscular Disease	**Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), Facioscapulohumeral muscular dystrophy (FSHD), and Amyotrophic Lateral Sclerosis (ALS)**	**Global function biomarkers**	**i) For the upper extremity 3D reachable workspace outcome measure, a global function marker in patients with upper extremity mobility limitation. ii) For use in efficacy testing of therapeutics targeting to improve upper extremity function.**	**Development of a scalable and sustainable remote measurement platform for upper extremity function will facilitate translational science and promises to be a novel tool for conducting clinical trials by reducing cost and participant burden while improving efficiency through automation.**
	Duchenne Muscular Dystrophy (DMD)	**Dystrophin as a biomarker, qualifying skeletal MRI as a biomarker and qualifying the assessment of upper extremity function based on the concept of 3-dimensional reachable workspace.**	**Dose selection, proof of concept, utilization in study (e.g. patient enrichment, patient stratification), PK/PD, disease progression (e.g. prognostic endpoint), treatment response (e.g. predictive endpoint, composite endpoint, etc.) and as surrogate endpoint.**	**There is an urgent unmet need to develop new treatments for DMD as there are currently no FDA approved therapies for DMD and no way to reverse the underlying condition.**
	Myotonic dystrophy (DM)	**i) Biomarkers for cardiac and central nervous system. ii) Predictive genetic biomarkers. CELF1 protein (upregulated in DM1 tissues, particularly in heart).**	**Biomarkers for patient selection and surrogate endpoints.**	**This RNA biomarker could be analyzed in any target tissue and it has a direct link to the disease process, so it is likely to be useful for determining target engagement of drugs that affect the root causes of the disease, as well as predicting drug effect.**
	Friedreich's Ataxia (FA)	**i) Frataxin protein, mRNA or miRNA biomarkers. ii) Structural and functional imaging of muscle, heart and central nervous system. iii) Secondary symptomatic measurements (e.g. vision,**	**i) Proof of principle in preclinical models and in early stage trials. ii) Demonstration of target engagement. iii) Demonstration of effective dose. iv) Potentially accelerated approval.**	**Selection of cohorts of patients that are likely to progress in a similar manner in the short term so that that cohort can be studied in a clinical trial.**

		gait, speech in FA). **iv) Markers which predict cardiac risk, in the central nervous system that can be used to signal response to treatment or target engagement and for patient selection.**		
Neurological and Neuropsychiatric Diseases	**Alzheimer's disease, Mood Disorders, Epilepsy, Huntington's disease, Alcohol Dependence, Schizophrenia and Parkinson's disease**	**Tau, Neurofilament proteins, alpha-synuclein, calbindin, Neuron-Specific Enolase, S100b, PSD95, drebrin.**	**i) Using Some custom biomarker panels (Imaging , Efficacy, Predictive, Diagnostic) as a link to imaging results and to longer term clinical assessments of disease activity/progression.** **ii) By serving as early signals of efficacy for more rapidly evaluating the impact of potential disease-modifying therapies.**	**Both neurological and neuropsychiatric disorders suffer from a lack of disease-relevant markers that could be used to assess early signals of efficacy in a clinical setting. Other than imaging modalities like MRS, DTI, PET and MRI, there is a definite need to better monitor drug-mediated effects on neurodegeneration, neuroinflammation and cognition including markers for synaptic plasticity and neurogenesis.**
		Neuro-immunology markers	**Diagnosis, stratification and outcome measures.**	**For patient stratification in clinical trials.**
		Tau imaging markers		**AD diagnosis and staging; progression monitoring, PD measurement.**
		Genetic & epigenetic biomarker signatures (AD and Mood disorders)		**Disease risk**
		Screening biomarkers for AD, Mood disorders (blood tests, neurofunctional and behavioral measurements)		**Patient enrichment for clinical trials.**

		Novel strategies to approach outcome measures (different than patient reported outcomes)		**N/A**
		Biomarkers of functional outcome measures		**Objective measures for motor dysfunction.**
		Imaging measures (PET, tMRJ) and physiological (EEG)		**For stratification purposes in CNS disorders in general.**
		Translocator Protein (TSPO) PET ligand	**Patient Selection**	**Neuroinflammatory biomarkers such as the TSPO PET Ligand should thus be considered in the context of experimental medicine to potentially enrich clinical study designs and improve the testing of clinical hypotheses.**
		Utilizing composite biomarker	**Identification of target population based on disease biology and/or drug target for predicting drug efficacy /response.**	**The field acknowledges that given the heterogeneity and complexity of CNS disorders, a single biomarker (e.g.. Gene, SNP, micro RNA, protein or metabolite) will be unlikely to identify a subpopulation and/ or explain predictive efficacy of a drug.**

		Phosphodiesterase(PDE)-10A PET ligand	**Diagnostic, Dose selection.**	**The PDE10A PET ligand will serve multiple purposes. Firstly it will confirm that a given drug enters the CNS, reaches and binds to the PDE10A enzyme. Furthermore, the PET ligand will enable the establishment of plasma exposure of a drug to target occupancy. This will be critical in determining the therapeutic dose range.**
	Alzheimer's Disease biomarker to identify subjects "at risk", which would help in patient stratification.	**N/A**	**Treatment Response.**	**N/A**
	Multiple Sclerosis	**N/A**		**N/A**
Oncology	**i) Cardio-vascular system, liver, kidney for safety(toxicity) biomarkers. ii) Efficacy biomarkers based on genomics are largely studied in oncology.**	**i) Patient stratification biomarkers ii) Drug efficacy and safety biomarkers**	**i) Proof of concept (POC) using pharmacodynamic biomarkers ii) Patient stratification in enrollment using drug efficacy (also subset of pharmacodynamic and safety biomarkers) iii) Monitoring clinical safety using safety biomarkers.**	**N/A**
	Cancer - all types, importantly NSCLC (Non-small-cell lung carcinoma).	**N/A**	**N/A**	**They will improve the efficiency of clinical decision making and potentially reduce overall health system cost, while improving outcomes if patients are directed to more effective treatments.**

	Pancreatic cancer	**CCK-B receptor SNP; rs1800843. The resulting splice isoform is termed as CCK-C receptor.**	**Screening for pancreatic cancer risk in patients with family history or chronic pancreatitis.**	**This biomarker is the only SNP found at a very high frequency (35-40%) in pancreatic cancer. In addition, further development of this biomarker may lead to the ability to select targeted therapies that regulate the pathways constitutively activated by CCK-C.**
	Pancreatic cancer	**HER2-amplified cancers, BrCa2; Mutant pancreatic cancer; A change in the levels of the CA-19-9 serum protein biomarker; Enumeration of circulating tumor cells; Levels of circulating tumor DNA.**	**i) As a predictive biomarker to determine if a targeted-treatment is efficacious enough for accelerated approval in pancreatic cancer patients whose tumor contains that biomarker. ii) A blood-based biomarker representing a surrogate endpoint for survival in pancreatic cancer clinical trials for accelerated approval of a therapeutic.**	**The use of biomarkers can aid in understanding the prediction, cause, diagnosis, progression, regression, or outcome of treatment of disease.**
	N/A	**i) Archived and fresh tumor biopsy assessment for classical tumor morphology ii) Blood or plasma monitoring. iii) Non-invasive surrogate biomarkers iv) Tumor infiltrating T-cell (CD3+CD8+ cytotoxic T cells and CD45RO+ memory T cells) quantification**	**i) Tumor staging immune-score classification surrogate endpoint to predict treatment outcome. ii) Immuno-oncology contextual assessment immune scoring: Tumor infiltrating T-cell (CD3+CD8+ cytotoxic T cells and CD45RO+ memory T cells) quantification.**	**Acceptance of a biomarker can be expedited with the generation of high quality clinical data. Surrogate endpoint measurements for the assessment of therapeutic efficacy can potentially offer greater flexibility for drug approval mechanisms and patient access to promising therapies.**

	N/A	**Circulating tumor cells (CTCs) and cell-free DNA (cfDNA)**	**i) Patient-selection biomarkers that help guide the use of immuno-oncology drugs.** **ii) Use of MRD data as surrogate biomarkers in some cancers to accelerate drug development.**	**Recent progress in analyzing circulating tumor cells (CTCs) and cell-free DNA (cfDNA) indicate these blood-based methods may significantly help to inform decision making in oncology, particularly in the solid tumor setting where access to tumor-derived material has traditionally been very difficult. They will also help speed the application of these promising drugs across all cancers and facilitate the testing of rational combinations of immuno-oncology drugs together and with other active therapies.**
	N/A	**Imaging biomarkers for chemotherapy response in cancer (FDG-PET/CT)**	**Utilization of FDG-PET as an endpoint and drug development tool.**	**FDG-PET treatment related response differences across trial is likely to predict the magnitude of the treatment effects seen in primary clinical outcome measures.**
	Solid Tumors.	**i) Minimal Residual Disease (MRD) as surrogate endpoint** **ii) Predictive biomarker**	**i) A surrogate marker such as Minimal Residual Disease could shorten the timelines for clinical trials.** **ii) The ability to follow the disease course and modify therapies to improve outcome based on predictors of early response to treatment, early detection of relapse/disease progression and identifying mechanisms of resistance.**	**RECIST criteria have been useful but are outdated. Therefore, there is an immediate need for sensitive markers for rapid effect of therapies on tumors that are not related to 2D variable measures.**
	NSCLC (Non-small-cell lung carcinoma)	**N/A**	**N/A**	**N/A**

	N/A	Cell-Free DNA	N/A	N/A
	N/A	Pharmacokinetic/ Pharmacodynamic biomarkers	N/A	N/A
	N/A	N/A	N/A	i) Biomarkers could be used to determine better dosing without having to go to MTD. ii) Biomarkers could be used to better understand the kinetics/ effectiveness of a drug.
Autoimmune and Inflammatory Diseases	Systemic Lupus Erythematosus (SLE)	SLE markers of disease activity and prediction of flare: C4d, C1q, CD27, IFN-a, other complement and IFN associated proteins , SNP and autoantibody (ANA, dsDNA, NMDA) panels	i) To improve the efficacy and decrease the adverse effects of immunosuppression. ii) Predict clinical manifestation, disease progression rates and pathogenic mechanisms of Lupus and Lupus nephritis and adjust therapy appropriately.	Need for biomarkers that forecast Lupus Nephritis flare well before thresholds of proteinuria, decreased renal function and urine sediment. Such a predictive biomarker could be followed serially and based on levels; treatment could be initiated before development of significant inflammatory in jnury in the kidney.
	Lupus Nephritis	Biomarkers predictive of renal flare, development of chronic kidney disease or reflect kidney histology at the time of flare: MCP-1, NGAL, Transferrin, FOXP3, CXCL10, MEPCR		
	Rheumatoid Arthritis (RA)	Biomarkers for vascular inflammation and CV risk in RA patients. FDG-PET/CT as a novel imaging biomarker to detect baseline and DMARD-associated changes in vascular inflammation of RA patients	i) Stratification od RA patients with elevated risk of CV co-morbities in standard of care. ii) Addition of an anti-inflammatory biologic.	The lack of an RA specific CV risk toll hampers evidence based guidelines and creates uncertainty for patients and providers in managing RA and its comorbidities.

	Rheumatoid Arthritis (RA)	**Highly sensitive MRI imaging of joints using the RA-MRI scoring system (RAMRIS)**	**RAMRIS s a surrogate to be used in place of bone erosion and joint space narrowing in registration clinical interventional trials in rheumatoid arthritis patients.**	**Because of the higher sensitivity and more detailed and quantitative nature of MRI imaging compared to clinical examination and basic X-ray films, RA clinical trials of shorter duration can be conducted using lower numbers of patients to assess the efficacy of experimental compounds.**
	Crohn's disease, Ulcerative colitis (UC)	**Anti-TNF, antibodies to anti-TNF and circulating anti-TNF**	**Diagnostic, Predictive, Imaging, Efficacy**	**A subset of patients does not respond to anti-TNF-a therapies from the onset of treatment or develop resistance to treatment over time. Biomarkers that can predict which patients will be resistant to anti-TNF treatment would assist in the development of novel therapies for this subpopulation.**
	Ankylosing Spondylitis (AS)	**Cox 1, RANKL; BMP-2, OPG, PINP, Sclerostin, DKK1**	**Prediction of AS patients with chronic low back pain at risk for radiographic progression to AS or increased progression with AS.**	**Little to no biomarkers for AS for disease diagnosis, activity/severity or therapeutic response.**
	Acute Immunotoxicity	**N/A**	**N/A**	**The major benefit would come if a biomarker specific for inflammation could be found, better than C-Reactive Protein (CRP) and if it could indicate tissue of origin.**
	Imaging Biomarkers	**Fluorodeoxyglucose (FDG), labeled with a positron emitting fluorine-18 [F-18]FDG ([F-18]FDG-PET/CT)**	**[F-18]FDG-PET/CT detection of inflammation-associated metabolic activity**	**[F-18]FDG-PET/CT can be used to detect lung parenchymal involvement at any chest X-ray stage, including therapy-resistant disease, and also provides information on extra-pulmonary disease.**

Hepatic Diseases	**Liver pathology: Non-Alcoholic Steatohepatitis (NASH), Non-Alcoholic Fatty Liver Disease (NAFLD), Primary Biliary Cirrhosis (PBC), Primary Sclerosing Cholangitis (PSC), Viral Hepatitis B (VHB) and C (VHC), Hepatocellular Carcinoma (HCC), Alcoholic Liver Disease (ALD) and Autoimmune hepatitis**	**Movel MRI imaging device that measures fibrosis/ inflammation in milliseconds and measures iron levels (in mg/g) and fat fraction (in %)**	**i) To measure the efficacy of new treatments for liver disease. ii) For drug development in clincial trials. iii) As a tool to aid clinicians in the assessment of patients with suspected liver disease to diagnose and to detect changes over time.**	**With the increasing prevalence of liver disease worldwide, there is an urgent clinical need for reliable methods to diagnose and stage liver pathology. Liver biopsy, the current gold standard, has severe limitations, i.e. invasiveness, complications (including death in 1:1000), discomfort, and substantial sampling-dependent and observer-dependent variability.**
	Fibrosis (Liver): NASH, PSC, PBC	**ALT, AST, AP for PSC; TIMP-1, Osteopontin, Collagen-1, Collagen fragments, MMPs, CK-18, CCL-2, FaL, NAFIC score, fibrosure, ELF test**	**N/A**	**N/A**
	N/A	**Plasma/serum miR-122, glutamate dehydrogenase (GLDH), arginase (ARG-1), sorbitol dehydrogenase (SDH) and glutathione S-transferase (GST-α)**	**N/A**	**N/A**
	Non Alcoholic Fatty Liver Disease (NAFLD)	**Liver cT1 and cT2**	**Biomarkers to determine Non Alcoholic Fatty Liver (NAFL) Activity Score (NAS) without performing histology.**	**It is a magnetic resonance imaging procedure; therefore non-invasive.**

	Anti-fibrotic activity	**Hepatic Venous Pressure Gradient (HVPG).**	**Hepatic Venous Pressure Gradient (HVPG) as a surrogate to measure anti-fibrotic activity.**	**Hepatic Venous Pressure Gradient (HVPG) should be qualified by FDA for use as a surrogate replacing liver transplant and death for measuring anti-fibrotic activity in patients with compensated cirrhosis in registration interventional clinical trials.**
	Safety biomarkers for Acute Hepatotoxicity (Non-clinical and Clinical)	**miRNA-122**	**i) Demonstration of organ toxicity. ii) Safety in dose escalation. iii) drug-induced liver injury, two context of use have been proposed by the IMI SAFE-T consortium.**	**A new biomarker that could discriminate between drug-induced liver injury at risk of progressing and drug-related adaptive processes.**
	Safety biomarkers for Chronic Hepatotoxicity (Non-clinical and Clinical)	**miRNA-123, Fibrosis marker and CK-18**	**Demonstration of organ toxicity without histopathology.**	**Biomarkers predicting chronic hepatotoxicity would translate to tremendous cost savings and lower risk for drug development but may benefit fewer programs than acute markers.**
Musculoskeletal Diseases	**Osteoarthritis (OA)**	**Urinary CTX-II and Urinary alpha-CTX-I), Serum C1M, C3M and CRPM**	**i) Identification of the right patient phenotype. ii) Early detection of efficacy. iii) Early decision making, prediction of responders.**	**N/A**
		Using MRI for direct visualization of joint structures including the cartilage, subchondral bone, menisci, synovial fluid and other tissues.	**Assessment of osteoarthritic knee joint structures by MRI.**	**MRI can allow for a sensitive and reliable joint marker, superior to that of radiography, of global joint structural changes along the cross-section and longitudinally.**

		Biomarkers that can enrich OA trials for progressors and biomarkers that could serve as more sensitive efficacy of intervention markers than the current joint space loss of plain radiographs.	**Burden of Disease, investigational, prognostic, efficacy of intervention, diagnostic and safety biomarkers.**	**Enrichment of trials for progressors can increase trial power and decrease trial costs due to requirement for lower subject number and shorter trial duration required to show a treatment effect.**
		Assessment of osteoarthritis joint structural changes by MRI with the change in cartilage volume used as a primary outcome.	**DMOAD RCTs in knee, hip, and hand osteoarthritis**	**Magnetic resonance imaging (MRI) to assess osteoarthritis joint structural changes and response to treatment of disease-modifying osteoarthritis drugs (DMOADs) in randomized controlled trials (RCTs).**
		Quantitative MRI cartilage morphometry, cartilage defects and bone marrow lesions; semi-quantitative analysis of bone shape and attrition and subchondral bone area; Bone trabecular integrity by facial signature analysis. **Serum and urine measures of bone and cartilage: Serum HA, PIIAMP, CTX-1, C2C, CI,2C, NTX-1, COMP, Urine CTX-1 & II, C2C, Coi21N02**	**To establish the predictive validity and responsiveness of disease progression biomarkers and assess the responsiveness of several imaging and biochemical markers pertinent to knee OA.**	**Assist in planning and design of clinical trials focused on facilitating scientific discovery and establishing efficacy of future disease-modifying regimens for knee OA.**
	Osteoporosis	**i) Bone quality biomarkers** **ii) Imaging biomarkers (with sufficient resolution to capture microstructure)**	**To be used for osteoporesis patient management and as a substitute for failure endpoints in randomized clinical trials.**	**These biomarkers may provide precise estimates of the relationship between treatment-related changes in imaging and fracture outcomes.**

Pulmonary Diseases	**Cystic Fibrosis**	**i) Sweat chloride and chloride conductance to determine CFTR activity ii) Serum, plasma and sputum, which might determine degree of inflammation iii) Nasal and intestinal epithelial cell**	**i) Qualification of CF biomarkers as surrogate endpoints. ii) Identification of biomarkers for use in targeting approved disease-modifying drugs to patients with rare mutations in whom these drugs are not yet indicated.**	**The CF research community faces a serious challenge in designing and executing trials of drugs for CF patients with especially rare mutations even though these agents are likely to be efficacious.**
	Fibrosis	**High resolution CT (HRCT)-based biomarkers**	**To provide quantitative assessment of therapeutic interventions based on structural changes in lung geometry as well as on functional changes in regional airway volumes and airway resistance.**	**N/A**
	Chronic Obstructive Pulmonary Disease (COPD)	**Biomarkers of recovered lung function or decline and prediction of risk for COPD or flare (exacerbation)**	**Genomic and proteomic biosignature(s) that predict accelerated lung function decline in COPD patients and provide a surrogate marker of FEV1.**	**No biomarker exists for pathogenesis of COPD that associated with a clinically important outcome or are known to be modified by an effective intervention to change the target outcome.**
	Chronic Obstructive Pulmonary Disease (COPD)	**N/A**	**A prognostic biomarker that predicts disease progression and exacerbation frequency that is responding to treatment options would decrease tremendously development timelines, and development costs.**	**N/A**
Renal Diseases	**Nephrotoxicity**	**Urinary osteopontin (OPN), Clusterin (CLU), Cystatin C (CysC), Kidney injury molecule-1 (KIM-1), N-Acetyl-beta-D-**	**N/A**	**N/A**

		glucosaminidase (NAG), Neutrophil gelatinase-associated lipocalin (NGAL), Total protein and Albumin		
	Autosomal Dominant Polycystic Kidney Disease (ADPKD)	N/A	Total Kidney Volume as an efficacy biomarker for ADPKD	N/A
	Acute Nephrotoxicity (Non-clinical and Clinical)	NGAL, Kim-1	Acute Kidney Injury (AKI) biomarkers at early stage and reversible stages of injury.	To demonstrate the Lowest observed adverse effect level (LOAEL) and organ toxicity. New candidate biomarkers with renal safety signals in animal toxicology studies that cannot be monitored using conventional biomarkers will be immensely important.
	Chronic Nephrotoxicity (Non-clinical and Clinical)	GFR, Kim-1	Novel biomarkers to detect GFR (other than creatinine clearance).	
Cardiovascular Diseases	Therapies in acute and chronic heart failure with reduced or preserved ejection fraction.	Natriuretic peptides (e.g. NT-proBNP, b-type natriuretic peptide [BNP]), ST2, and Cystatin C	Phase II studies should include biomarkers as primary endpoints to aid in assessing the efficacy and dose selection of potential heart failure therapies.	i) Applications for heart failure. ii) Applications for Acute Coronary Syndrome. iii) As an outcome measure in clinical trials of therapeutic efficacy. iv) Drug-induced cardiotoxicity.
	Heart Failure	i) Imaging biomarkers ii) A blood/urine based panel of biomarkers representing cardiac functionality, cardiac damage, fibrosis in various organ systems, renal function and fluid overload.	Cardiac MRI images as biomarkers to provide multi-parametric quantitative regional and global metrics of cardiac tissue abnormalities.	Using cardiac MRI, measurement of edema volume (using T2 mapping), fibrosis (utilizing late gadolinium enhancing volume for focal lesions and extracellular volume form T1 mapping pre and post–contrast), tissue phase mapping and wall motion would be possible.
	Safety Biomarkers for Acute Cardiotoxicity (Non-clinical and Clinical)	i) Cardiac Troponin-I (cTnI) ii) Fatty-acid-binding proteins (FABP)	i) Demonstration of organ toxicity without histopathology ii) Demonstration of organ	Acute clinical cardiotoxicity biomarkers are immensely important to developing new drugs in the clinical safety

		iii) QT interval	toxicity iii) No observable adverse effect level (NOAEL) iv) Biomarker relating to major adverse cardiac events (MACE) endpoints	arena.
	Safety Biomarkers for Chronic Cardiotoxicity (Non-clinical and Clinical)	i) N-terminal fragment of proatrial natriuretic peptide (NT-proANP) and brain natriuretic peptide (BNP) ii) hs-Troponin I iii) Ejection fraction		i) Biomarkers distinguishing reversible from irreversible "injury" with strong pathophysiologic evidence and clinical event correlates. ii) Biomarkers that qualitatively and quantitatively, can predict and accurately identify and confirm when a change in an acute clinical cardio toxicity biomarker will result in chronic clinical cardiotoxicity.
Protein Misfolding Diseases	Amyloid Light-chain (AL) amyloidosis	N-terminal pro b-type natriuretic peptide(NT-proBNP), proteinuria	Endpoint for accelerated approval pathway in AL amyloidosis.	i) Great predictor of survival in AL amyloidosis. ii) Great predictor of delaying or stopping patients from progressing to dialysis.
		NT-proBNP	As a surrogate endpoint for accelerated approval in AL amyloidosis with cardiac involvement.	The biomarker has an extremely strong correlation with survival in many studies. As a surrogate endpoint, it could reduce time to develop new treatments through clinical development.

	Protein amyloid diseases, specifically, transthyretin amyloidosis with polyneuropathy and/or cardiomyopathy phenotypes.	**Non-native Transthyretin (NNTTR)**	**i) Identification of patients who can benefit from the TTR amyloid disease modifying drugs.** **ii) Efficacy biomarker which provides mechanistic link bridging the currently used pharmacodynamics biomarker.** **iii) In dose-setting studies to optimize efficacious dose.** **iv) A surrogate biomarker reasonably likely to predict clinical outcome.**	**The change in NNTTR levels is quantitative and can be measured within a few months after drug treatment. Qualifying it as a surrogate biomarker has the potential to significantly shorten the required time of a clinical trial, drastically reducing the cost of drug development, expediting drug availability to patients.**
	ATTR (Transthyretin) amyloidosis and AL amyloidosis; including disease-related dysfunction of the heart, kidneys and liver.	**i) NT-proBNP** **ii) Urinary albumin** **iii) Modified Neuropathy Impairment Score +7 and Norfolk Quality of Life-Diabetic Neuropathy in patients with ATTR-FAP**	**In the context of a pivotal study for approval, the use of a validated biomarker as a surrogate endpoint for accelerated approval (for cardiac and renal involvement).**	**Biomarkers should be used for diagnosis and staging, as well as for assessing the response to therapy. There remains a significant need to utilize expedient surrogate endpoints based on biomarkers in order to provide therapeutics to patients, within a reasonable timeframe, in rare fatal diseases.**
Metabolic Diseases	**Diabetes (Type 1)**	**i) islet autoantibodies** **ii) Diagnostic biomarkers** **iii) Prognostic biomarkers** **iv) Predictive biomarkers** **v) Pharmacodynamic biomarkers**	**i) To distinguish between type 1 and type 2 diabetes.** **ii) To stratify patients based on risk for developing symptomatic type 1 diabetes and/or rate of progression of the disease.** **iii) For identifying subgroups of patients likely to respond to a therapy.** **iv) For more efficient clinical trials and identification of efficacious therapies.**	**The lifetime risk of developing symptomatic type 1 diabetes approaches 100% once two or more islet autoantibodies are detected in genetically at-risk children. The detection of two or more islet autoantibodies increases the rate of progression to symptomatic type 1 diabetes. The number of detectable islet autoantibodies correlates with risk.**

	Diabetes	**Beta cell function measures**	**Benefit for tracking drug effect on disease progression.**	**N/A**
	Diabetic Nephropathy (DN)	**Monocyte Chemoattractant Protein-1 (MCP-1), Urine albumin-to-creatinine ratio (UACR), KIM-1**	**MCP-1 measurement in the urine could be a promising biomarker to establish the effect of a compound on kidney inflammation. The later is also associated with a higher risk for end stage renal disease (ESRD) and chronic kidney disease (CKD3) stage.**	**KIM-1 is a sensitive and specific biomarker for proximal tubular injury which could be helpful to predict the outcome of clinical trials with respect to regression or progression of the disease.**
Infectious Disease	**Vaccines against Pneumococcal disease**	**N/A**	**Testing the efficacy of PCV vaccines against invasive pneumococcal disease (IPD)**	**N/A**
	Acute Bacterial Skin and Skin Structure Infections (ABSSSI), Community-Acquired Bacterial Pneumonia (CABP), Hospital-Acquired Bacterial Pneumonia (HABP) and Ventilator Associated Bacterial Pneumonia (VABP).	**N/A**	**Development of Patient Reported Outcomes Instruments to assess how a patient feels, functions and survives for ABSSSI, CABP, HABP and VABP.**	**N/A**

Pancreatic Diseases	**Safety biomarkers for Acute Pancreatic Toxicity (Non-clinical and Clinical)**	**Acute pancreatic toxicity is not commonly encountered in drug development and to date, no specific biomarker has been identified that could be considered for qualification.**	**i) Demonstration of absence of toxicity.** **ii) Demonstration of organ toxicity without histopathology. The benefit of new qualified biomarkers of pancreatic toxicity should demonstrate correlations with the gold standard and are therefore appropriate to monitor for the effect with the ultimate goal of using them to demonstrate the lack of effect in humans.**	**N/A**
	Safety biomarkers for Chronic Pancreatic Toxicity (Non-clinical and Clinical)	**N/A**	**N/A**	**N/A**
Traumatic Brain Injury (TBI)	**N/A**	**i) Glial fibrillary acidic protein (GFAP) and its breakdown products),** **ii) Ubiquitin C-terminal hydrolase- L1** **iii) Tau (p-tau), S100b** **iv) aII- Spectrin Breakdown Products (SBDP 150, SBDP 145, SBDP120, SNTF)** **v) Myelin Basic Protein (MBP).** **vi) Neoron Specific Enolase (NSE)** **viii) Neurofilament protein-light chain (NF-L), neurofilament protein heavy chain (NF-H) (including phospho-neurofikament H)**	**i) Use of TBI protein biomarker as a patient stratification tool to select for TBI patients who are most likely to respond to a specific therapeutic treatment in a clinical trial setting.** **ii) Use of TBI protein biomarker as a response-indicator biomarker.** **iii) Use of a TBI protein biomarker to track efficacy of TBI therapies.**	**There is a critical need for simple, bio fluid-based biomarkers capable of measuring injury severity and injury mechanism and selecting patients for trials of targeted therapeutic drug development.**

		Pathoanatomic lesions on brain magnetic resonance imaging (MRI).	**Use of pathoanatomic lesions on brain MRI as a diagnostic tool to evaluate patients with mTBI and to measures clinical outcome in patients with mTBI.**	**Brain MRI is a non-invasive technology widely available and has great sensitivity. Therefore, as a new biomarker, it can be quickly operationalized into practice for drug development trials.**
Miscellaneous	**Rare diseases**	**N/A**	**N/A**	**N/A**
	Immuno-oncology, Pain medications, Neuroscience/Psychiatric medications, Nutrigenomics /Nutritional medicine.	**N/A**	**N/A**	**Increased drug safety application- certain genotypes may need to avoid specific medicines/alter doses. Also there may be increased efficacy for certain drugs in specific populations based on biomarkers, certain drugs could be marketed to precise populations.**
	Drug use and biomarker interaction effect on current drug efficacy and effectiveness.	**BRAF (v-Raf murine sarcoma viral oncogene homolog B)**	**N/A**	**N/A**
	Oncology, Non-alcoholic Steatohepatitis (NASH) and progression to cirrhosis and hepatocellular carcinoma, Chronic Kidney Disease (CKD), Toxicity (pulmonary, cognitive, auditive, renal, hepatic, gastro-intestinal, cardiac toxicity).	**N/A**	**N/A**	**i) Early detection of patient safety risks ii) Identification of patients at high risk of disease progression iii) Replacement of invasive assessments with non-invasive methods**

	Fall Detection	**N/A**	**Fall reduction as a FDA-qualified surrogate for the traditional six minute walk.**	**N/A**

N/A : not available