2022 IIS Strategic Priorities

Contents

Body Contouring: Coolsculpting, CoolTone

CoolSculpting

1. To assess the impact of different treatment regimens using CoolSculpting® alone or in sequence with other treatment modalities.
2. To understand factors that optimise patient selection, treatment and management.
3. To explore novel indications for cryolipolysis.

CoolTone

1. To assess the impact of different treatment regimens using CoolTone alone or in sequence with other treatment modalities.
2. To further elucidate the mechanism of action for electromagnetic stimulation.
3. To enhance understanding of comprehensive patient outcomes following treatment.

Things to consider for the investigator:
Limited funds may be available to support proposals

Facial Aesthetics: Botox/Vistabel, Fillers (Juvederm, Vycross, Hylacross, HArmonyCa), Kybella/Belkyra

Botox/Vistabel Priorities:

1. Impact of adherence to a long-term treatment plan
2. Impact of labelled dose and regular repeat dosing on PROs/OROs
3. Innovative clinical, PRO/ORO measures and predictive models of treatment effect/outcomes
4. Outcomes in diverse and generational populations
5. Novel aesthetic uses

Filler Priorities:

1. Correlation of rheologic/physiochemical properties with clinical benefit/impact to patient
2. Correlation of volume/treatment planning with PRO/OROs
3. HArmonyCa data generation/demonstration of clinical benefit and impact on PROs/OROs; demonstration of the impact of treatment on skin architecture
4. Data supporting longer term efficacy/safety of products than demonstrated in development trials
5. Development/use of novel objective measures of clinical outcomes/use of sophisticated objective measures beyond photonumeric scales (e.g. video, 3d imaging, volumetric analysis, etc.)
6. Use of Aesthetics portfolio in diverse populations (skin type, ethnicity, age, congenital/acquired deformity, gender realignment, etc.)
7. Real world evidence using the Allergan Aesthetics range of fillers
8. Use of product portfolio to establish facial harmony/balance
9. Novel aesthetic uses

Kybella/Belkyra Priorities:

1. Novel aesthetic uses in the face and body

Pan Facial Priorities:

1. Use of Allergan Aesthetics portfolio as part of a sequential treatment plan, demonstrating the psychosocial impact and impact on investigator/patient/observer reported outcomes
2. Impact of adherence to a non-surgical facial aesthetic treatment plan – short-term and long-term outcomes
3. Innovative solutions to measure, predict and optimize outcomes
4. Innovation which improves upon the ability to deliver safe outcomes for patients
5. Impact of Allergan Aesthetics portfolio on overall skin health

Things to consider for the investigator:

Limited funds may be available to support proposals

Plastics and Regenerative Medicine: Breast Implants, ADMs, Fat Grafting

Breast Implant Portfolio:

Enhancing scientific knowledge to improve clinical outcomes:

- Immediate & long-term patient outcomes with Natrelle Inspira smooth implants and tissue expanders
- Systemic symptoms reported by patients with breast implants (SSBI/BII): etiology, pathogenesis, epidemiology and management
- BIA-ALCL: mitigation, etiology, pathogenesis, epidemiology and treatments
- Supporting best practice techniques:
- Infection control techniques to improve patient outcomes (e.g. Keller funnel, aseptic technique)
- Keller funnel clinical outcomes measures
- Patient/implant matching for optimal outcomes (cohesivity matching)
- Global best practice surgical techniques to optimize outcomes with Allergan Aesthetics Breast Implant portfolio
- Using Allergan Aesthetics breast surgical products to address clinical needs and optimize patient outcomes

Regenerative Medicine Portfolio:

ADM Portfolio (Artia, AlloDerm and Strattice)

- Scientifically differentiate integration and encapsulation of ADM using histology and/or outcomes measures
- Patient outcomes using Allergan Aesthetic ADMs for the benefit of patients requiring soft tissue reinforcement or repair
- Global best practice technical considerations to maximize patient outcomes

Fat grafting benefits

- Advance the understanding of patient outcomes using Revolve/Envi including patient/surgeon satisfaction, durability and graft retention

Things to consider for the investigator:

Limited funds may be available to support proposals

CNS – Migraine: OnabotulinumtoxinA/BoNTA from AbbVie (Botox), Ubrogepant (Ubrelvy), Atogepant (Qulipta)

AbbVie is dedicated to enabling all people with migraine disease, which affects one in seven people worldwide, to achieve migraine freedom so they can live their best lives. We are committed to pursuing and providing treatment options that stop or reverse migraine attacks (acute treatments), as well as those that reduce the frequency and severity of migraine attacks (preventive treatments).

The Migraine therapeutic area is comprised of three assets:

- OnabotulinumtoxinA (Botox) approved for the preventive treatment of headaches in those with Chronic Migraine
- Ubrogepant (Ubrelvy) approved for the acute treatment of Migraine with or without aura for adults in the US only
- Atogepant (Qulipta) approved for preventive treatment of episodic migraine in adults in the US only

Things to consider:

- Studies will only be considered for compounds that have received regulatory approval for at least one indication in the country of interest.
- Limited funds may be available to support proposals

Proposals for the topics listed below will <u>NOT be considered</u>:

- OnabotulinumtoxinA vs Placebo, vs other toxins, vs mAbs (monoclonal antibodies)
- Ubrogepant vs Placebo, vs other acute treatments for migraine
- Atogepant vs Placebo, vs other preventive treatments for migraine
- Pediatric Studies
- Placebo controlled studies for ubrogepant consistency of effect, early treatment or treatment when pain is mild, treatment during premonitory/prodrome phase

Priority will be given to proposals investigating the following areas:

<u>Migraine Disease State</u>

- Characterize and describe disease state across the migraine spectrum, regardless of treatment administered.
- Impact of disease across the migraine spectrum
- Impact of disease management (of AbbVie and non-AbbVie products) on disease state
- Impact of COVID, COVID vaccines and COVID-related treatments on disease outcomes in patients treated with OnabotulinumtoxinA, Ubrogepant and/or Atogepant

<u>OnabotulinumtoxinA/BoNTA from Abbvie (Botox) - Chronic Migraine</u>

- Effect on migraine co-morbidities (e.g., neck pain, depression, anxiety, etc.) in chronic migraine patients

- Preclinical/clinical data on MoA in migraine and synergistic effects in combination treatment with anti-GCRP mAbs/gepants
- Effect on QoL and/or return to daily activities
- Impact on health care resource utilization
- Post-traumatic Headache (PTH) or primary headache (HA)
- Long-term data in CM
- Switching from mAbs to OnabotulinumtoxinA
- Combination treatment of adding anti-CGRP mAbs/gepants to a chronic migraine patient

Ubrogepant (Ubrelvy) - Acute Treatment of Migraine

- Real world data on Ubrogepant + other gepants
- Ubrogepant + other acute treatments for migraine
- Ubrogepant + CGRP preventive treatments for migraine
- Ubrogepant + OnabotulinumtoxinA treatment
- Safety and efficacy of Ubrogepant for acute treatment of migraine attacks
- Impact of Ubrogepant management on disease state

Atogepant (Qulipta) - Migraine Prevention

- Atogepant + Ubrogepant
- Atogepant + OnabotulinumtoxinA
- Atogepant + non-CGRP treatments
- Switching from other CGRP treatments to Atogepant
- Long term, real world safety and effectiveness of Atogepant for preventive treatment of migraine
- Effect on QoL, work productivity and/or return to daily activities
- Impact on co-morbidities
- Impact on health care resource utilization
- Impact of Atogepant management on disease state

CNS – Neurotoxin Therapeutics – Botox (OnabotulinumtoxinA): Toxin Science, Spasticity and Movement Disorder, Urology

For the purposes of this document the IIS Strategic Priorities will be described for these indications:

- Toxin Science and New Indications
- Spasticity and Movement Disorders (SMD)
- Urology

For other Neurotoxin Therapeutics and for Botox Cosmetics indications, please refer to the applicable sections.

Things to consider:
Limited funds may be available to support proposals

Toxin Science and Novel Indications

Priorities

- Real world evidence of clinical and health economic outcomes of Botox utilization vs other toxins, including the consequences of non-medical toxin switching.
- Botox utilization studies in multi-indication patients
- Novel Botox applications beyond current labelled indications
- Data generation in following areas
    - Non-classical mechanism of action (non-striated muscle)
    - Pain, sensory, anti-inflammatory mechanisms of action
    - Studies on topics related to clinical practice
    - Preclinical studies assessing Botox vs other toxin

Spasticity

Priorities

- Botox for treatment of pain associated with spasticity
- Studies assessing the applicability of tools and biomarkers as predictors for early spasticity diagnosis
- Clinical and/or Pharmacoeconomic impact of early diagnosis and intervention
- Impact of treatment adherence/discontinuation on pharmacoeconomic and functional outcomes
- Real world safety and utilization of Botox (assessing muscles, doses and retreatment)
- Real world observations describing impact of Botox treatment on comorbidities (e.g. depression/anxiety) and/or patient reported outcomes (including but not limited to patient/physician satisfaction, functional impairment, pain relief, quality of life etc.)
- Real world studies assessing patient specific functional goal attainment after treatment with Botox
- Optimization of Botox therapy with pattern-based treatment paradigms and/or utilization of new technologies, and/or training tools.
    - Studies that assess pharmacodynamics (including objective or sensitive measures of treatment response) and/or clinically meaningful duration of Botox effects

Movement Disorder

Priorities

- Botox for treatment of pain associated with movement disorder
- Clinical and/or Pharmacoeconomic impact of early diagnosis and intervention
- Studies assessing approaches/predictors for prompt diagnosis and early intervention with Botox for Cervical Dystonia to obtain optimized patient outcomes
- Real world observations describing impact of Botox on comorbidities (e.g., depression/anxiety) and/or patient reported outcomes (including but not limited to patient/physician satisfaction, functional impairment, pain relief, quality of life etc.)
- Optimization of Botox therapy with utilization of new technologies, training tools and/or treatment paradigms
- Studies that assess pharmacodynamics and/or clinically meaningful duration of Botox effects
- Impact of treatment adherence/discontinuation on pharmacoeconomic and functional outcomes

Urology

Priorities

- Studies to assess long-term real-world economics, safety and/or effectiveness of Botox
- Assessment of treatment procedure paradigms, which can include impact on treatment adherence and/or patient satisfaction
- Studies to assess variables that impact time between diagnosis and advancement to third line therapies, including cycling on oral medications
- Impact of treatment adherence/discontinuation on pharmacoeconomic and functional outcomes

Proposals will NOT be considered for the following:

- Studies assessing novel/developmental toxins (toxins other than Botox) under evaluation by AbbVie
- Head-to-Head clinical trials assessing Botox vs other toxins
- Studies conflicting with current research and development programs
- For Spasticity - Assessment of anticoagulants pre/post injection procedure
- For SMD - Imaging studies with no clear patient reported outcomes
- For Urology – Evaluation of Botox for Premature Ejaculation (PE) or Benign Prostatic Hypertrophy (BPH)

CNS – Psychiatry – Vraylar (Cariprazine): Bipolar Disorder I, Schizophrenia

Vraylar (Cariprazine) is an orally active atypical antipsychotic. It is a partial agonist at central dopamine D3/D2
and serotonin 5-HT1A receptors and has antagonist activity at serotonin 5-HT2A receptors.

We welcome proposals from Investigators from under-represented groups.

Vraylar is approved in the US for adults with:

- Bipolar Disorder I (BP-I) - depressive, manic and mixed episodes
- Schizophrenia

Priority will be given to proposals to investigate the following areas:

- Investigation of disease states where Vraylar's pharmacology matches with the underlying biology of psychiatric illnesses, including but not limited to:
  - Bipolar Disorder II (BP-II)
  - Combination therapy in BP-I (e.g., valproate or lithium)
  - Attention Deficit and Hyperactive Disorder (ADHD)
  - Post-Traumatic Stress disorder (PTSD)
  - Borderline personality disorder
  - Generalized Anxiety Disorder (GAD)
  - Effect of Vraylar on endophenotypes in psychiatric disorders

- Understanding the impact of Vraylar on the following in BP-I populations:
  - Sexual functioning
  - Functional outcomes / QoL / work productivity
  - Cognition and cognitive impairment
  - Severe mixed episodes where both symptom poles (manic and depressive) are simultaneously significantly syndromic

- Additional areas of interest for the approved indications (BP-1, schizophrenia) include:
  - Increasing accuracy of BP-I Disorder diagnosis
  - Real world experience with and implementation of Rapid Mood Screener
  - Response of gut microbiome to treatment with Vraylar
  - Variance in the response to Vraylar based on the status of the gut microbiome.
  - Burden of disease
  - Novel outcomes related to treatment with Vraylar
  - Pharmacogenetic predictors of Vraylar response
  - Clinical relevance and prognostic value of BP-I maintenance treatment selection based on polarity index of medication

Proposals in the following areas <u>will NOT be considered</u>:

- Indications for which Vraylar has been or is being evaluated:
  - Adjunctive Major Depressive Disorder (MDD)
  - Pediatric BP-I disorder
    - Pediatric schizophrenia
    - Maintenance treatment of BP-I disorder in adults

- Irritability associated with Autism Spectrum Disorder (ASD)
- Negative symptoms in Schizophrenia
- Populations at high risk for impulse control dysfunction/compulsive behavior
- Patients at high risk for seizures
- Preclinical or pharmacokinetic studies (unless requesting drug product only)
- Populations and/or indications under consideration by AbbVie

Other factors to consider:

- Studies can only be initiated following regulatory/market approval in the country of interest.
- Vraylar is expected to receive marketing approval in Canada for BP-I and Schizophrenia in 2022.
- Funding decisions are based on the quality of the proposal and availability of funds.

Eye Care: Durysta, XEN 45/63, Ozurdex, AGN-190584 Pilocarpine 1.25% ophthalmic solution (Vuity)

Durysta Priorities

- RWE on effectiveness and duration of IOP control with Durysta
- Effectiveness of subsequent treatments after Durysta
- Effectiveness of Durysta after SLT
- Safety profile in RW clinical setting
- Study of impact on topical AEs profile (including OSD) of switch from drops to Durysta
- RWE on Durysta´s efficacy and safety across ethnic groups (African-Americans, Asian, Hispanic)
- Limitations of SOC

Ozurdex Priorities

- Structural biomarkers in DME (cytokine profile, treatment response to Ozurdex)
- Use in phakic patients with DME
    - First and second line use
    - Pre-surgical in cataract surgery
- Sequential use (Ozurdex as 1L) of Ozurdex and aVEGF
- Intertreatment intervals
- IOP safety profile of Ozurdex in relationship to posology

XEN 45/63 Priorities*

- Evaluation of patient outcomes via novel surgical techniques
- Effectiveness and safety after failure of MIGS procedures
- Comparative evaluation of XEN45 and XEN63
- Effectiveness and safety of XEN vs Preserflo
- Prospective effectiveness and safety data *vs.* Trabeculectomy
- Impact of COVID 19 on Glaucoma progression and IOP control
- Effectiveness and safety when implanted after 2 drops
- Effectiveness and safety of XEN in ACG

*Wherever possible, long-term data and POAG sub-group analysis desirable

Notable considerations for the investigator: Pediatric use IIS proposals will not be considered

AGN-190584 Pilocarpine 1.25% ophthalmic solution (Vuity) Priorities

- Data on the management of presbyopia across all ranges of visual acuity (near, intermediate, and distance)
- Increasing the scientific body of evidence evaluating the mechanism of action of AGN-190584 Pilocarpine 1.25% in presbyopia
- Evaluation of AGN-190584 Pilocarpine 1.25% used complementary to other refraction/surgical techniques for the management of presbyopia
- Evaluation AGN-190584 Pilocarpine 1.25% in additional patient sub-types
- Evaluation of patient's use patterns and outcomes with AGN-190584 Pilocarpine 1.25% for presbyopia

Immunology – Gastroenterology: Risankizumab & Upadacitinib

No new interventional studies will be considered for Humira (adalimumab) in 2021, except for COVID-19 vaccine related studies as noted below.

COVID-19 studies will be considered as related to vaccine impact on AbbVie's marketed Immunology products or the impact of these marketed therapies on the safety and efficacy of vaccines.

Any clinical/interventional studies with upadacitinib and risankizumab can only be initiated following regulatory/market approvals for respective indications in the country of interest. For preclinical studies utilizing outside of approved indications only *ex-vivo*, *in-vitro or in-silico* studies will be considered.

1. Predictive and prognostic factors of disease severity and response to therapy in IBD (adult and pediatric)
2. Optimal monitoring of symptoms and inflammation in IBD (adult and pediatric)
3. Exploration of drug mechanisms and targeted therapy approaches in IBD
4. Broadening the knowledge about the role of early and sustained control of inflammation to prevent disease worsening or optimize long-term outcomes in IBD
5. Global burden of IBD (total cost of illness, quality of life, co-morbidities, unmet needs)
6. Evaluation of biomarkers in IBD and identification of potential disease phenotypes linked to differentiated pathophysiology
7. Exploration of mechanisms of disease (disease state and novel therapeutic targets in IBD)
8. Broadening the knowledge of IL23 and JAK pathways in IBD
9. Prevention and treatment of pouchitis, fistulizing, and structuring disease

Immunology – Dermatology: Adalimumab (HUMIRA), Risankizumab (SKYRIZI), Upadacitinib (RINVOQ)

Clinical interventional studies will be considered only for compounds that have regulatory approval for use.

COVID-19 studies will be considered as related to vaccine impact on AbbVie's marketed Immunology products or the impact of these marketed therapies on the safety and efficacy of vaccines.

Use of Adalimumab (Humira) is restricted to retrospective research or as comparator only.

Dermatology / All Indications

Compounds: Adalimumab (Humira), Risankizumab (SKYRIZI), Upadacitinib (RINVOQ)
Priority consideration will be given to applications proposing to investigate the following areas of interest:

1. Development and use of novel technological tools and devices for referral, diagnosis, assessment, disease management, and monitoring.
2. Remote and virtual, monitoring and disease management – challenges associated with remote environment.
3. Impact of treat to target strategies, treatment goals and initiatives to advance quality of care in managing disease.
4. Assessment of the impact/benefits of achieving and maintaining high levels of clearance over the long term.
5. Understanding treatment patterns, including dosing, sequencing, and compliance, including persistence, adherence, adverse events, and outcomes.

Dermatology / Psoriatic Disease

Compounds: Risankizumab (SKYRIZI)

Priority will be given to applications proposing to investigate the following:

- In vitro or in vivo research of risankizumab or IL-23 in the pathogenesis of psoriasis, psoriatic arthritis, or associated comorbidities
- Epidemiology, associated comorbidities, cumulative life course impairment (CLCI), and markers for early detection
- Impact of risankizumab on CLCI
- Impact of early intervention and disease modification of risankizumab in psoriasis across all severities (including mild to moderate)
- Effectiveness and safety of risankizumab in special psoriasis areas
- Impact of risankizumab on psoriatic comorbidities, including prevention of comorbidities
- Real World Evidence or interventional use of risankizumab
- Impact of risankizumab in PsA, including impact on musculoskeletal symptoms, extra articular manifestations, structural joint damage, patient reported outcomes (including pain and fatigue) and skin outcomes

Dermatology / Hidradenitis Suppurativa (HS)

Compound: Adalimumab (Humira)

Priority will be given to applications proposing to investigate the following:

- Disease prevalence and natural course of disease, including progression

- Practical diagnostic and monitoring tools that aid in disease classification, assessment of disease severity, activity progression, flares and response to treatment
- Pathogenesis of HS
- Biomarkers and phenotypes of HS
- Patient types/segments and their needs with respect to treatment and disease management
- Impact of early referral, diagnosis and treatment in HS including impact on progression, and the consequences of underdiagnosed / undertreated disease
- Economic burden

Dermatology / Atopic Dermatitis (AD)
Compound: Upadacitinib (RINVOQ)

Priority will be given to applications proposing to investigate the following:

- Epidemiology, natural course of the disease, including co-morbidities and CLCI, management, and burden of AD
- Pathogenesis and systemic nature of AD
- Understanding skin pain and itch in AD
- Clinical and biomarker characterization of different AD endotypes (phenotypes)
- Effectiveness and safety of upadacitinib in AD, including AD sub-types, ethnicities and variants, optimal treatment regimens, and characterization of adverse event profiles
- Long-term impact of use and patient experience with topical steroids
- Understanding the importance of multi-dimensional disease control (speed of onset, importance of itch control, rapid response, long-term control, CLCI)
- Impact of Upa on AD co-morbidities

Dermatology / Vitiligo
Compound: Upadacitinib (RINVOQ)

Priority will be given to applications proposing to investigate the following:

- Disease pathogenesis
- The natural course of disease, including disease activity and progression
- Burden of disease, including co-morbidities, psychosocial impact (stigma, mental health), access to care, and cost (direct and indirect), as well as the cumulative long-term impact of disease
- Disease scoring and assessment measures
- Treatment goals, from both the HCP and patient perspective

Dermatology / other inflammatory skin diseases

- Research to understand the pathogenesis, disease course, and CLCI of other inflammatory skin diseases
- Efficacy/effectiveness and safety of Upa in other inflammatory skin diseases

Immunology – Rheumatology: Upadacitinib (RINVOQ)

No new interventional studies will be considered for Humira (adalimumab) in 2021, with the exception of pediatric and COVID-19 vaccine related studies as noted below.

COVID-19 studies will be considered as related to vaccine impact on AbbVie's marketed Immunology products or the impact of these marketed therapies on the safety and efficacy of vaccines.

Clinical interventional studies will only be considered for compounds that have regulatory approval for use for at least one indication in that country.

Upadacitinib is a selective and reversible JAK inhibitor that is being evaluated in rheumatoid arthritis [RA], psoriatic arthritis [PsA], axial spondyloarthritis [axSpA] and giant cell arteritis [GCA].

For Risankizumab in PsA please refer to the Dermatology Strategic Priorities.

Rheumatology / Overarching

Compounds: Upadacitinib
Indications: RA, PsA, axSpA, GCA
Additional indications which are asset agnostic include polymyalgia rheumatica [PMR], systemic lupus erythematosus [SLE], primary Sjogren's syndrome [pSS]

- Adherence and persistence with JAK-inhibitors in inflammatory diseases
- Understanding JAK-related pain mechanisms
- Role of JAKi on extra-musculoskeletal manifestations
- Impact of Upadacitinib treatment via imaging modalities
- Understanding burden of systemic glucocorticoid treatment
- Mechanistic basis for and potential risk factors associated with Herpes Zoster with JAK inhibition
- Non-clinical pharmacological assessments of JAK inhibitor differentiation
- Understanding unmet needs, characteristics, burden of disease, treatment patterns/strategies, economic assessments, novel outcomes and assessments (including aspirational cure)
- Roles of JAKs in disease progression
- Prognostic biomarkers predictive of therapeutic response and/or disease progression
- Epidemiology and risk factors associated with VTEs, MACE, malignancies, and mortality
- Assessment of step-down approaches of concomitant medications (e.g., methotrexate, glucocorticoids, NSAIDs, opioids)
- Outcomes associated with patients achieving and/or maintaining remission
- Assess the benefit and understand the barriers of goal directed / treat-to-target therapy
- Understanding telemedicine/remote monitoring assessment approaches to optimize patient care

Oncology: Venetoclax (ABT-199)

Venetoclax is a BCL2 inhibitor with scientific rationale for evaluation across a broad variety of Hematologic malignancies/disorders. Consideration will be given to real-world evidence, preclinical, and clinical applications in 2022.

Priority will be given to applications proposing to investigate the following areas:

- Novel therapeutic combinations
- Novel clinical indications where there is scientific rationale and unmet medical need
- Evaluation of real-world data including but not limited to treatment patterns, outcomes, quality of life, and patient preferences
- Evaluation of mechanisms of resistance
- Evaluation of novel and additional clinical endpoints and/or biomarkers (including, but not limited to, MRD)
- Research that is focused on understanding the effectiveness, immunogenicity and safety of SARS-CoV-2 vaccines in patients treated with Venetoclax and disease outcomes in populations at risk of COVID-19 may be considered

Notable considerations for the investigator:

- Limited funds may be available to support proposals
- Clinical interventional IIS may be considered once the safety profile has been established for compounds prior to regulatory approval for use
- Adult solid tumor proposals will not be accepted

Oncology: Navitoclax (ABT-263)

Navitoclax (ABT-263) is a BCL-XL/BCL-2 inhibitor with scientific rationale for evaluation across several hematologic malignancies, particularly myeloproliferative neoplasms. Consideration will be given to both preclinical and clinical applications in 2022.

Priority will be given to applications proposing to investigate the following areas within MPN:

- Novel therapeutic combinations
- RWE outcomes
- Evaluation of novel and/or exploratory predictive models or biomarkers
- Evaluation of novel and additional clinical endpoints
- Exploration of navitoclax combination therapy in special patient populations
- Evaluation of preclinical or correlative effects of BCL-XL inhibition

Things to consider for the investigator:

- Clinical indications other than MPN are of lower priority
- Limited funds may be available to support proposals
- Solid tumor proposals will not be accepted
- Clinical interventional IIS may be considered once the safety profile has been established for compounds prior to regulatory approval for use

Oncology: Epcoritamab, NHL

Epcoritamab is a CD3xCD20 bispecific antibody with scientific rationale for evaluation in Non-Hodgkin Lymphomas (NHL). Consideration will be given to real-world evidence, preclinical, and clinical applications in 2022.

Consideration will be given to applications proposing to investigate the following areas:

- Evaluation of Epcoritamab management in various patient settings
- Novel clinical indications where there is scientific rationale
- Evaluation of novel and/or exploratory predictive models or biomarkers
- Evaluation of novel and additional clinical endpoints
- Evaluation of real-world data including but not limited to treatment patterns and patient reported outcomes

Considerations for the investigator:

- Limited funds may be available to support proposals
- Clinical interventional IIS may be considered once the safety profile has been established for compounds prior to regulatory approval for use.

Oncology: Telisotuzumab vedotin (Teliso-V), Non-small cell lung cancer (NSCLC)

Teliso-V is an antibody drug conjugate (ADC) targeting c-Met with scientific rationale for evaluation in non-small cell lung cancer. Consideration will be given to both preclinical and clinical applications in 2022.

Consideration will be given to applications proposing to investigate the following areas:

- Evaluation of Teliso-V as a monotherapy or in combination in NSCLC clinical indications where there is scientific rationale (excluding non-squamous NSCLC)
- Evaluation of novel and/or exploratory predictive models or biomarkers
- Evaluation of novel and additional clinical endpoints

Considerations for the investigator:

- Limited funds may be available to support proposals
- Pediatric proposals will not be accepted
- Clinical interventional IIS may be considered once the safety profile has been established for compounds prior to regulatory approval for use.

Specialty – Hepatology – Maviret/Mavyret: Hepatitis C Virus (HCV)

AbbVie is committed to support global efforts to meet WHO target of HCV elimination as a major public health threat by 2030.

In this context, AbbVie is interested in scientific study proposals addressing any of the following priority areas:

1. Research aiming to explore sustainable solutions and models, including 8-week treatment, to allow simplification of the HCV care continuum and/or accelerate the path to elimination, in the following populations: A) high incidence of HCV, B) high risk of HCV transmission, C) sub -optimal linkage to care AND D) high unmet needs (e.g.: PWID, immigrants, incarcerated). Examination of models that successfully incorporate non-liver specialists into the HCV care, including but not limited to addiction specialists, OB/GYN, psychiatrist, nurses and primary care physicians.

2. Clinical and economic outcomes of 8-week treatment in patients with acute and recently acquired HCV to enable further simplification of HCV care across disease stages.

3. Epidemiological research in HCV populations of interest (e.g., PWID, immigrants from high-prevalence countries, incarcerated, psychiatric patients, pregnant women).

Specialty – COVID-19

AbbVie is committed to further understand the impact of the COVID-19 pandemic. Due to the rapidly evolving landscape of SARS-CoV-2, COVID-19 vaccines, therapies and emerging variants Abbvie is not actively seeking to repurpose on market therapeutics. The following outlines the activities Abbvie may consider:

- Epidemiological, surveillance, preclinical and clinical research that may impact marketed Abbvie therapies used in COVID-19 and other emerging viral pandemics.

Specialty – Neuroscience – Duopa/Duodopa: Parkinson's Disease

Disease State
Parkinson's Disease

- Disease burden/Progression: Further understand the characteristics and/or burden of Parkinson's disease (PD) inadequately controlled by optimized oral therapy, including but not limited to patient, caregiver, and healthcare resource utilization.
- Management: Clinical Utility of diagnostics or technology to identify signs of Advancing Parkinson's Disease and resultant changes in care.
- Patient Perspective: Evaluate reasons why PD patients uncontrolled on oral therapy refuse, accept, or hesitate to initiate invasive treatment options.

Continuous dopaminergic stimulation (CDS)

- Evaluate short and long-term benefits of CDS vs pulsatile stimulation, including but not limited to disease modification and prevention/delay of motor complications.
- Investigate indicators/markers (including but not limited to laboratory, clinical, imaging) to support the translation of continuous Levodopa infusion into CDS benefits.
- Evaluate preclinical effects of CDS on neuroinflammation.

Levodopa Carbidopa Intestinal Gel/Carbidopa Levodopa Enteral Suspension (LCIG/CLES)

- Evaluate LCIG/CLES efficacy and safety in subpopulations of advanced PD (APD) patients uncontrolled on orals.
- Understanding the use of LCIG/CLES in combination with or after failure with other "device-aided therapies".
- Characterize APD medication management to achieve monotherapy with LCIG/CLES.
- Further understanding the characteristics of patients likely to derive benefit from LCIG/CLES.
- LCIG/CLES management/system:
    - Efficacy and safety of treatment modalities.
    - Understanding the impact of multi-disciplinary care models in APD.
- Additional areas:
    - Evaluate LCIG/CLES in other Parkinsonisms
    - Evaluation of APD treatment with Duo(do)pa with innovative imaging techniques
    - Evaluation of Biomarkers in APD patients treated with Duo(do)pa

Specialty – Oriahnn, Orilissa, LoLo, Liletta: Uterine Fibroids, Endometriosis

Oriahnn
Uterine Fibroids

- Impact of elagolix /elagolix + add back on disease and/or symptom recurrence following surgeries/procedures aimed to address symptomatic UF.
- Impact of elagolix /elagolix + add back on delaying or avoiding surgery related to symptomatic UF.
- Concurrent use of progestin only contraceptives with elagolix + add back to assess prevention of pregnancy.

Orilissa
Endometriosis

- Role of elagolix in delaying and/or avoiding surgical intervention or impact on pain recurrence post-surgery.
- Impact of elagolix on the efficacy of hormonal contraceptives.
- Synergistic treatment approaches in conjunction with elagolix for endometriosis related pain.

Contraceptives
LoLo and Liletta

- Evaluation of novel uses of contraceptive products LoLo and Liletta.

Other Areas of Interest

- Novel uses of elagolix/elagolix + AB

Endo-Metabolic: CREON

Abbvie is interested in scientific study proposals that would address the following priority clinical areas:

1. Burden of exocrine pancreatic insufficiency (EPI) disease and impact of treating EPI in, but not limited to:
    a. Acute Pancreatitis
    b. Celiac Disease
    c. GI surgeries that could result in EPI

2. Outcomes in EPI patients treated with CREON® (pancrelipase) with underlying conditions of EPI, excluding chronic pancreatitis/ pancreatectomy in adults.

3. Novel approaches (clinical tools, biomarkers, devices) that
    a. Accelerate/ease the diagnosis of EPI
    b. Improve adequate pancreatic enzyme replacement therapy (PERT) dosing
    c. Improve PERT adherence
    d. Assess outcome of PERT treatment beyond stool fat measurements

Anti-Infectives: Avycaz (ceftazidime/avibactam), Dalvance (dalbavancin), Teflaro (ceftaroline fosamil)

Key Focus Areas: Avycaz (ceftazidime/avibactam)

- Comparative clinical and/or microbiologic data in infections caused by carbapenem-resistant Enterobacterales (CRE), extended-spectrum beta lactamase (ESBL) producing bacteria, and multi-drug resistant (MDR) Pseudomonas aeruginosa
- Studies evaluating the impact of early appropriate therapy on clinical outcomes in high-risk patients with suspected or documented resistant Gram-negative infections
- Studies (pre-clinical and clinical) evaluating emergence of resistance of Gram-negative bacteria, including prevalence of resistance, mechanisms of resistance, and strategies for prevention
- Clinical outcomes in patients with Gram-negative bacteremia
- Clinical outcomes in special populations (i.e., immune-compromised, CF patients, pediatrics, transplant)

Key Focus Areas: Dalvance (dalbavancin)

- Economic outcomes and patient centric data demonstrating the impact in reduced hospitalizations, expressed in reduced LOS or admission avoidance
- Clinical outcomes against Gram (+) infections in unique patient populations, such as immunocompromised patients or people who inject drugs
- Clinical outcomes in patients other than ABSSSI (i.e., infected implantable devices, persistent bacteremia, endocarditis, osteomyelitis)

Key Focus Areas: Teflaro (ceftaroline fosamil)

- Comparative time to clearance data of *S. aureus* bacteremia vs standard of care (vancomycin, daptomycin)
- Clinical and/or microbiological outcomes in hospitalized ABSSSI and CABP patients with significant co-morbidities (e.g., diabetes, obesity, immune-compromised), including evaluation of early and sustained clinical responses
- Dose optimization and/or outcomes in difficult to treat infections, including but not limited to methicillin resistant *S. aureus* (MRSA) bacteremia, MRSA pneumonia, osteomyelitis, diabetic foot infection, catheter-related infection

GI Care: Eluxadoline

AbbVie is interested in scientific study proposals that would address the following priority areas:

1. Burden of Irritable Bowel Syndrome with Diarrhea (IBS-D) and impact of multi-symptom treatment on patient outcomes and resource utilization

2. Efficacy and continuing safety of Eluxadoline to treat additional patient populations including, but not limited to:
    a. Functional diarrhea
    b. Fecal incontinence
    c. Persistent IBS-D symptoms in ulcerative colitis patients in inflammatory remission
    d. Persistent IBS-D symptoms in Crohn's disease patients in inflammatory remission

3. Novel real-world clinical efficacy and continuing safety outcomes data in IBS-D patients

GI Care: Linaclotide

AbbVie is interested in scientific study proposals that would address the following priority areas:

1. Burden of Irritable Bowel Syndrome with Constipation (IBS-C) or Chronic Idiopathic Constipation (CIC) and impact of multi-symptom treatment on patient outcomes and resource utilization

2. Efficacy and safety of linaclotide to treat constipation and/or abdominal symptoms in additional patient populations including, but not limited to:
    a. Parkinson's disease
    b. Multiple sclerosis
    c. Functional abdominal pain
    d. Geriatric patients
    e. Cystic fibrosis

3. Linaclotide effect on clinical visceral nerve hypersensitivity

4. Novel clinical tools and/or biomarkers that:
    a. Increase the ease of confident diagnosis of IBS-C and CIC
    b. Improve patient clinical experience and/or adherence to treatment
    c. Assess novel outcomes of IBS-C and CIC treatment