2020 IIS Strategic Priorities

Contents

Hepatology - Compound: Glecaprevir and Pibrentasvir

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 which address any of the following priority areas:

1. HCV elimination, especially studies addressing populations with high risk of HCV transmission.
   - Sustainable solutions and models which allow simplification of the HCV care continuum and/or accelerate the path to elimination
   - Models that successfully incorporate non-liver specialists into the HCV care
   - Clinical and economic outcomes of patients with recently acquired HCV

2. Clinical and economic outcomes of simplification of hepatitis C treatment, including benefits of 8-week treatment duration and its impact on elimination.

3. HCV epidemiology in regions which have evolving, limited, or no epidemiological information.

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

Dermatology / Psoriatic Disease

Compounds: Adalimumab (HUMIRA)*, Risankizumab (SKYRIZI)

1. In vitro or in vivo research of risankizumab or IL-23 in the pathogenesis of psoriasis or associated comorbidities.
2. The impact of early intervention of risankizumab on psoriasis or use in less severe (moderate) psoriasis.
3. Epidemiology of psoriasis and psoriatic arthritis, associated comorbidities and markers for early detection of psoriasis and psoriatic arthritis.
4. Evaluate the effectiveness and safety of risankizumab in special areas (genital, scalp, nail, etc.).
5. Impact of treatment goals and initiatives to advance quality of care in managing psoriasis and/or psoriatic arthritis.
6. Real World Evidence or interventional use of risankizumab: patient reported outcomes, health economic and healthcare resource utilization, long-term durability and safety and treatment patterns associated with psoriasis and comorbidities.
7. Understanding treatment compliance, persistence, and adherence for psoriatic diseases.

*No prospective studies for Adalimumab (Humira) will be considered. Adalimumab (Humira) studies should be restricted to psoriatic arthritis.

Dermatology / Hidradenitis Suppurativa (HS)

Compounds: Adalimumab (HUMIRA)*

1. Real World Evidence examining natural course of the disease.
2. Practical diagnostic and monitoring tools that aid in disease classifications, activity, progression, and response to treatment. (time to diagnosis and referral)
3. RWE examining the humanistic and economic burden of underdiagnosed/undertreated hidradenitis suppurativa.
4. RWE examining the clinical and patient reported outcomes of treatment with immunologic therapy for HS.
5. Translational research to further explore the pathogenesis of HS and other inflammatory skin diseases.

*No prospective studies for Adalimumab (Humira) will be considered.

Dermatology / Atopic Dermatitis (AD)

Compound: Upadacitinib (RINVOQ)

1. Epidemiology, and progression, education, management, comorbidities, and/or humanistic/economic burden of AD.
2. Translational and clinical research to further explore the pathogenesis of AD and other inflammatory skin diseases.
3. Systemic nature of moderate to severe AD.
4. Tools and markers that aid classification/endotype and evaluation of AD.

Immunology-Gastroenterology - Compound: Risankizumab, and Upadacitinib

Clinical interventional studies with upadacitinib & risankizumab are not supported.

For preclinical studies utilizing upadacitinib and risankizumab, only *ex-vivo*, or *in-vitro* 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 progression in IBD

5. Global burden of IBD (total cost of illness, quality of life, co-morbidities)

6. Evaluation of novel and/or exploratory biomarkers in IBD

7. Exploration of mechanisms of disease (disease state and novel therapeutic targets in IBD)

8. Broadening the knowledge of IL23 and JAK 1 pathways in IBD.

Immunology-Rheumatology - Compound: Upadacitinib

Any clinical studies with upadacitinib can only be initiated following regulatory/market approvals for respecitve indications in the country of interest.

No new interventional studies will be considered for Humira (adalimumab) in 2020.

Overarching:

1. Understand impact of Janus Kinase (JAK) signaling and inhibition of JAK signaling in rheumatologic diseases with high disease burden/unmet need, where clinical studies are not yet underway.
2. Understand mechanistic basis for, and potential risk factors associated with risk of Herpes Zoster with JAK inihibition, including strategies to mitigate risk of Herpes Zoster in patients treated with JAK inhibitors
3. Understand the epidemiology and risk factors associated with VTEs across: Giant Cell Arteritis (GCA), Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), axial Spondyloarthritis (ax-SpA)
4. Further understanding of JAK related pain mechanisms
5. Development and validation of novel tools to measure patient relevant outcomes (e.g., function, pain, sleep, mood)

New Indication & Pipeline

6. Understanding the role of JAKs in Giant Cell Arteritis (GCA) disease pathogenesis
7. Understanding the role of JAKs and Bruton's Tyrosine Kinase (BTK) in RA disease pathogenesis
8. Further understanding of pathogenesis of the following diseases: GCA
9. Further understandings of unmet needs and burden of disease in the treatment of GCA
10. Understanding of potential biomarkers related to GCA, PsA, ax-SpA, and RA
11. Understanding of outcome measures or clinical assessment tools for GCA

Rheumatoid Arthritis

12. Understand potential biomarkers predictive of upadacitinib efficacy response
13. Understand mechanistic basis for effectiveness of upadacitinib across patient populations such as monotherapy, combination therapy, post treatment with csDMARDs, bDMARDS, with our without methotrexate
14. Understand patient characteristics associated with non-adherence to methotrexate
15. Develop and evaluate mechanisms to optimize adherence to oral therapies
16. Step down or sparing of methotrexate and/or corticosteroids in patients responding to upadacitinib plus Methotrexate and/or corticosteroids
17. Further understanding of clinical, imaging, patient reported and economic outcomes associated with patients achieving remission (including sustainability of remission) with upadacitinib.
18. Understand impact of upadacitinib treatment on novel PRO measures
19. Understanding the role of JAKs in Rheumatoid Arthritis disease pathogenesis
20. Further understanding of unmet needs and burden of disease in the treatment of RA with biologic or tsDMARD monotherapy
21. Understanding barriers and benefits when implementing goal directed therapy regarding patient disease outcomes
22. Understanding the role of JAK inhibitors in extra articular manifestations (EAMs) of RA including but not limited to: interstitial lung disease, secondary Sjogren's

Axial SpA & PSA

23. Real-world treatment patterns and with current and emerging therapeutic options in SpA diseases
24. New insights into epidemiology and burden of MSK signs and symptoms, comorbidities, and health economic outcomes in SpA
25. Deepen understanding of the pathophysiology of SpA and role and mechanism of IL-23 and JAK 1-selective inhibition

Axial SpA

26. Impact of residual axial (spinal) inflammation on clinically meaningful and patient-relevant long-term outcomes (e.g., physical function, disease progression including structural progression)

PsA

27. Develop and validate treatment targets for different domains of PsA. (eg joints, skin, axial, enthesitis, etc.)
28. Defining progression/worsening of PsA in long-term (beyond radiographic inhibition)

Neuroscience - Parkinson's Disease – Compound: Duopa/Duodopa

Parkinson´s Disease

1. 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.
2. Management: Identify the right time for intervention (and provide referral, if needed) using different tools (i.e. Tools/Criteria; technology based objective measures (TOM)).

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

1. LCIG Mode of Action (MoA): Continuous dopaminergic stimulation (CDS)
    1. Short and long-term benefits of CDS vs pulsatile
2. Evaluate LCIG/CLES efficacy and safety in subpopulations of advanced PD (APD) patients including, but not limited to: elderly (>75 years of age), cognitively impaired, patients with impulse control disorders (ICDs), difficult to treat dyskinesia, freezing of gait, difficult to treat prominent NMS, and axial symptoms in whom oral treatments no longer offer benefits.
3. Understanding the use of LCIG/CLES in combination with or after failure with other "device-aided therapies" (e.g. DBS).
4. Characterize APD medication management to achieve monotherapy with LCIG/CLES and describe the patient population that benefits most from monotherapy.
5. Further understanding the characteristics of LCIG/CLES patient population and responders, clinical assessment tools, and key clinical and/or health economic outcomes, including but not limited to:
    1. Patient and caregiver-related outcomes, preferences, self-efficacy (patient/caregiver experience), activities of daily living (ADL), quality of life (QoL);
    2. Non-motor symptoms (NMS);
    3. Retrospective long-term efficacy and safety outcomes; and
    4. Using TOM (e.g. wearable devices, biosensors, and others) as surrogates of efficacy and safety of LCIG/CLES in APD patients.
6. LCIG management/system:
    1. Efficacy and safety of treatment modalities including but not limited to outpatient titration, and use for a duration of > 16 hours/day,
    2. Understanding the impact of multi-disciplinary care models in APD, and
    3. Evaluation of new tubing technologies and/or placement procedures with the goal to enhance efficacy and safety of LCIG delivery.
7. Additional focus areas:
    1. Identify the role of the gut microbiome in APD patients in the response to the presence of LCIG/CLES, and

Evaluate LCIG/CLES in other Parkinsonisms

Oncology - Compound: Veliparib (ABT-888)

Veliparib is a PARP inhibitor with scientific rationale for evaluation across a broad variety of tumor types. Consideration will be given to both preclinical and clinical applications in 2020.

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

- Novel therapeutic combinations/regimens
- Novel clinical indications where there is scientific rationale
- Evaluation of novel and/or exploratory biomarkers (disease state and therapeutic targets)

Things to consider for the investigator:

- Limited funds may be available to support proposals

Oncology - Compound: Venetoclax (ABT-199)

Venetoclax is a BCL2 inhibitor with scientific rationale for evaluation across a broad variety of Hematologic malignancies and solid tumors. Consideration will be given to both preclinical and clinical applications in 2020.

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

- Novel therapeutic combinations
- 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 mechanisms of resistance to apoptosis pathways

Notable considerations for the investigator:

- Limited funds may be available to support proposals

Oncology - Compound: Navitoclax (ABT-263)

Navitoclax (ABT-263) is being studied in multiple hematological malignancies. Consideration will be given to both preclinical and clinical applications in 2020.

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

- Novel therapeutic combinations
- 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 mechanisms of resistance to apoptosis pathways

Things to consider for the investigator:

- Limited funds may be available to support proposals

Endo-Metabolic - Compound: Creon

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

1. Burden of EPI disease and Impact of treating EPI in, but not limited to:
    a. Acute Pancreatitis
    b. Diabetes (Types 1, 2, and 3c)
    c. IBS, Celiac Disease, IBD
    d. GI surgeries associated with EPI

2. Outcomes in exocrine pancreatic insufficiency (EPI) patients treated with CREON® (pancrelipase) in chronic pancreatitis, or pancreatic cancer.

3. Novel approaches (clinical tools, biomarkers, devices)
    a. That accelerate/ease the diagnosis of EPI
    b. Improve adequate PERT dosing
    c. Improve adherence for patients
    .
4. New approaches beyond traditional stool fat measurements that assess outcomes of PERT treatment

Women's Health - Benign Gynecologic Diseases

Endometriosis Related Priorities

- Impact of elagolix use on surgical outcomes and disease recurrence
- The role of elagolix in disease modification in the three phenotypes of endometriosis (endometriomas, superficial endometriosis and deep endometriosis)
- Differentiation of GnRH analog MOA and clinical implications (including appropriate in vivo and in vitro non-human models)
- Predictors of response/non-response including Inflammation, pain pathways, degree of fibrosis
- Predictors of tolerability (i.e., can we predict who will have low tolerance to hypoestrogenemia: predictors of bone turn-over, high risk of hot flashes, who will be better served with add-back)
- Synergistic treatment approaches in conjunction with elagolix, (therapeutic approaches that are supplemental/synergistic to endometriosis, including central sensitization)

Uterine Fibroids Related Priorities

- Impact of elagolix use pre and post-surgery on uterine fibroids outcomes and disease recurrence
- Impact on elagolix safety and efficacy with concurrent use with contraceptives
- Pathophysiology of heavy menstrual bleeding in uterine fibroids – impact of medical therapy
- Synergistic treatment approaches in conjunction with elagolix to manage uterine fibroids and related symptoms

Women's Health – Other areas of interest

- Novel clinical applications of elagolix with a focus on Women's Health
- Management of bleeding and pain in women with adenomyosis
- Management of premenstrual dysphoric disorder (PMDD) and/or premenstrual syndrome (PMS)
- Management of menstrual migraines
  Management of breast tenderness/pain