NOVARTIS

Investigator initiated trials / studies (clinical) and investigator initiated research (non-clinical)

As part of our commitment to delivering innovative therapies to patients worldwide, Novartis believes in the need to support ethical independent clinical and non-clinical research conducted by qualified third-party investigators.

The value of the scientific research produced by third party sponsors is key to complementing Novartis-sponsored research by helping us to better understand the benefit/risk profile of our therapies, as well as enabling us to explore new opportunities addressing unmet medical needs.

The proposed research must offer meaningful scientific objectives and be supported by a valid study design. Privacy rights, safety and welfare of patients and animals shall be fully secured.

IITs are defined by Novartis as “studies with scientific and medical merit developed and sponsored by an independent investigator or academic sponsor. An IIT may be a clinical study conducted without the participation of Novartis, for which the IIT sponsor requests Novartis to provide either funding, drug product or both.”

IIRs are defined by Novartis as “non-clinical research conducted by an independent third-party sponsor to evaluate the effects, properties or profile of a Novartis drug that is conducted in animals or in vitro assays or utilizes previously collected human tissue*.”

Note: Any monetary request intended for a specified purpose to support medical/scientific research, education, policy initiatives, and patient advocacy activities, where Novartis will receive no benefit, should not be considered as IIT or IIR as these are classified as Grants. Read more information for Grants.

Novartis position on Investigator Initiated Trials (IITs) and Investigator Initiated Research (IIRs) (189 KB) IIT guidance for investigators (719 KB)

Strategic areas of interest

We welcome unsolicited research proposals from qualified investigators in our strategic areas of interest which we list below. Well-thought through studies that enhance our delivery of innovative therapies to more patients worldwide, enhance patient care, and align with our strategic areas of interest will be considered. If you have questions on any steps of the process or wish to discuss your study concept, please feel free reach out to your local Novartis contact (e.g. MSL, Medical Advisor) for support.

To broaden Novartis’ Commitment to Patients and Caregivers and encourage the wider research ecosystem to improve outcomes for patients and change the practice of medicine, we encourage qualified investigators to inform their research proposals and project executions with the insights of and engagement with people living with conditions of study. We encourage the research community to actively seek out and listen to insights from the patient community to inform design, operations, and meaningful use of participant data for and with patients. Consider the available resources from TransCelerate’s Patient Experience Initiative, the IMI PARADIGM Patient Engagement Toolbox, and PFMD.org to enhance your project.

- Global – Strategic areas of interest
- US – Strategic 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^2)
    - 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^2 (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^2

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^2
- 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 spontaeous 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

Remibrutinib in RMS

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 paraclinical 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

Beyond GU

- 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

Oncology

Tisagenlecleucel (Kymriah)

- Essential factors for selecting patients for Kymriah (tisagenlecleucel) therapy to improve safety and/or response for their approved indications
- Essential factors for sequencing Kymriah (tisagenlecleucel) therapy with other therapies and determining outcomes for their approved indications
- Novel combinations of therapies with Kymriah (tisagenlecleucel) to improve response and/or safety for their approved indications
- Study outcomes of Kymriah (tisagenlecleucel) administered at various sites (e.g., in-patient, out-patient, community hospital, community practice) for their approved indications

Asciminib (Scemblix)

CML-CP in Earlier Lines (1L & 2L)

- Sequencing of TKIs, clinical efficacy, and safety in real-world setting
- Patient – reported outcomes (PROs) and Quality of life issues with current CML therapies
- Biomarkers for TFR and safety
- Long-term safety and tolerability
- Studies aiming to improve the eligibility to attempt TFR and reduce the risk of relapse after TFR attempts
- Response to asciminib in patients with pre-existing BCR::ABL1 mutations other than T315I, or treatment approaches in patients with emerging mutations under asciminib, including compound mutations

CML- BC and Ph+ ALL

- Efficacy and safety of Asciminib in selected ALL settings (PH+, Ph-Like)
- Exploratory high-risk advanced phase CML populations such as patients with additional genomic alterations
- TKI- based combinations addressing high unmet need populations (CML-AP/BC)

Out of scope

- Use of Non BCR-ABL diseases

Iptacopan (Fabhalta)

With Drug

- Mechanistic studies in PNH
- Studies evaluating complement factors associated with or predictive of treatment outcome in PNH
- Studies evaluating effectiveness, safety and management of Iptacopan in PNH patients treated in the real-world setting
- Studies evaluating PNH treated patients in the context of bone marrow disorders, such as AA, in the real-world setting
- Studies evaluating the role of factor B inhibition in hematologic complement mediated diseases

Without drug

- Complement mediated diseases in Hematology
- Role of complement system in disease evolution
- Approaches to facilitating and expediting diagnosis
- Identification of biomarkers that leads to better characterization, management or correlation with outcomes
- Burden of disease (clinical, economic, and/or humanistic burden)
- Epidemiology studies (incl. registries)

Out of scope

- Pediatric studies
- Clinical trials exploring different dosing regimens as currently investigated
- Clinical trials combining Iptacopan with immunosuppressant and anti-C5 treatments
- Head-to-head comparisons
- Studies in other non complement mediated hematologic diseases

Ribociclib (Kisqali)

HR+/HER2- Studies in Breast Cancer

- Exploring ribociclib with novel/emergent compounds
- Utilizing real-world data (RWD) and/or digital health technologies
- Enhances the treatment experience of patients

Out of scope

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

[177Lu]Lu-PSMA-617 (Pluvicto)

- Investigating retreatment or extended treatment with ^{177}Lu-PSMA-617
- Real-world evidence in prostate cancer for ^{177}Lu-PSMA-617
- Health disparities in advanced prostate cancer

177Lu DOTATATE (Lutathera) / 68Ga DOTATATE (Netspot)

GEP & Bronchopulmonary NET

- Re-treatment/Re-challenge with Lutathera (after initial 4 cycles)
- Combinations with other agents with potential to improve efficacy
- Sequencing studies
- Long-term safety
- Efficacy/Safety of Lutathera in specific patient subgroups

Other SSTR+ Tumors

- Role of Lutathera in the management of patients with other SSTR-positive tumors

NETSPOT for Imaging

- Role of Netspot in GEP-NET and other SSTR2+ tumors

FAP [177Lu] Lu-FAP-2286

Imaging Studies in FAP-expressing solid tumors

- Role of FAP PET in diagnosis, staging, clinical decision-making, and treatment response
- Studies exploring FAP PET as an imaging biomarker: Correlation with other biomarkers such as

histological/molecular/genetic subtype
- Understanding FAP expression in benign/inflammatory processes in relation to FAP RLT safety and patient selection for therapy

Therapeutic Studies

- Role of 177Lu-FAP RLT in FAP-expressing solid tumors
- Use of 177Lu-FAP RLT in combination with standard of care therapies and/or immuno-oncology agents
- Studies investigating the effect of 177Lu-FAP RLT in cancer-associated fibroblasts and tumor microenvironment
- Evaluation of optimal dosing regimens in subpopulations and combinations
- Correlation of RLT efficacy with predictive biomarkers and FAP PET uptake
- Studies exploring alternate routes of administration to improve safety and efficacy

^{225}Ac-PSMA-617 / ^{225}Ac-PSMA-R2

- Investigating alternative dosing regimens (cycles, frequency) with ^{225}Ac-PSMA-617 in mCRPC
- Radioligand therapy in neoadjuvant setting for localized prostate cancer
- Use of ^{225}Ac-PSMA-617 in adjuvant setting in combination with EBRT + ADT +/- abiraterone in patients with localized prostate cancer post prostatectomy with N1M0 on PSMA PET
- Use of ^{225}Ac-PSMA-617 post definitive therapy for localized prostate cancer with biochemical recurrence and PSMA-PET M0 disease
- Use of PSMA-targeted PET imaging agents in prostate cancer (e.g., patient selection, treatment assessment)
- Use of ^{225}Ac-PSMA-617 in combination with other agents in mHSPC or mCRPC
- Treatments up-regulating PSMA expression in prostate cancer
- Use of >6 cycles of ^{225}Ac-PSMA-617 in patients with mHSPC or mCRPC
- Use of ^{225}Ac-PSMA-617 in prostate cancer patients with distinct mutations (e.g., PTEN-loss, AKT, DDR)
- Use of ^{225}Ac-PSMA-617 in patients with low or no PSMA expression in mCRPC
- Real-world evidence in prostate cancer for ^{225}Ac-PSMA-617
- Health disparities in advanced prostate cancer
- Sequencing with 177Lu-PSMA-617

CRM
Pelacarsen

Non-drug IITs

<u>Epidemiology associated with elevated Lp(a)</u>

- Patient characterization, identification, and genetic risk across sub-groups
- Association & impact on different types of CVD (ischemic stroke, PAD), polyvascular disease, and other CV-related diseases

<u>Distinct and unique pathophysiology of Lp(a) related to CVD</u>

- Insights on the pro-thrombotic mechanisms impacted by Lp(a)
- Unique features of Lp(a)

<u>Patient perception on contribution of Lp(a) to CVD and CV risk</u>

<u>Lp(a) testing and global CV risk management</u>

- Implementation of Lp(a) testing in CVD risk evaluation
- Clinical and economic value of Lp(a) testing

Out of scope

- Comparison / association with LDL-C
- Non-cardiovascular related diseases

Inclisiran (Leqvio)

- ASCVD MOA – atherosclerotic plaque composition/changes
- Differentiation of inclisiran vs other LLTs in Real World setting – e.g., adherence, implementation

Atrasentan for IgAN Indication (Vanrafia)

Disease-related: including but not limited to IgAN, FSGS, Alport Syndrome, post-kidney transplant

- Studies evaluating the role of the endothelin pathway in proteinuric kidney diseases (e.g. IgAN, FSGS, Alport Syndrome, post-kidney transplant).
- Innovative diagnostic approaches beyond biopsy and prognostic approaches for IgAN and FSGS.
- Approaches to improve profiling (biomarkers, genetics, imaging, histopathology) of patients with IgAN and FSGS.
- Epidemiological studies and burden of disease (clinical, economic and/or humanistic burden) in patients with proteinuric kidney diseases.
- Patient journey mapping and practice change initiatives to improve outcomes and reduce disparities.

Drug-related

- Studies evaluating pre-clinical, mechanistic and clinical effects of atrasentan in patients with proteinuric kidney diseases (included, but not limited to IgAN, and post-kidney transplant), including biomarker analyses, specific patient subgroups, and broader physiological impacts (e.g. inflammation, fibrosis, and pain).
- Studies on combination strategies with atrasentan in IgAN.

Out of scope

- Pediatric studies (with drug).
- Studies exploring different dosing regimens than currently FDA-approved dose.
- Head-to-head comparisons with other approved products.
- Studies including patients with eGFR <15 ml/min/1.73m^2 (CKD stage 5).

Iptacopan

Disease-related: including but not limited to IgAN, C3G, IC-MPGN, aHUS, LN, AAV, FSGS, post-kidney transplant, IgAV with nephrits

- Studies evaluating the role of the complement system in complement-mediated kidney diseases.
- Innovative diagnostic approaches beyond biopsy and prognostic approaches for complement-mediated kidney diseases.
- Approaches to improve profiling (i.e. biomarkers, genetics, imaging, histopathology) of patients with complement-mediated kidney diseases.
- Epidemiological studies and burden of disease (clinical, economic and/or humanistic burden) in patients with complement-mediated kidney diseases.
- Patient journey mapping and practice change initiatives to improve outcomes and reduce disparities.

Drug-related

- Studies evaluating pre-clinical, mechanistic, and clinical effects of iptacopan in patients with complement-mediated kidney diseases (e.g. IgAN, C3G, IC-MPGN, aHUS, post-kidney transplant, IgAV with nephritis) including biomarker analyses, and specific patient subgroups (e.g. high crescent, RPGN, corticosteroid-resistant).
- Studies on combination strategies with iptacopan in IgAN.

Out of scope

- Pediatric studies (with drug).
- Head-to-head comparisons with other approved products.

- Studies including patients with GFR <20 ml/min/1.73m^2.

Neuroscience

Ofatumumab (Kesimpta)

Multiple Sclerosis

- The experience of use of OMB in sub-populations of RMS (e.g., AA and Hispanic patients, and age)
- The impact of OMB on MS comorbidities and patient-centric outcomes
- The therapeutic role of OMB in MS: Efficacy, safety, tolerability, use in treatment naive patients
- The impact of OMB on both fluid and digital biomarkers in MS
- The MS pathophysiology (including MoA of OMB and its effects on MS pathophysiology) and burden of disease of MS (including impact of OMB)
- The innovative neuroimaging techniques used to measure biomarkers of MS disease/MS inflammation/axonal integrity and function (including effects of OMB)
- The long-term impact on the immune system and long-term safety with B-cell therapies
- Different B-cell depleting therapies have a differential impact on the functioning of the immune system over time, especially on the non-B-cell compartment

Remibrutinib

Multiple Sclerosis

- The impact on CNS – BBB transmigration, microglial impact (activation)
- The impact on biology of progression – PET imaging impact, cognition, fatigue, depression outcomes
- The impact on imaging – SELs, PRLs, cortical lesions impact
- The role for remibrutinib in sequencing of treatments
- The proteome profiling effects of remibrutinib

Myasthenia Gravis

- Impact of remibrutinib on gMG
- Development of biomarkers and endpoint exploration for clinical trial use

Zolgensma IV

In Scope

- Demonstrating or validating care needs for SMA populations post Zolgensma IV Treatment-safety related items
- Value of Zolgensma IV : Cost of care, Quality of life, and Caregiver Burden-Cost effectiveness
- Methods/Processes to assess the efficacy and durability of Zolgensma IV (e.g. bulbar function)
- Biomarkers for efficacy

Out of Scope

- Clinical Trials involving Zolgensma IV re-dosing
- Study of Zolgensma IV alternative doses/maximum dose
- Basic Science research that request use of Zolgensma IV

OAV101 IT

In Scope

- Interventional Studies of OAV101 IT in patients not included in clinical trials (e.g. independently ambulant SMA patients, patients >18 years, severe scoliosis) and patients with AAV9 titers >1:50
- Non-interventional Studies of OAV101 IT assessing sleep, bulbar function, scoliosis and respiratory function, head steadiness and independence.
- Studies on biomarkers assessing clinical response to OAV101 IT

Out of Scope

- Clinical Trials involving OAV101 IT re-dosing or OAV IT dosing following OAV IV
- Study of OAV101 IT alternative doses/maximum dose
- Head-to-head comparison with other therapies and combination with other MDT
- Studies of OAV101 IT in patients under 2 years of age.
- Comparative studies between Zolgensma IV and OAV101 IT

Immunology
Ianalumab

- Sjogren's disease US epidemiology
- Sjogren's disease classification and clinical assessment
- Sjogren's disease progression: use of ultrasounds, clinical assessments and or biomarkers
- Sjogren's symptoms: evidence generation with existing PROs or new SjD symptom modalities
- Sjogren's disease organ domains: generation of evidence in key disease domains
- Sjogren's disease and concomitant conditions (i.e., rheumatoid arthritis, lupus, etc.) and outcomes
- Sjogren's disease in subpopulations (AA, Hispanic, etc.) and outcomes
- Sjogren's disease burden: clinical, social, economical, and humanistic aspects

Remibrutnib -Urticaria

Disease Related Research

- Population-based epidemiology studies; studies investigating the impact of urticaria on patients; studies of real-world treatment patterns (incl. e.g. overuse of corticosteroids, impact on sleep); studies of patient preference, patient experience and satisfaction (qualitative).
- Studies employing digital technology e.g. *in silico* models, AI-enabled/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/CindU observational studies and secondary use of data.

Clinical Studies

- Studies with Remibrutinib in CSU/CindU,
- Poof of concepts in new allergic and dermatologic indications.

Mechanistic Studies

- Mechanistic studies assessing the effects of Remibrutinib on mast cells, basophils, B-cells and other relevant immune pathways *in vitro* or *ex vivo.*

Optional 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.

How do I submit an IIT/IIR request?

IIT/IIR requests are submitted via the Novartis Grants, External Studies and Managed Access System or GEMS portal. Please submit your concept by clicking here.

Guidance on using the GEMS portal is available here:

Novartis GEMS portal external user guide (PDF 0.2 MB)

For IIT related questions, please contact the medical team in your Novartislocal country office.

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