

# IIT Global Areas of Interest

Cardiovascular, Renal & Metabolism

## Atrasentan (Vanrafia)

Without drug (IgAN, FSGS)

- Diagnosis and classification
  - Additional ways to foster (earlier) diagnosis of IgAN and FSGS beyond biopsy
  - Validate outcome measures (endpoint validation, validation of definitions) including patient-related outcomes, treatment targets, partial remission / remission and relapse criteria in IgAN
- Pathophysiology and biomarkers
  - Studies evaluating the mechanism of anemia with ERAs
  - Role of the endothelin system in IgAN and FSGS
  - Identification of approaches that lead to better characterization, management and/or correlation with outcomes in IgAN and FSGS (eg identification of biomarkers, genetic analysis, novel imaging technologies or biopsy-based studies)
- Disease burden
  - Burden of disease (clinical, economic and/or humanistic burden) in IgAN and FSGS
  - Epidemiological studies - Prevalence, treatment patterns and RWE, sex/geography differences (incl. registries) in IgAN and FSGS
  - Disease characteristics and clinical outcomes in patients with skin of color, ethnic minorities, or populations so far underrepresented in clinical trials. Gender related differences.
  - Gaps in the optimal care and management of IgAN and FSGS patients
  - Impact of patient education programs
  - Patient perspective on disease, treatment options and QoL

With Drug (IgAN, FSGS)

- Mode of action
  - Mechanistic studies using atrasentan in IgAN and FSGS, including biomarkers, biopsy and novel imaging techniques (eg MRI)
  - Studies evaluating non-hemodynamic effects of atrasentan in IgAN and FSGS
  - Studies evaluating the effects of atrasentan on pain in IgAN and FSGS
- Treatment optimization
  - Studies evaluating novel implementation protocols in IgAN
  - Evaluation/biomarker analysis of subgroups of patients included in the overall study populations in the atrasentan CDP
  - Studies in IgAN utilising SGLT2i and/or other novel treatments in combination with atrasentan
  - Studies evaluating the early use of atrasentan initiated alongside RASi +/- SGLT2i, or atrasentan alone in IgAN
- Expanded populations in IgAN
  - Studies of atrasentan in patients with IgAN with less severe disease (eg. lower proteinuria >0.5g/d)
  - Studies of atrasentan in patients with IgAN in more severe disease (eg. CKD stage 4, eGFR 15-29 ml/min/1.73m<sup>2</sup>)
  - Studies evaluating atrasentan in transplant patients with recurrent IgAN

Out of scope (IgAN, FSGS)

- Pediatric studies in IgAN and FSGS
- Studies exploring different dosing regimens to those currently being evaluated in current clinical development programs for IgAN and FSGS
- Head-to-head comparisons with other treatments for IgAN and FSGS
- Studies in IgAN including patients with eGFR <15 ml/min/1.73m<sup>2</sup> (CKD stage 5)

## **Inclisiran (Leqvio®)**

### Studies within the label population

- Long-term safety and tolerability
- Health-related quality of life (HrQoL)
- Implementation science and/or quality system improvement programs (ex. clinical care pathways)
- Early post-event implementation
- Stroke
- PAD
- LDL-C lowering in under-represented population
- Adherence vs. other LLTs

### Mechanistic Studies in secondary prevention

- Remodeling, fibrosis, inflammation
- Plaque burden regression/modification
- CABG graft remodeling

### Mechanistic Studies in primary prevention and/or patients with statin-intolerance

- Remodeling, fibrosis, inflammation
- Plaque burden regression/modification
- Assessment techniques (IVUS, echo, CCTA, OTC, MRI) must be guidelines validated (pending vascular bed assessment)

### Out of scope:

- Studies in off-label populations (with respect to geographies)
- Efficacy, safety and tolerability studies with inclisiran in pediatric population (<18 y)
- Studies in adults with HoFH and/or different populations than ASCVD and ASCVD equivalent
- CVOT trials
- Head-to-head efficacy/safety studies with other lipid lowering therapies
- Pre-Clinical Proposals (separate process)

### Studies involving drug for any indication(s) currently in clinical development and not yet approved

## **Iptacopan (Fabhalta)**

### **Without drug** (IgAN, C3G, IC-MPGN, aHUS, LN, AAV, FSGS)

- Additional ways to foster (earlier) diagnosis of glomerulopathies, beyond biopsy including diagnostic research leveraging use of artificial intelligence in IgAN, C3G, IC-MPGN, aHUS, LN, AAV, FSGS
- Identification of approaches that lead to better characterization, management and/or correlation with outcomes in IgAN, C3G, IC-MPGN, aHUS, LN, AAV, FSGS eg identification of biomarkers, genetic analysis or biopsy-based studies
- Burden of disease (clinical, economic and/or humanistic burden in IgAN, C3G, IC-MPGN, aHUS, LN, AAV
- Epidemiological studies - Prevalence, treatment patterns and RWE, sex/geography differences (incl. registries) in IgAN, C3G, IC-MPGN, aHUS, LN, AAV
- Role of the complement system in complement mediated kidney diseases

### **With drug** (IgAN, C3G, IC-MPGN)

- Mechanistic studies using iptacopan including biopsy in IgAN C3G, IC-MPGN
- Subgroups of patients that are included in the overall study population in indications in the iptacopan development program in IgAN, C3G, IC-MPGN
- Studies evaluating iptacopan in transplant patients with recurrent IgAN or recurrent C3G
- Evaluation/biomarker analysis for subgroups of patients included in the overall study population in IgAN, C3G and IC-MPGN
- Preclinical research studies in IgAN, C3G and IC-MPGN

- Studies investigating combination, sequencing of targeted treatments in IgAN

#### **Out of scope** (with drug)

- Pediatric studies
- Studies exploring different dosing regimens to those currently being evaluated in current clinical development program
- Head-to-head comparisons
- Studies including patients with GFR <20 ml/min/1.73m<sup>2</sup>

#### **Pelacarsen**

##### Without drug

- Epidemiology associated with elevated Lp(a)
  - Patient characterization, identification, and genetic risk across sub-groups
  - Plaque characteristics and differences across patient sub-groups
  - Association & impact on different types of CVD (ischemic stroke, CAVS, PAD), various vascular beds, and other diseases (e.g., AF, kidney disease, diabetes)
- Distinct and unique pathophysiology of Lp(a)
  - Insights on the pro-inflammatory or pro-thrombotic mechanisms impacted by Lp(a)
  - Unique features of Lp(a)
- Quantification of Lp(a) role in CV risk assessment tools
  - Quantification of Lp(a) contribution to global CV risk and in light of other CV risk factors
  - Risk score calculators incorporating Lp(a)
  - Patient perception on contribution of Lp(a) to CVD and CV risk
- Lp(a) testing and global CV risk management
  - Implementation of Lp(a) testing in CVD management pathways
  - Clinical and economic value of Lp(a) testing
  - Guidance on management of currently modifiable risk factors in the setting of elevated Lp(a)

##### Out of scope:

- Comparison / association with LDL-C
- Studies involving drug for any indication(s) currently in clinical development and not yet approved

#### **Sacubitril/Valsartan (Entresto)**

##### **Heart Failure**

- RWE or Implementation Science studies on improvements of HF care through increase in GDMT
- RWE studies with sac/val in Chronic Heart Failure with reduced EF
- RWE studies with sac/val in Chronic Heart Failure with mildly-reduced or preserved EF - in geographies where it is in-label
- RWE studies with sac/val in HTN - in geographies where it is in-label

##### Out of scope:

- Comparative effectiveness studies vs other MoA, e.g. SGLT2i, MRA, BB
- Studies in non-cardiovascular disease
- Studies in patients with valvular disorders not related to HF
- Studies in children (<18 years)
- Mechanistic Studies in HF including but not limited to those looking at:
  - Remodeling, fibrosis, inflammation
  - Cardiac function (including diastolic function)
  - Cardiac biomarkers
- Studies in populations with specific, less well studied / documented HF etiologies, e.g. chemotherapy /toxicity induced HF

## **Zigakibart**

### Without drug

- Diagnosis and classification
  - Additional ways to foster (earlier) diagnosis of glomerulopathies (IgAN), beyond biopsy and its impact on outcomes
  - Validate outcome measures (endpoint validation, validation of definitions) including patient-related outcomes, treatment targets, partial remission / remission and relapse criteria in IgAN
- Pathophysiology and biomarkers
  - Role of APRIL system in IgAN, Gd-IgA1 and autoantibodies in IgAN Including the subtype characterisation
  - Identification of approaches that lead to better characterization, management and/or correlation with outcomes in IgAN eg identification of biomarkers, genetic analysis or biopsy-based studies
  - Predictive models for APRIL inhibition responses across disease phenotypes/genotypes
- Disease burden
  - Burden of disease (clinical, economic and/or humanistic burden) in IgAN
  - Epidemiological studies - Prevalence, treatment patterns and RWE, sex/geography differences (incl. registries) in IgAN Disease characteristics and clinical outcomes in patients with different racial and ethnic backgrounds, or populations so far underrepresented in clinical trials. Gender related differences.
  - Gaps in the optimal care and management of IgAN patients
  - Impact of patient education programs
  - Patient perspective on disease, treatment options and QoL

### With drug

- Pre-clinical
  - Mechanistic studies in IgAN
  - Preclinical evaluations aimed at demonstrating MoA-pathway activity and/or differentiation
- Clinical
  - Evaluation of zigakibart in expanded IgAN patient populations: Transplant patients with recurrent IgAN, IgA vasculitis with nephritis patients, Low proteinuria (0.5 – 1 g/d)

### Out of scope

- Pediatric studies
- Studies exploring different dosing regimens to those currently being evaluated in current clinical development program
- Head-to-head comparisons
- The value of tight control (treat to target) versus conventional management strategies in IgAN
- Risk prediction models for which patients may develop hypogammaglobulinemia
- Preclinical (comparison) studies (vs APRIL/BAFF or APRIL/BLyS) and other IgAN treatments
- Duration and withdrawal of therapy / impact of treatment breaks
- Combination evidence
- Studies including patients with GFR <20 ml/min/1.73m<sup>2</sup>
- Vaccine titer studies or b-cell subset characterization

### Gene Therapies

## **Zolgensma IV**

### **Areas of interest by product**

- Demonstrating or validating care needs for SMA populations post OAV101 Treatment-safety related items
- Expansion of treatment with OAV101 to patient populations not included in clinical trials (e.g. older/heavier, 4 copies, switch therapy, ambulatory)
- Value of OAV101: Cost of care, Quality of life, and Caregiver Burden-Cost effectiveness
- Methods/Processes to assess the efficacy and durability of OAV101 (e.g. bulbar function)
- Biomarkers for efficacy

## **Out of scope**

- Clinical Trials involving OAV 101 re-dosing
- Study of OAV101 alternative doses/maximum dose
- Head-to-head comparison with other therapies and combination with other MDT
- Basic Science research that request use of OAV101

## **OAV101 IT**

### **Areas of interest by product**

- Interventional Studies of OAV IT in patients not included in clinical trials (e.g. ambulant SMA patients, severe scoliosis)
- Non-interventional Studies of OAV IT assessing sleep, bulbar function, scoliosis and respiratory function, head steadiness and independence.
- Studies on biomarkers assessing clinical response to OAV IT

## **Out of scope**

- Clinical Trials involving OAV 101 re-dosing
- Study of OAV101 alternative doses/maximum dose
- Head-to-head comparison with other therapies and combination with other MDT
- Basic Science research that request use of OAV101

## Global Health

### **Adakveo, Ryverna (Crizanlizumab, SEG101)**

- Studies with crizanlizumab in sickle cell disease and related complications
  - e.g- renal, leg ulcer, stroke, AVN, adolescents with SCD, priapism, splenic sequestration, VOCs
- Mechanistic studies with crizanlizumab
- Predictors of response to crizanlizumab
- SCD biomarkers

#### Out of scope:

- IIT requests from countries outside of US, SSA, Brazil
- IIT requests in non-SCD indications

### **HU, HU-FCT (Hydroxyurea)**

- Studies with HU in sickle cell disease and organ protection
  - e.g., spleen, lungs, kidneys
- Societal and economic impact of HU/HU-FCT on LMIC
- Studies with HU-FCT looking at treatment/stroke prevention in LMIC
- HU-FCT preference by caregivers

#### Out of scope

- IIT requests from countries outside of SSA, Brazil and India
- IIT requests in non-SCD indications

## Immunology

### **Ianalumab**

#### **Clinical data, outcomes & RWE (with drug):**

- RWE studies on clinical effectiveness and safety of Ianalumab in Sjogren's disease
- Clinical outcomes with Ianalumab across different manifestations and domains of Sjogren's disease
- Clinical outcomes with Ianalumab by gender, race, skin of colors, ethnic minorities and access to health care systems in Sjogren's disease
- Research investigating clinical impact of Ianalumab on Sjogren's disease systemic and organ complications such as

neuropathies, interstitial lung disease, renal disease, vasculitis, etc

#### **Implementation Science/HCS research.**

- Population-based epidemiology studies investigating the impact of autoimmune diseases on patients; comorbidities; studies of real-world treatment patterns (incl. e.g. overuse of corticosteroids, delays in systemic therapies initiation or Treat-to-Target approaches, etc)
- Identification of predictors and patient characteristics associated with rapid progression or poor outcomes in autoimmune diseases
- Impact of early intervention and treat-to-target on patient outcomes
- Impact of systemic treatments on prevention or reduction of long-term comorbidities and complications in autoimmune diseases
- Research utilizing novel imaging modalities for early diagnosis and monitoring of treatment responses
- Research evaluating treatment impact on patients' symptoms, such as fatigue, pain, mental and sexual well-being,
- Research evaluating patients perspectives in terms of unmet needs, current treatment satisfaction, disease management, treatment adherence, PROs, and shared decision-making across autoimmune diseases

#### **Exploratory/ mechanistic studies:**

- Role of B-cells in the pathogenesis of Sjogren's disease, Systemic Lupus Erythematosus, Systemic Sclerosis, and other autoimmune conditions
- Impact of BAFF blockade on Sjogren's disease, Systemic Lupus Erythematosus, Systemic Sclerosis, and other autoimmune conditions
- Identification and validation of new clinical outcome measures or PROs for clinical trials or real-world practice use across autoimmune diseases
- Studies employing digital or AI based technologies e.g. in silico models, machine learning techniques, telemedicine etc. to support clinical diagnosis, clinical management, prediction of disease trajectories, prediction of treatment responses

#### **Out of scope**

- Studies on safety topics e.g. infections (tuberculosis, HIV, viral hepatitis), high-risk patients
- Studies with combination biologics
- Clinical comparative studies with other treatments
- Pediatric studies
- Studies exploring different dosing regimens as currently investigated

#### **Secukinumab (Cosentyx)**

#### **Indications: axSpA (axial spondyloarthritis), incl. r-axSpA (radiographic) and nr-axSpA (non-radiographic)**

#### **Clinical data, outcomes & RWE:**

- Long term RWE studies on clinical efficacy, structural progression & safety of secukinumab
- Clinical outcomes with Secukinumab across different manifestations of axSpA , by gender and race

#### **Implementation Science/HCS research.**

- Identification of Predictors of structural progression and treatment algorithm related to structural progression
- Impact of early intervention and treat-to-target on patient outcomes
- impact of Secukinumab on prevention or reduction of Comorbidities
- Research Use of Novel imaging modalities for early diagnosis, pathogenesis of disease and monitoring of Secukinumab response
- Evaluate the impact of Secukinumab and treatment strategy to reduce Fatigue and pain

#### **Exploratory/ mechanistic studies:**

- New classification criteria of AxSpA and differences in pathogenesis of axSpA vs. axial PsA.
- Role of IL-17A in the pathogenesis of axial, peripheral manifestations and comorbidities of AxSpA
- Role of IL-17A across the spectrum of spondyloarthritides (SpA)

#### **Out of scope**

- Studies on safety topics e.g. infections (tuberculosis, HIV, viral hepatitis), high-risk patients
- Studies with combination biologics
- Clinical comparative studies with other treatments

### **Indications: Psoriatic arthritis (PsA)**

#### **Clinical data, outcomes and RWE:**

- Long term RWE studies on clinical efficacy, inhibition of structural progression & safety of secukinumab
- Long term RWE studies on efficacy, safety and treatment strategy in juvenile PsA (JPsA) and enthesitis-related arthritis (ERA)
- Clinical outcomes with Secukinumab in key manifestations of PsA, by gender, race, ethnic minorities and access to health care systems
- Clinical outcomes with Secukinumab in specific phenotypes (Axial PsA, skin predominant , nail/dactylitis, Oligoarticular predominant)

#### **Implementation Science/HCS research:** cost-effectiveness, resource utilization and guideline implementation

- Impact of early treatment and treat-to-target on patient outcomes and resource utilization
- Impact of Secukinumab on prevention or reduction of Comorbidities (e.g.CV, metabolic)
- Research studies on Novel imaging for early diagnosis and monitoring of Secukinumab response
- Evaluate the impact of Secukinumab to reduce Fatigue and pain

#### **Exploratory/ mechanistic studies:**

- Role of IL-17A in the pathogenesis of Axial PsA and differences with pathogenesis of. axial PsA vs axSpA
- Roles of different cytokine pathways in the key manifestations of PsA notably axial disease, enthesitis, nail-dactylitis

#### **Out of scope**

- Studies on safety topics e.g. infections (tuberculosis, HIV, viral hepatitis), high-risk patients
- Studies with combination of other biologics
- Comparative studies with other treatments

### **Indications: Psoriasis (PsO)**

#### **Clinical data, outcomes and RWE:**

- Long term RWE studies on clinical efficacy, & safety of secukinumab, risk factors and prevention of the transition period of PsO to PsA
- Clinical outcomes with Secukinumab by gender, race, skin of colors, ethnic minorities and access to health care systems
- Long term RWE studies on efficacy, safety and treatment strategy in pediatric PsO

#### **Implementation Science/HCS research:**

- Impact of early intervention strategy on disease modification in PSO and resource utilization
- Research program designed for early diagnosis and characterization of PSO patients at risk of PsA : disease burden, risk factors, screening tools/app, novel imaging

#### **Exploratory/ mechanistic studies:**

- role of IL-17A in the pathogenesis of the transition period PsO to PsA
- Mechanistic study of Secukinumab in Early PsO

### **Out of scope**

- Studies on safety topics e.g. infections (tuberculosis, HIV, viral hepatitis), high-risk patients
- Studies with combination other biologics
- Comparative studies with other treatments

## **Indications: Hidradenitis Suppurativa**

### **Clinical data, outcomes and RWE:**

- Early intervention with Sec and impact on disease progression (including imaging techniques, such as ultrasound)
- Clinical outcomes in subpopulations (e.g. disease phenotypes, Black / African American, super-responders,..)
- Integrating surgical procedures with the administration of Secukinumab for the treatment of HS. (effectiveness and Safety)
- HS comorbidities (Mental Health, Obesity, CV)
- Effects of lifestyle intervention on HS treatment with Secukinumab

### **Implementation Science / HCS research:**

- Quality of care, cost-effectiveness, resource utilization, and guidelines implementation
- AI/ML algorithms and big data approach to improve diagnosis and treatment of HS
- Development and validation of scoring tools / PROs

### **Exploratory/ mechanistic studies:**

- Translational research on pathophysiology - role of IL-17A and other pathways in HS over the course of the disease , and in specific aspects of the disease e.g., "Fistula/tunnel development"
- Biomarkers to predict disease and treatment outcomes

### **Out of scope**

- Comparative studies with other treatments
- Combination studies for Secukinumab with other biologic agents
- IV dosing for HS

## **Indications: GCA and PMR**

### **Pathophysiology and biomarkers**

- Biomarkers to monitor subclinical disease activity, predict prognosis and treatment outcomes
- Effects of a mechanism-based approach to therapy
- Pathways involved in refractory/flaring GCA
- Biomarkers to predict drug/GC toxicity

### **Diagnosis and classification**

- Standardization of clinical trial endpoints
- Validation of the definition of remission, response, relapse and disease subtypes of importance
- Use of the different imaging techniques for vascular activity, damage assessment and follow-up

### **Treatment and treatment outcomes**

- Implementation Science/HCS research: quality of care, cost-effectiveness, resource utilization, and guidelines implementation
- Disease characteristics and clinical outcomes in patients with skin of color, ethnic minorities, or populations so far underrepresented in clinical trials. Gender related differences

- Assessment of prognosis by demographic, clinical and histological data
- Predictors of response, remission or relapse
- Validation of patient-reported outcomes
- Predictive models for IL-17A inhibition responses across disease phenotypes
- Effect of secukinumab on the development of future vascular complications

#### **Out of scope**

- Effect of secukinumab on the development of future vascular complications
- Combination studies of secukinumab with other biologic agents
- The role of ultrasound for guiding temporal artery biopsy, specific treatment of organ complications

#### **Remibrutinib in Chronic Urticaria**

**Disease:** Chronic Urticaria – CSU (chronic spontaneous urticaria) and CindU (chronic inducible urticaria)

**Product:** Remibrutinib

#### **Areas of interest by product**

##### Disease Related Research:

- Population-based epidemiology studies; studies investigating the impact of urticaria on patients; comorbidities; studies of real-world treatment patterns (incl. e.g. overuse of corticosteroids, impact on sleep)
- Studies investigating biomarkers in urticaria aiming to identify predictors of chronic urticaria in patients with acute episodes, biomarkers predictive of treatment response, biomarkers correlating with the time-course of CSU, biomarkers of permanent remission or relapse, including with remibrutinib
- Studies employing digital technology e.g. *in silico* models, machine learning techniques, telemedicine etc. to predict disease trajectories, treatment response, disease modification, etc.
- Studies investigating innovative tools to support urticaria management, e.g. digital applications, sleep related
- Long-term CSU observational registries and secondary use of data
- Studies investigating patient preference

##### Clinical Studies:

- Studies with remibrutinib in CindU
- Studies with remibrutinib focusing on angioedema only

##### Mechanistic Studies

- Mechanistic studies assessing the effects of remibrutinib on mast cells, basophils, B-cells *in vitro* or *ex vivo*
- Studies investigating the disease modifying potential of remibrutinib, including pre-clinical *in vitro* or *ex vivo* research

#### **Out of scope**

- Head-to-head comparisons of remibrutinib with other active treatments
- Studies investigating remibrutinib in combination with biologics
- Alternative dosing regimens to 25 mg b.i.d developed in the CSU phase 3 clinical program

#### Neuroscience

#### **Ofatumumab (Kesimpta) and siponimod (Mayzent) - Multiple sclerosis (MS)**

- Focus on prognosis and diligent monitoring of patients with MS (including data and digital):
  - Markers for disease prognosis, disease monitoring, and/or risk mitigation
  - New or improved quantitative outcome measures in MS, including next-generation technology and patient assessment technologies
  - Integration of markers/outcome measures to establish disease stability or disease control, disease progression
- Mechanistic studies looking at differentiating Novartis compounds from other DMTs

**Disease:** Relapsing Multiple Sclerosis

**Product:** Remibrutinib

### **Areas of interest by product**

#### Follow the science

- Impact on the immune system in and outside the CNS – clinical and preclinical studies
- Direct CNS effects (i.e. microglial activity, synaptogenesis, neuronal function) and correlation with clinical outcomes beyond relapses (e.g. PIRA, disability improvement) and with some patient outcomes (e.g. cognition, fatigue)
- Impact on chronic inflammation and correlation with linked clinical and preclinical outcomes (disability measures, such as EDSS/MSFC, imaging measures, fluid biomarkers)

#### Safety related:

- BTKi – vaccine response
- Pregnancy registries (in line with initiatives already in place)

#### Identify unmet need under current DMTs:

- Patient preference
- Tolerability and safety concerns (what, when, to whom – patient profile-)
- Effectiveness gaps under HET (what, when, to whom – patient profile -)

### **Out of scope**

*Progressive phenotypes of MS (naSPMS or PPMS); hepatotoxicity*

Oncology

### **Asciminib (Scemblix)**

Studies in adult patients Chronic Myeloid Leukemia in Chronic Phase (CML-CP) in early treatment lines, investigating:

- Long-term safety and tolerability
- Clinical efficacy and safety in real-world setting
- Treatment sequencing
- Patient-reported outcomes (PROs) and Quality of Life (QoL)
- Patients with CML-CP and additional T315I mutation
- Response to asciminib in patients with pre-existing mutations other than T315I or treatment approaches in patients with emerging mutations under asciminib, including compound mutations

Studies exploring additional high-need patient populations other than CML-CP:

- Patients with Philadelphia-positive acute lymphoblastic leukemia (Ph+ALL)
- Exploratory high risk CML populations such as patients with additional genomic alterations
- CML-AP/BC

Studies in Treatment Free Remission (TFR)

- Studies aiming to improve deep molecular responses, increase the eligibility for TFR attempts or reduce the risk of relapse after treatment discontinuation
- Combination approaches of asciminib with non-ATP-TKI compounds

Studies providing insight into mechanistical action of asciminib, potential on- and off target effects and its use against additional mutations in patients with CML.

Out of scope:

- Use of asciminib in ABL-independent diseases

## Iptacopan (LNP023)

### With Drug

1. Mechanistic studies in Paroxysmal Nocturnal Hemoglobinuria (PNH);
2. Studies evaluating factors associated with or predictive of treatment outcome in PNH;
3. Studies exploring preferences in oral treatment administration approaches in PNH

### Without Drug

1. Role of complement system in complement-mediated PNH, Immune Thrombocytopenia Purpura (ITP) and Cold Agglutinin Disease (CAD);
2. Approaches to facilitating and expediting diagnosis of PNH and CAD;
3. Identification of biomarkers that leads to better characterization, management or correlation with outcomes in PNH, ITP and CAD;
4. Burden of disease (clinical, economic, and/or humanistic burden) – PNH and CAD;
5. Epidemiology studies (incl. registries) – PNH and CAD

### Out of scope:

- Pediatric studies
- Studies exploring different dosing regimens as currently investigated
- Any study, which combines iptacopan with immunosuppressant and anti-C5 treatments
- Head-to-head comparisons
- Studies in other hematology diseases

\*\* Strategic areas of interest for iptacopan (IgAN, C3G, aHUS, MN, LN), please also refer to the Cardiovascular, Renal & Metabolism section

### [177Lu] Lu-DOTA-TATE (Lutathera®)

- Studies (other than prospective design) describing optimal timing and sequence of treatment in advanced or metastatic GEP-NET patients
- Studies of Lutathera in advanced or metastatic NET patients in combination with other anti-cancer treatments, including chemotherapy (also bolus 1L), immuno-oncology therapies, tyrosine kinase inhibitors (TKIs), PARP-inhibitors, CDK4/6 inhibitors, or other upcoming treatments (if supported by MoA rationale)
- Retrospective studies describing long-term safety or health economic aspects
- Studies on biomarkers to predict and prognosticate treatment in GEP-NET

### [177Lu] Lu-PSMA-617 (Pluvicto®)

#### Indication: Prostate Cancer

- mHSPC, mCRPC - **Sequencing RWE** - Sequential use of different radioligand therapies (alpha- or beta-emitter); Treatment optimization
- HRLPC, BCR - **Combinations** - Efficacy and safety of 177Lu-PSMA-617 combinations to overcome resistance and to improve efficacy outcomes
- mHSPC (OMPC) - **Low volume disease** - Efficacy and safety of 177Lu-PSMA-617 in low volume disease
- mHSPC - **Alternative dosing** - Adaptive and alternative treatment regimens with 177Lu-PSMA-617 monotherapy or in combinations
- HRLPC, BCR - **Treatment effect in earlier stages** - Efficacy and safety of radioligand therapy (alpha- or beta-emitter)
- mHSPC, mCRPC - **Subpopulations** - Impact of 177Lu-PSMA-617 efficacy and safety in patient populations with sub-optimal outcomes, including patients distinct mutations (e.g., PTEN-loss, AKT, DDR), patients CNS mets, liver mets etc.
- All disease stages - **Long-term safety** - Retrospective analysis to predict long-term safety events
- HRLPC, mHSPC, 1L-2L mCRPC - **Translational Research** - Treatment effect on disease biology
- HRLPC, mHSPC, 1L-2L mCRPC - **Imaging** - Understanding PSMA expression in different stages of prostate cancer

- Brain Metastasis (secondary malignancies)
- Ovarian Ca
- NSCLC
- GBM: microenvironment and translational research (MoA deeper understanding)
- GBM: Other mode of administration in GBM (not IV)
- Hepatocellular Carcinoma
- High grade gliomas
- Others PSMA-expressing/PET-avid tumors
- Imaging studies
- Pediatric indications

### **Ribociclib (Kisqali)**

- HR+/HER2- studies in breast cancer
  - Exploring data on CDK4/6 inhibitor rechallenge
  - Exploring ribociclib with novel/emergent compounds
  - Utilizing real world data and/or digital health technologies
  - Utilizing patient reported outcomes (PRO)

Out of scope:

- Any area outside HR+/HER2- breast cancer
- Any study in overlap with ongoing Novartis-sponsored/supported studies

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### **List of links present in page**

1. <https://www.novartis.com/node/662876>
2. <https://www.novartis.com/node/662876/printable/print>
3. <https://www.novartis.com/node/662876/printable/pdf>