Clinical Trial Summary

July 2024

Better Health, Brighter Future

Overview of Clinical Trials

	LCM[1]		NME[2]
GASTROINTESTINAL AND INFLAMMATION	ENTYVIO IV – Pediatric CD/UC ENTYVIO IV GvHD – Prophylaxis ENTYVIO IV – UC Combo Induction ENTYVIO IV – CD Combo Induction ENTYVIO IV – Optimal Treatment Target ALOFISEL – Pediatric Complex Perianal Fistulas in CD Maralixibat – PFIC, ALGS	Zasocitinib (TAK-279) – Plaque Psoriasis x2 Zasocitinib (TAK-279) – Active Psoriatic Arthritis Zasocitinib (TAK-279) – Crohn's Disease, UC ADZYNMA (TAK-755) – cTTP, iTTP Fazirsiran – AATD Assoc. Liver Disease Mezagitamab – ITP, IgAN TAK-227 – Active Celiac Disease Zamaglutenase – Active Celiac Disease	TAK-101 – Celiac Disease Rusfertide – Polycythemia Vera
NEUROSCIENCE		Soticlestat – DS, LGS TAK-861 – NT1, NT2 Danavorexton – OSA, Postanesthesia Recovery	TAK-341 – Multiple System Atrophy TAK-594 – Frontotemporal Dementia
ONCOLOGY	ICLUSIG – CML ICLUSIG – 1L Ph+ ALL NINLARO – In-class Transition (MM6)	Dazostinag – Solid Tumors TAK-500 – Solid Tumors TAK-186 – EGFR+ Solid Tumors	TAK-280 – B7-H3+ Solid Tumors TAK-012 – AML Mirvetuximab – PROC
OTHER RARE DISEASES	ADYNOVATE – Pediatric HemA, HemA China VONVENDI – Pediatric vWD LIVTENCITY – Pediatric CMV Infection Post Transplant		
PLASMA-DERIVED THERAPIES	HYQVIA – PID, CIDP/MMN Japan TAK-881 – PID TAK-330 - Prothromplex – DOAC Reversal GLOVENIN-I – AE Japan		
VACCINES	QDENGA – Dengue Vaccine		

1. LCM: Life cycle management programs or marketed assets in development seeking new indications, new geographic expansions, fulfillment of regulatory requirements, new formulations/method of use, and/or enhancement in commercial/competitive profile.
2. NME: New molecular entity

Overview of Clinical Trials

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ENTYVIO (VEDOLIZUMAB):
GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB

Study	NCT04779320	NCT04779307
Indication	Crohn's disease in pediatric patients	Ulcerative colitis in pediatric patients
Phase	**Phase III**	**Phase III**
# of Patients	N = 120	N = 120
Target Patients	Pediatric patients with Crohn's disease between 2 to 17 years old at the time of randomization for Study NCT04779320	Pediatric patients with ulcerative colitis between 2 to 17 years old at the time of randomization for Study NCT04779307
Arms/ Intervention	**Induction period:** • Subjects ≥30 kg will receive open–label vedolizumab, 300 mg IV • Subjects >15 to <30kg open–label vedolizumab, 200 mg IV • Subjects 10 to 15 kg open–label vedolizumab 150 mg IV **Maintenance period:** • ≥30 kg weight cohort): Vedolizumab IV 300 mg or 150 mg (Q8W) • >15 <30 kg weight cohort: Vedolizumab IV 200 mg or 100 mg (Q8W) • 10 to 15 kg weight cohort: Vedolizumab IV 150 mg or 100 mg (Q8W	**Induction period:** • Subjects ≥30 kg will receive open–label vedolizumab, 300 mg IV • Subjects >15 to <30kg open–label vedolizumab, 200 mg IV • Subjects 10 to 15 kg open–label vedolizumab 150 mg IV **Maintenance period:** • ≥30 kg weight cohort): Vedolizumab IV 300 mg or 150 mg (Q8W) • >15 <30 kg weight cohort: Vedolizumab IV 200 mg or 100 mg (Q8W) • 10 to 15 kg weight cohort: Vedolizumab IV 150 mg or 100 mg (Q8W
Primary endpoint and key secondary endpoint(s)	**Primary:** • Co-primary 1 (based on PCDAI): Clinical remission at Week 54 • Co-primary 2 : Endoscopic response at Week 54 **Secondary:** • Clinical and endoscopic remission at Week 14 • Clinical and endoscopic remission at Week 54 • Sustained clinical and endoscopic remission at Week 54 • Corticosteroid-free remission at Week 54 • PK/AVA	**Primary:** • Clinical remission at Week 54, based on the modified Mayo score **Secondary:** • Clinical remission at Week 14 • Sustained clinical remission at Week 54 • Sustained endoscopic remission • Endoscopic response at Week 14 and at Week 54 • Corticosteroid-free clinical remission at Week 54 • PK/AVA
Study start date	April 2022	October 2021

ENTYVIO (VEDOLIZUMAB): *GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB*

Study	NCT03657160
Indication	Graft-versus-Host Disease (GvHD) prophylaxis IV
Phase	**Phase III**
# of Patients	N = 343
Target Patients	Patients undergoing allogeneic hematopoietic stem cell transplantation (Allo-HSCT) in the prophylaxis of intestinal acute GvHD (aGvHD)
Arms/Intervention	• **Arm 1:** Vedolizumab 300 mg at Days -1 (baseline), +13, +41, +69, +97, +125, and +153 • **Arm 2:** Placebo at Days -1 (baseline), +13, +41, +69, +97, +125, and +153
Primary endpoint and key secondary endpoint(s)	**Primary:** • Intestinal aGvHD-free survival by Day +180 after Allo-HSCT
Study start date	February 2019

ENTYVIO (VEDOLIZUMAB): *GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB*

Study	NCT06095128	NCT04259138[1]
Indication	Ulcerative colitis (UC)	Ulcerative Colitis (UC)
Phase	**Phase IV** ***ExiGem***	**Phase IV** ***VERDICT***
# of Patients	N = 65	N = 660
Target Patients	Adult (18 to 65) patients with moderate to severely active ulcerative colitis who have failed no more than 2 TNF antagonists.	Moderately to severely active UC
Arms/ Intervention	Vedolizumab (IV) 300 mg + Tofacitinib (PO) 10 mg • Participants will receive Vedolizumab 300 mg , intravenous (IV) infusion, at Week 0, Week 2 and Week 6 along with Tofacitinib 10 mg, tablets, orally, twice daily from Week 0 to Week 8. • Participants with clinical response at Week 8 will transition to receive vedolizumab 300 mg IV infusion every 8 weeks (Q8W) through Week 46.	Participants will be randomized to 1 of 3 groups, each with a different treatment target. Treatment targets will be defined as: **Group 1:** corticosteroid-free symptomatic remission **Group 2:** corticosteroid-free endoscopic + symptomatic remission **Group 3:** corticosteroid-free histological + endoscopic + symptomatic remission Participants will be assigned a treatment algorithm (A,B, or C) based on their existing UC treatment at the time of entry. Treatment algorithms may include the use of vedolizumab.
Primary endpoint and key secondary endpoint(s)	Percentage of Participants Achieving Clinical Remission at Week 8 Based on Complete Mayo Score • Clinical remission based on complete Mayo Score is where a participant achieves complete Mayo Score ≤2 points with no individual subscore >1 at Week 8.	Difference in Time to UC-related Complication Between Treatment Target Groups 1 and 3 (Time Frame: From the date of treatment target achievement until the date of first UC-related complication until end of study (Week 96), whichever came first)
Study start date	January 2024	September 2020

 1. Collaborative study led by Alimentiv in collaboration with Takeda

ENTYVIO (VEDOLIZUMAB): *GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB*

Study	NCT06045754
Indication	Crohn's disease (CD)
Phase	**Phase IV** ***EXPLORER 2.0***
# of Patients	N = 150
Target Patients	Adults (18 to 65) with moderate to severe Crohn's disease who have experienced inadequate response, loss of response or intolerance to either one prior interleukin [IL] antagonist (Cohort 1) or tumor necrosis factor inhibitor [TNFi] (Cohort 2).
Arms/Intervention	**Part A, Cohort 1**: Vedolizumab + Adalimumab • Participants will receive vedolizumab IV 300 mg, at Weeks 0, 2, and 6, then every 8 weeks (Q8W) until Week 22 and adalimumab SC 160, 80, and 40 mg at Weeks 0, 2, and 4, respectively, then 40 mg every 2 weeks (Q2W) until Week 26. **Part A, Cohort 2**: Vedolizumab + Ustekinumab • Participants will receive vedolizumab IV 300 mg, at Weeks 0, 2, and 6, then Q8W until Week 22 and ustekinumab IV 520, 390, or 260 mg (weight-based), then SC 90 mg 8 weeks after initial IV dose, then Q8W until Week 24. **Part B: Vedolizumab Monotherapy** • Participants who achieve clinical remission in Part A will receive vedolizumab IV 300 mg monotherapy, Q8W from Week 30 until Week 46.
Primary endpoints	**Part A:** Percentage of Participants Achieving Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 26 • Clinical remission is defined as a CDAI score of ≤150 points. **Part B:** Percentage of Participants in Clinical Remission Based on the CDAI at Week 52 • Clinical remission is defined as a CDAI score of ≤150 points.
Study start date	March 2024

ENTYVIO (VEDOLIZUMAB): *GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB*

Study	NCT06227910
Indication	Crohn's Disease (CD)
Phase	**Phase IIIb** ***VICTRIVA***
# of Patients	N = 396
Target Patients	The participant has a confirmed diagnosis of moderately to severely active CD
Arms/Intervention	1. Experimental: Induction Period: Vedolizumab + Upadacitinib: Participants will receive vedolizumab 300 mg intravenous (IV) infusion at Weeks 0, 2, 6 and 10 along with upadacitinib 45 mg, orally, once daily (QD) during the 12-week Induction Period. 2. Placebo Comparator: Induction Period: Vedolizumab +Placebo: Participants will receive vedolizumab IV 300 mg infusion, at Weeks 0, 2, 6 and 10 along with upadacitinib matched placebo, orally, QD during the 12-week Induction Period. 3. Experimental: Maintenance Period: Vedolizumab Monotherapy: Participants who achieve a CDAI reduction of ≥70 points from baseline at Week 12 will receive vedolizumab 300 mg IV infusion (monotherapy) every 8 weeks (Q8W) during the 40-week Maintenance Period. The Q8W vedolizumab monotherapy may be escalated to Q4W as per protocol-specified criteria.
Primary endpoint and key secondary endpoint(s)	1. To evaluate whether dual targeted therapy (DTT, vedolizumab and upadacitinib) during induction improves clinical and endoscopic outcomes by Week 12, compared with vedolizumab monotherapy, in participants with moderately to severely active CD. 2. To evaluate further the short-term clinical and endoscopic benefits of DTT during induction, compared with vedolizumab monotherapy, in participants with moderately to severely active CD.
Study start date	Estimated August 2024

ENTYVIO (VEDOLIZUMAB): *GUT-SELECTIVE ANTI-α4β7 INTEGRIN MAB*

Study	NCT06249555	NCT06257706
Indication	Crohn's Disease (CD)	Crohn's Disease (CD)
Phase	**Phase IV** ***VOICE***	**Phase IV** ***VECTORS***
# of Patients	N = 300 (estimated)	N = 304 (estimated)
Target Patients	Participant is an adult 18 years of age or older with confirmed CD, as per standard clinical criteria which may include symptoms, endoscopy, histopathology, and imaging.	Adults aged 18 to 80 years with Moderately-to-severely active CD at baseline defined by a CDAI score of 220 to 450 inclusive and SES-CD, excl. the presence of narrowing component, ≥6 (or ≥4 for participants with isolated ileal disease)
Arms/ Intervention	**Two arm study:** • Group one will include participants who will be starting Vedolizumab as part of routine care. Dose, frequency and duration are not mandated as part of the study and are determined by the health care provider. • Group two will include participants who will be starting an IL-23 antagonist as part of routine care. Dose, frequency and duration are not mandated as part of the study and are determined by the health care provider.	**Group 1** will be treated over 48 weeks to achieve a target of corticosteroid-free IUS-based outcomes + clinical remission + biomarker remission. At Week 22 and 30, the IUS-based component of the target will be IUS response and at Week 38, the final treatment target will be TMH. **Group 2** will be treated over 48 weeks to achieve a target of corticosteroid-free clinical remission + biomarker remission. **Intervention**: All participants will begin a vedolizumab induction regimen of 300 mg IV at Weeks 0, 2, 6, and 10 followed by vedolizumab 300 mg IV every 8 weeks starting at Week 14. Treatment may be modified at Weeks 22, 30, and/or 38 based on the results of the target assessment at each of these time points.
Primary endpoint and key secondary endpoint(s)	Time to meaningful clinical improvement in pain interference, defined as a ≥ 2-point decrease in the PROMIS Pain Interference-SF T-score	Percentage of participants with Corticosteroid-free Endoscopic remission in group 1 and group 2 at week 48
Study start date	March 2024	February 2024

ALOFISEL/CX601 (DARVADSTROCEL): *ALLOGENEIC EXPANDED ADIPOSE-DERIVED STEM CELLS (ASC)*

Study	NCT04701411
Indication	Complex Perianal Fistulas in Crohn's - Pediatric
Phase	**Phase III**
# of Patients	N = 20
Target Patients	Pediatric subjects with Crohn's Disease aged 4 to <18 years, with complex perianal fistula(s), whose perianal fistulas were previously treated and have shown an inadequate response.
Arms/Intervention	Open Label, Single Group Assignment: • Darvadstrocel (Cx601), 24 mL suspension of 120 million cells as a perilesional injection, once on Day 0
Primary endpoint and key secondary endpoint(s)	**Primary:** • To evaluate the efficacy of darvadstrocel in combined remission at Week 24 for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years. **Secondary:** • To evaluate the efficacy of darvadstrocel in clinical remission at Week 24 and Week 52 for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years. • To evaluate the efficacy of darvadstrocel in clinical response at Week 24 and Week 52 for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years. • To evaluate the efficacy of darvadstrocel in time to clinical remission up to Week 52 for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years. • To evaluate the efficacy of darvadstrocel in time to clinical response up to Week 52 for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years. • To evaluate the efficacy of darvadstrocel on relapse by Week 52 in pediatric subjects with combined remission at Week 24. • To evaluate the safety of darvadstrocel for the treatment of complex perianal fistula in pediatric subjects with CD aged 4 to <18 years over 52 weeks.
Study start date	June 2021

MARALIXIBAT (TAK-625):
IBAT (ILEAL BILE ACID TRANSPORTER) INHIBITOR

Study	NCT05543187	NCT05543174
Indication	Progressive Familial Intrahepatic Cholestasis (PFIC)	Alagille Syndrome (ALGS)
Phase	**Phase III** **Japan**	**Phase III** **Japan**
# of Patients	N = 5	N = 7
Target Patients	Patients with Progressive Familial Intrahepatic Cholestasis	Patients with Alagille Syndrome
Arms/Intervention	TAK-625 orally, twice daily (BID) for 4 weeks as Dose Escalation Period. The dose in Dose Escalation Period will be increased weekly, 150 mcg/kilograms (kg), 300 mcg/kg, 450 mcg/kg, and 600 mcg/kg. After Dose Escalation Period, TAK-625 600 mcg/kg (or maximum tolerated dose [MTD]), orally, BID up to study completion	TAK-625 200 mcg per kilogram, orally, once daily for 1 week. After that, TAK-625 400 mcg per kilogram, orally, once daily after Week 1

Primary endpoint and key secondary endpoint(s)	**Primary:**
	• Change in the Average Morning ItchRO (Obs) Severity Score between Baseline and Average of Week 15 through Week 26
	Key Secondary:
	• Change in the Average Morning ItchRO (Obs) Frequency Score between Baseline and Average of Week 15 through Week 26
	• Change of Total sBA Levels from Baseline to Week 26
	• Percentage of Participants who Achieve sBA Well Control from Baseline through Week 26
	• Change in the ItchRO (Obs) Weekly Average Severity between Baseline and Average of Week 15 through Week 26
		Primary:
		• Change of Fasting Serum Bile Acid (sBA) Levels from Week 18 to Week 22
		Key Secondary:
		• Change from baseline to Week 18:
		  ◦ Fasting sBA levels.
		  ◦ Pruritus as measured by ItchRO (Obs): weekly average severity (based on daily maximum of morning and evening severity scores).
		  ◦ Pruritus as measured by ItchRO (Obs): weekly average morning severity.
		• Change from Week 18 to 22:
		  ◦ Pruritus as measured by ItchRO (Obs): weekly average severity (based on daily maximum of morning and evening severity scores).
		  ◦ Pruritus as measured by ItchRO (Obs): weekly average morning severity.

Study start date	January 2023	January 2023

ZASOCITINIB (TAK-279):
TYK2 – INHIBITOR, ORAL

Study	NCT06088043	NCT06108544
Indication	Moderate-to-Severe Plaque Psoriasis	Moderate-to-Severe Plaque Psoriasis
Phase	**Phase III** ***LATITUDE PSORIASIS***	**Phase III** ***LATITUDE PSORIASIS***
# of Patients	N = 600	N = 1000
Target Patients	Patients with moderate-to-severe plaque psoriasis	Patients with moderate-to-severe plaque psoriasis
Arms/Intervention	• **Arm 1:** TAK-279 tablet for oral administration • **Arm 2:** Apremilast for oral administration • **Arm 3:** Matching placebo	• **Arm 1:** TAK-279 tablet for oral administration • **Arm 2:** Apremilast for oral administration • **Arm 3:** Matching placebo incl. withdrawal and re-treatment period
Primary and Secondary Objective(s)	**Primary Objective:** • Evaluate efficacy of TAK-279 orally administered for 16 wks, compared to placebo **Secondary Efficacy Objectives:** • Evaluate whether TAK-279 orally administered for 16 wks is superior to placebo • Evaluate whether TAK-279 orally administered is superior to apremilast after 16, 24, and 52 weeks of treatment with TAK-279 or apremilast **Secondary Safety Objective:** • Evaluate safety and tolerability of TAK-279 orally administered when compared to placebo and apremilast	**Primary Objective:** • Evaluate efficacy of TAK-279 orally administered for 16 wks, compared to placebo **Secondary Efficacy Objectives:** • Evaluate whether TAK-279 orally administered for 16 wks is superior to placebo • Evaluate whether TAK-279 orally administered is superior to apremilast after 16 and 24 wks of treatment with TAK-279 or apremilast • Evaluate maintenance and durability of efficacy of TAK-279 during withdrawal and re-treatment period **Secondary Safety Objective:** • Evaluate safety and tolerability of TAK-279 orally administered when compared to placebo and apremilast • Evaluate safety of retreatment after withdrawal
Study start date	November 2023	November 2023

ZASOCITINIB (TAK-279):
TYK2 – INHIBITOR, ORAL

Study	NCT05153148
Indication	Active Psoriatic Arthritis
Phase	**Phase II**
# of Patients	N = 260
Target Patients	Participants with active psoriatic arthritis
Arms/Intervention	• Regimen 1: TAK-279 at a dose of 5 mg will be orally administered once daily (QD) for 12 weeks. • Regimen 2: TAK-279 at a dose of 15 mg will be orally administered once daily (QD) for 12 weeks. • Regimen 3: TAK-279 at a dose of 30 mg will be orally administered once daily (QD) for 12 weeks. • Regimen 4: Matching placebo, identical to TAK-279 but without active ingredient.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Proportion of subjects achieving at least an American College of Rheumatology (ACR) 20 response [Time Frame: Day 1 to Week 16]
Study start date	January 2022

ZASOCITINIB (TAK-279):
TYK2 – INHIBITOR, ORAL

Study	NCT06233461	NCT06254950
Indication	Crohn's Disease	Ulcerative Colitis
Phase	**Phase II**	**Phase II**
# of Patients	N = 268	N = 207
Target Patients	Moderately to Severely Active Crohn's Disease	Moderately to Severely Active Ulcerative Colitis
Arms/Intervention	• **Arm 1:** TAK-279 Dose 1 for oral administration • **Arm 2:** TAK-279 Dose 2 for oral administration • **Arm 3:** TAK-279 Dose 3 for oral administration • **Arm 4:** Matching placebo	• **Arm 1:** TAK-279 Dose 1 for oral administration • **Arm 2:** TAK-279 Dose 2 for oral administration • **Arm 3:** Matching placebo
Primary endpoint and key secondary endpoint(s)	**Primary:** • Percentage of Participants With Endoscopic Response Based on Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 12 **Key secondary:** • Percentage of Participants Achieving Clinical Remission Based on the Crohn's Disease Activity Index (CDAI) at Week 12 • Percentage of Participants Achieving Clinical response Based on CDAI at Week 12 • Percentage of Participants Achieving Endoscopic Remission Based on SES-CD at Week 12	**Primary:** • Percentage of Participants Achieving Clinical Remission at Week 12 Based on Modified Mayo Score (mMS) **Key secondary:** • Percentage of Participants Achieving Clinical Response at Week 12 Based on Modified Mayo Score (mMS) • Endoscopic improvement and Endoscopic remission based on mMES
Study start date	March 2024	June 2024

ADZYNMA (TAK-755):
REPLACEMENT OF THE DEFICIENT ADAMTS13 ENZYME

Study	NCT03393975	NCT05714969
Indication	Congenital Thrombotic Thrombocytopenic Purpura (cTTP)	Immune Thrombotic Thrombocytopenic Purpura (iTTP)
Phase	**Phase III**	**Phase IIb**
# of Patients	N = up to 68	N = 40
Target Patients	Patients diagnosed with severe cTTP in prophylactic and on-demand treatment	Adult patients diagnosed with iTTP experiencing an acute event

Arms/Intervention	Prophylaxis Treatment Cohort: 6 + 6 months cross over of TAK-755 vs SoC followed by 6 months TAK-755 extension
	• **Arm 1:** TAK-755 followed by SOC
	• **Arm 2:** SOC followed by TAK-755
	(Patients are also eligible to enter the prophylaxis study upon completion of acute treatment)
		• **Acute Phase:**
		  • **Arm 1:** TAK-755 40 IU/kg BID
		  • **Arm 2:** TAK-755 80 IU/kg BID
		• **Post-acute Phase:**
		  • 80 IU/kg 2-3x weekly (3 – 6-week duration)

Primary endpoint and key secondary endpoint(s)	**Primary:** • Incidence of acute TTP episodes in subjects receiving prophylactic treatment with either TAK-755 or SoC.	**Primary:** • Incidence of adverse events, serious adverse events, and adverse events of special interest. **Secondary:** • Achievement of clinical response without on-study plasma exchange.
Study start date	October 2017	March 2023

FAZIRSIRAN (TAK-999): *ALPHA-1 ANTITRYPSIN SILENCING RNAI*

Study	NCT05677971
Indication	Alpha-1 Antitrypsin Deficiency Associated Liver Disease (AATD-LD)
Phase	**Phase III** ***The Redwood Study***
# of Patients	N = 160
Target Patients	Patients with PiZZ AATD-LD with METAVIR stage F2, F3, or F4 liver fibrosis.
Arms/Intervention	• Arm 1: Fazirsiran subcutaneous injection at Day1, Week 4 and every 12 weeks thereafter • Arm 2: Placebo
Primary endpoint and key secondary endpoint(s)	**Primary:** • Reduction from baseline of at least 1 stage of histologic fibrosis METAVIR staging in the centrally read liver biopsy in AATD-LD with METAVIR stage F2 and F3 fibrosis. **Key Secondary:** • Evaluate percent change from baseline in intrahepatic Z-AAT protein. • Evaluate the decrease in fibrosis in the centrally read liver biopsy in AATD-LD with METAVIR stage F2 – F4. • Evaluate the impact on progression in disease (liver related clinical event). • Evaluate changes from baseline in serum Z-AAT protein. • Evaluate changes from baseline in intrahepatic Z-AAT protein polymer burden. • Evaluate changes from baseline in portal inflammation. • Evaluate changes from baseline in liver stiffness with Vibration-Controlled Transient Elastography (VCTE). **Safety:** • Evaluate the safety and tolerability of Fazirsiran compared with placebo with an emphasis on central pulmonary function tests & CT densitometry yearly
Study start date	March 2023

MEZAGITAMAB (TAK-079): *ANTI-CD38 ANTIBODY*

Study	NCT04278924	NCT05174221
Indication	Persistent/Chronic Primary Immune Thrombocytopenia (ITP)	IgA Nephropathy (IgAN)
Phase	**Phase II**	**Phase Ib**
# of Patients	N = 54	N = 16
Target Patients	Patients ≥18 years of age with persistent/chronic primary ITP	Patients ≥18 years of age with primary IgA Nephropathy in combination with stable background medication

Arms/Intervention	• Part A: 2 dose groups and placebo added to stable background therapy
	  • Arm A1: Matching placebo (n=8-12 pts)
	  • Arm A2: TAK-079 100 mg (n=8-12 pts)
	  • Arm A3: TAK-079 300 mg (n=8-12 pts)
	• Part B: Following interim analysis. 1 dose group and placebo (600 mg) added to stable, standard background therapy.
	  • Arm B1: Matching placebo (n=4- 6 pts)
	  • Arm B2: TAK-079 600 mg (n=8-12 pts)
		• TAK-079 600 mg subcutaneous injection, once weekly for 8 weeks then once every 2 weeks for 16 weeks in the Main Study.
		• Same dosing regimen will be repeated in Long-term extension (LTE) Retreatment Period.

Primary endpoint and key secondary endpoint(s)	**Primary**: • Percentage of patients with TEAEs including Grade 3 or higher events, SAEs, and AEs leading to TAK-079 discontinuation.	**Primary**: • Percentage of participants with one or more TEAEs, Grade 3 or Higher TEAEs, SAEs, and AEs leading to TAK-079 discontinuation.
Study start date	November 2020	July 2022

TAK-227 / ZED1227:
TRANSGLUTAMINASE INHIBITOR, PO

Study	EudraCT: 2020-004612-97 [1]	EudraCT: 2023-506150-21 [1]
Indication	Active Celiac Disease (symptoms and small intestinal mucosal injury consistent with active celiac disease despite a gluten free diet)	Active Celiac Disease (symptoms and small intestinal mucosal injury consistent with active celiac disease despite a gluten free diet)
Phase	**Phase IIb**	**Phase IIb**
# of Patients	N = 400	N = 92
Target Patients	Adults with celiac disease, with incomplete response to the gluten-free diet.	Adults with celiac disease, with incomplete response to the gluten-free diet.
Arms/Intervention	• Arm 1: TAK-227 10 mg 3 times daily, 30 minutes before each major meal • Arm 2: TAK-227 25 mg 3 times daily, 30 minutes before each major meal • Arm 3: TAK-227 50 mg once a day, 30 minutes before breakfast, Placebo capsules 30 minutes before lunch and before dinner • Arm 4: Placebo capsules 3 times daily 30 minutes before each major meal	• Arm 1: TAK-227 25 mg three times daily, 30 minutes before each major meal, plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) • Arm 2: Placebo capsules three times daily 30 minutes before each major meal, plus thrice weekly study provided gluten exposure (approximately 500 mg gluten)
Primary endpoint and key secondary endpoint(s)	**Primary:** • Improvement in histological findings AND Non-Stool GI Specific Symptom Score Change OR Diarrhea Severity Score (both measured with Celiac Disease Symptom Diary (CDSD)) **Key Secondary:** • Change in histological findings; Change in CDSD GI Total Severity Score; • Change in duodenal mucosal inflammation measured as the density of CD3-positive intraepithelial lymphocytes (IELs)	**Primary:** • Improvement of celiac disease symptoms as assessed by Celiac Disease Symptom Diary (CDSD) in celiac disease subjects experiencing symptoms and having mucosal damage on a gluten-free diet. **Key Secondary:** • Changes in duodenal mucosal morphology as measured by morphometry (villous height to crypt depth, VH:CrD), • Changes in the severity of non-stool gastrointestinal (GI) symptoms (abdominal pain, bloating, nausea) as assessed by CDSD.
Study start date	August 2021	April 2024

 1. Trial managed by Dr. Falk Pharma GmbH, Germany

ZAMAGLUTENASE (TAK-062): *GLUTENASE, PO*

Study	NCT05353985
Indication	Active Celiac Disease (symptoms and small intestinal mucosal injury consistent with active celiac disease despite a gluten free diet)
Phase	**Phase II**
# of Patients	N = 357
Target Patients	Adults and adolescents with celiac disease, with incomplete response to the gluten-free diet.
Arms/Intervention	Cohort 1: • Arm 1: TAK-062 600 mg three times daily, plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) • Arm 2: Placebo three times daily, plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) Cohort 2: • Arm 1: TAK-062 placebo three times daily, plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) • Arm 2: TAK-062 150 mg three times daily plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) • Arm 3: TAK-062 300 mg three times daily plus thrice weekly study provided gluten exposure (approximately 500 mg gluten) • Arm 4: Placebo three times daily without study provided gluten exposure • Arm 5: TAK-062 600 mg three times daily without study provided gluten exposure • Arm 6: TAK-062 150mg three times daily without study provided gluten exposure
Primary endpoint and key secondary endpoint(s)	**Primary:** • Change in GI symptom severity score (Celiac disease symptom diary) **Key Secondary:** • Change in biopsy or histological findings using upper endoscopy
Study start date	December 2022

TAK-101:
NANOPARTICLE ENCAPSULATING GLIADIN, IV

Study	NCT04530123
Indication	Celiac Disease
Phase	**Phase II**
# of Patients	N = 108
Target Patients	Adult patients with history of biopsy-proven well-controlled celiac disease on a gluten-free diet for a minimum of 6 months.
Arms/Intervention	Cohort 1: • Group A: Two infusion doses of placebo on Days 1 and 8 + 1 infusion dose of 2 mg/kg TAK-101 at Week 24 • Group B: One infusion dose of 2 mg/kg TAK-101 on Day 1 followed by 1 infusion dose of placebo on Day 8 + 1 infusion dose of 2 mg/kg TAK-101 at Week 24 • Group C: Two infusion doses of 2 mg/kg TAK-101 on Days 1 and 8 + 1 infusion dose of 2 mg/kg TAK-101 at Week 24 Cohort 2: • Group D: Two infusion doses of placebo on Days 1 and 8 + 1 infusion dose of 2 mg/kg TAK-101 at Week 24 • Group E: One infusion dose of 4 mg/kg TAK-101 on Day 1 followed by 1 infusion dose of placebo on Day 8 + 1 infusion dose of 4 mg/kg TAK-101 at Week 24 • Group F: Two infusion doses of 4 mg/kg TAK-101 on Days 1 and 8 + 1 infusion dose of 4 mg/kg TAK-101 at Week 24 • Group G: Two infusion doses of 1mg/kg TAK-101 on Days 1 and 8 + 1 infusion dose of 1mg/kg TAK-101 at Week 24
Primary endpoint and key secondary endpoint(s)	**Primary:** • Reduction in Day 15 IFN-γ SFUs based on results of gliadin-specific ELISpot **Key secondary:** • Safety and tolerability as assessed by AEs, IRs, CRS, physical examinations, vital signs, and clinical laboratory testing, including liver tests. • Change in Celiac Disease Symptom Diary version 2.1 3-day average score from Day 1 to post-gluten challenge on Day 15 and Weeks 8, 14, and 20 • Change from pre- to 4 hours post-gluten challenge in plasma IL-2 on Day 15 and Weeks 8, 14, and 20
Study start date	August 2022

RUSFERTIDE (TAK-121): *HEPCIDIN MIMETIC*

Study	NCT05210790[1]
Indication	Polycythemia vera
Phase	**Phase III** ***The VERIFY Study***
# of Patients	N = 293
Target Patients	Patients with Polycythemia vera with confirmed Hct ≥45% and that is ≥3% higher than baseline Hct or Hct ≥48% who require phlebotomy on a frequent basis (≥3 PHL in 28 weeks prior to randomization or ≥5 PHL in 52 weeks prior to randomization)
Arms/Intervention	**Part 1A:** • Randomized, double-blind, placebo-controlled, add-on parallel-group period for 32 weeks. Subjects randomized 1:1 in a blinded fashion to 32 weeks of add-on rusfertide or placebo treatment. Rusfertide or placebo will be added-on to each subject's ongoing therapy for PV. Randomization will be stratified by ongoing PV therapy. **Part 1B**: • Open-label treatment phase during which all subjects who complete Part 1a will receive rusfertide for 20 weeks (Wk 32 thru Wk 52). **Part 2:** • Long term extension for 104 weeks during which all subjects who complete Part 1b will continue to receive rusfertide.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Proportion of patients achieving a response (Weeks 20-32 inclusive) who receive rusfertide compared to placebo. Response is defined as absence of PHL eligibility (Confirmed Hct ≥45% and that is ≥3% higher than baseline Hct or Hct ≥48%) **Key Secondary:** • Mean number of phlebotomies between Weeks 0 through 32 (inclusive). • Proportion of subjects with all Hct values <45% between Week 0 through Week 32 (inclusive). • Mean change from baseline in total fatigue score based on PROMIS® Short Form 8a at Week 32. • Mean change from baseline in total score based on the Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 at Week 32.
Study start date	April 2022

 1. Trial managed by Protagonist Therapeutics

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SOTICLESTAT (TAK-935): *CH24H INHIBITOR, ORAL*

Neuroscience

Study	NCT04940624	NCT04938427
Indication	Dravet Syndrome (DS)	Lennox–Gastaut Syndrome (LGS)
Phase	**Phase III**	**Phase III**
# of Patients	N = 144	N = 270
Target Patients	Dravet Syndrome patients 2-21 years of age with ≥4 convulsive seizures per 28 days during the 4–6-week prospective Baseline Period	Lennox-Gastaut Syndrome patients 2-55 years of age with ≥8 Major Motor Drop (MMD) seizures per 28 days during the 4–6-week prospective Baseline Period
Arms/Intervention	• 1:1 soticlestat:placebo randomization ratio	• 1:1 soticlestat:placebo randomization ratio
Primary endpoint and key secondary endpoint(s)	**Primary:** Percent change from baseline in convulsive seizure frequency per 28 days in subjects receiving soticlestat compared with placebo during the full treatment period (Maintenance period for EMA registration). • Proportion of responders defined as those with ≥50% reduction from baseline in convulsive seizures • Percent change from baseline in frequency of all seizures • CGI-I (clinician). • Care GI-I (caregiver). • CGI-I Seizure Intensity and Duration. • CGI-I Non-seizure Symptoms (communication, disruptive behavior, alertness). • Change in QI-Disability score.	**Primary** : Percent change from baseline in MMD seizure frequency per 28 days in subjects receiving soticlestat compared with placebo during the full treatment period (Maintenance period for EMA registration). • Proportion of responders defined as those with ≥50% reduction from baseline in MMD seizures • Percent change from baseline in frequency of all seizures • CGI-I (clinician). • Care GI-I (caregiver). • CGI-I Seizure Intensity and Duration. • CGI-I Non-seizure Symptoms (communication, disruptive behavior, alertness) • Change in QI-Disability score.
Study start date	September 2021	October 2021

TAK-861:
OREXIN 2R AGONIST, ORAL

Neuroscience

Study	NCT05687903	NCT05687916
Indication	Narcolepsy Type 1	Narcolepsy Type 2
Phase	**Phase IIb**	**Phase IIb**
# of Patients	N= 100	N= 60
Target Patients	Participants with Narcolepsy Type 1	Participants with Narcolepsy Type 2
Arms/Intervention	• TAK-861 Dose 1 • TAK-861 Dose 2 • TAK-861 Dose 3 • TAK-861 Dose 4 • Placebo	• TAK-861 Dose 1 • TAK-861 Dose 2 • Placebo
Primary endpoint and key secondary endpoint(s)	**Primary:** • Change from Baseline to Week 8 in Mean Sleep Latency **Secondary:** • Change from Baseline to Week 8 in Epworth Sleepiness Scale (ESS) Total Score • Weekly Cataplexy Rate at Week 8	**Primary:** • Change from Baseline to Week 8 in Mean Sleep Latency **Secondary:** • Change from Baseline to Week 8 in Epworth Sleepiness Scale (ESS) Total Score
Study start date	January 2023	January 2023

TAK-861:
OREXIN 2R AGONIST, ORAL

Neuroscience

Study	NCT06470828
Indication	Narcolepsy Type 1 (NT1)
Phase	**Phase III** ***The First Light***
# of Patients	N = 152
Target Patients	Participants with Narcolepsy Type 1
Arms/Intervention	• TAK-861 Dose 1 • TAK-861 Dose 2 • Placebo
Primary endpoint and key secondary endpoint(s)	**Primary:** • Change from Baseline to Week 12 in Mean Sleep Latency measured through MWT **Key Secondary:** • Change from Baseline to Week 12 in Epworth Sleepiness Scale (ESS) Total Score • Change from Baseline to Week 12 in Weekly Cataplexy Rate • Change from Baseline in number of Lapses on the 3 Post Meridiem (PM) Psychomotor Vigilance Test (PVT) Session at Week 12 • Change from Baseline in Patient Global Impression of Change (PGI-C) Score at Week 12 • Change from Baseline in Narcolepsy Severity Scale for Clinical Trials (NSS-CT) Total Score at Week 12 • Change from Baseline in Functional Impacts of Narcolepsy Instrument (FINI) Domain Scores at Week 12 • Change from Baseline in Short Form-36 Survey (SF-36) Mental and Physical Component Scores at Week 12 • Occurrence of at least 1 TEAE during the study including the follow-up period, as applicable.
Study start date	July 2024

DANAVOREXTON (TAK-925): *OREXIN 2R AGONIST, IV*

Neuroscience

Study	NCT05180890	NCT05814016
Indication	Obstructive Sleep Apnea (OSA)	Postanesthesia Recovery
Phase	**Phase I**	**Phase IIa**
# of Patients	N = 18	N = 180
Target Patients	Patients With Obstructive Sleep Apnea	Moderate to severe obstructive sleep apnea patients undergoing general anesthesia for abdominal surgery
Arms/Intervention	• Low dose • High dose • Placebo	• Danavorexton high dose • Danavorexton low dose • Placebo
Primary endpoint and key secondary endpoint(s)	**Primary:** • Number of Participants With at Least one Treatment-emergent Adverse Event (TEAE) **Secondary:** • Change From Baseline in Upper Airway Collapsibility Index (UACI) • Apnea-Hypopnea Index (AHI) Observed During Overnight Polysomnographys (PSGs)	**Primary:** • Number of Participants who Maintain Respiratory Stability for 120 Minutes in the Postanesthesia Care Unit **Secondary (selected):** • Number of Episodes of Respiratory Instability per Participant Within 120 Minutes in the PACU • PK parameters • Number of Participants with At Least One Occurrence of Treatment-Emergent Adverse Events
Study start date	March 2022	May 2023

TAK-341:
ALPHA-SYNUCLEIN ANTIBODY, IV

Study	NCT05526391
Indication	Multiple System Atrophy
Phase	**Phase II**
# of Patients	N = 138
Target Patients	Patients With Multiple System Atrophy
Arms/Intervention	Q4wk IV infusion of TAK-341 or Placebo (1:1)
Primary endpoint and key secondary endpoint(s)	**Primary:** • Change from Baseline in a Modified Unified Multiple System Atrophy Rating Scale Part I at Week 52 **Secondary (selected):** • PK parameters • Change From Baseline in Scales for Outcomes in Multiple System Atrophy - Autonomic Dysfunction Total Score and Clinical Global Impression-Severity Score
Study start date	November 2022

TAK-594 / DNL593:
PROGRANULIN PTV, IV AND SC

Neuroscience

Study	NCT05262023[1]
Indication	Frontotemporal Dementia
Phase	**Phase I/II**
# of Patients	N = 106
Target Patients	Healthy volunteers / Participants with symptomatic FTD
Arms/Intervention	• **Part A:** SRD in Healthy Participants • **Part B:** Multiple doses in participants with symptomatic FTD harboring the GRN mutation • **Part C:** optional 18-month OLE period available for all participants who complete Part B
Primary endpoint and key secondary endpoint(s)	**Primary:** • Incidence, severity, and seriousness of treatment-emergent adverse events (TEAEs) • Incidence of treatment-emergent clinically significant abnormalities in safety laboratory values • Change from baseline in vital sign measurements (systolic and diastolic blood pressure, heart rate, respiratory rate, body temperature) • Change from baseline in electrocardiogram (ECG) results including PR, QRS, and QTcF intervals • Incidence of treatment-emergent clinically significant abnormalities in physical/neurological examination findings • Change from baseline in Columbia-Suicide Severity Rating Scale (C-SSRS; Parts B and C only) **Secondary:** • Serum PK
Study start date	February 2022

1. Trial managed by Denali

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ICLUSIG (PONATINIB): *BCR-ABL INHIBITOR*

Study	NCT02467270	NCT03589326
Indication	Chronic myeloid leukemia (CML)	Ph+ acute lymphoblastic leukemia (ALL)
Phase	**Phase II** ***OPTIC***	**Phase III** ***Ph+ALLCON***
# of Patients	N = 283	N = 245
Target Patients	Patients with resistant chronic phase chronic myeloid leukemia	Patients with newly-diagnosed Ph+ ALL
Arms/Intervention	• Ponatinib 45 mg once daily • Ponatinib 30 mg once daily • Ponatinib 15 mg once daily	• Cohort A: Ponatinib/reduced intensity chemotherapy until progressive disease (PD) or stem cell transplant (SCT) • Cohort B: Imatinib/reduced intensity chemotherapy until PD or SCT
Primary endpoint and key secondary endpoint(s)	**Primary:** Percentage of Participants With Molecular Response (MR2: <=1% Breakpoint Cluster Region-Abelson Transcript Level) as Measured by the International Scale (BCR-ABL1IS) at Month 12 [Time Frame: 12 months after the first dose of study treatment]	**Primary:** • Number of participants with Minimal Residual Disease (MRD) - Negative Complete Remission (CR) [Time frame: From Cycle 1 through Cycle 3 (approximately 3 months) (Cycle length is equal to 28 days)] **Secondary:** • EFS
Study start date	August 2015	January 2019

NINLARO (IXAZOMIB):
ORAL PROTEASOME INHIBITOR

Oncology

Study	NCT03173092
Indication	Non-transplant eligible patients with newly diagnosed multiple myeloma
Phase	**Phase IV** ***MM6***
# of Patients	N = 141
Target Patients	Patients with multiple myeloma previously receiving a bortezomib-based induction. In-class (proteasome inhibitor) transition after 3 cycles of bortezomib-based therapy. PFS/OS follow up for up to 2.5 years.
Arms/Intervention	• Ixazomib 4 mg + lenalidomide 25 mg + dexamethasone 40 mg • IRd treatment to be given up to 39 cycles • Transition from a bortezomib based regimen to IRD (ixazomib, lenalidomide, dexamethasone) may allow the long-term proteasome inhibition to be maximized while maintaining a manageable safety profile.
Primary endpoint and key secondary endpoint(s)	**Primary:** Progression Free Survival (PFS) at 2 years. **Key secondary:** Time to next therapy (TTNT), relative dose intensity (RDI) of the oral regimen, overall survival (OS), electronic patient reported outcomes (ePRO) and actigraphy (activity/sleep) data.
Study start date	September 2017
Publications	• Rifkin et al Blood Cancer Journal 2023; DOI 10.1038/s41408-023-00912-9 • Richter et al JNCCN 2023; DOI: 10.6004/jnccn.2023.7058 • Rifkin et al Future Oncology 2023; 10.2217/fon-2023-0272 • Girnius et al. Blood (2023) 142 (Supplement 1): 6677 • Boccia et al. EHA 2024 (abstract P1969)

DAZOSTINAG (TAK-676): *STING AGONIST*

Oncology

Study	NCT04420884	NCT04879849
Indication	Solid tumors	Solid tumors
Phase	**Phase I/II**	**Phase I**
# of Patients	N = 336	N = 34
Target Patients	• Dose escalation (Part 1): Adult patients with advanced or metastatic solid tumors • Expansion cohorts (Parts 2 and 3): 1. Adult patients with SCCHN 1L PD-L1+ or SCCHN 1L all comers 2. Adult patients with 3L+ MSI-H/dMMR CRC or 3L MSS/pMMR CRC	Adult patients with advanced or metastatic solid tumors
Arms/Intervention	Part 1: • Arm 1: Dose escalating single agent TAK-676, starting with safety lead-in at 0.1 mg IV on Days 1, 8, 15 in 21-day cycles, and capping at 2.5 mg IV on Days 1, 8 and 15 in a 21-day cycle. • Arm 2: Dose escalating TAK-676 along above parameters in combination with fixed dose pembrolizumab at 200mg IV administered on D1 in a 21-day cycle. Parts 2 and 3: • TAK-676 at RP2D level on Days 1, 8, and 15 in 21-day treatment cycles with fixed dose pembrolizumab at 200mg IV administered on D1 in a 21-day cycle. Part 2B only - starting with safety lead-in, addition of carboplatin/cisplatin and 5-FU on D1 in 21-day cycle.	• Image-guided radiation therapy between Day -8 and Day -1 followed by fixed dose pembrolizumab at 200 mg IV administered on D1 of a 21-day cycle in combination with dose escalating TAK-676, starting at 0.2 mg IV and capping at 2.5 mg IV on Days 1, 8 and 21 in a 21-day cycle.
Primary endpoint and key secondary endpoint(s)	**Primary:** Safety and tolerability **Secondary:** Recommended Phase 2 dose (RP2D), overall response rate (ORR), progression free survival (PFS), overall survival (OS)	**Primary:** Safety and tolerability **Secondary:** Recommended Phase 2 dose (RP2D), overall response rate (ORR)
Study start date	August 2020	July 2021

TAK-500:
STING AGONIST ANTIBODY DRUG CONJUGATE

Oncology

Study	NCT05070247
Indication	Solid tumors
Phase	**Phase I/II**
# of Patients	N = 306
Target Patients	Dose escalation: - adult patients with advanced or metastatic solid tumors Expansion cohorts: - adult patients with locally advanced or metastatic non-squamous 2L and 3L NSCLC, 3L RCC, or 2L PDAC.
Arms/Intervention	• Arm 1: Dose escalating single agent TAK-500 starting at 8 microgram per kilogram (mcg/kg), infusion, intravenously, once on Day 1 of each 21-days treatment cycle, once every 3 weeks (Q3W), for up to 1 year • Arm 2: Dose escalating TAK-500, infusion, intravenously, once on Day 1 of each 21-days treatment cycle (Q3W), along with pembrolizumab 200 milligram (mg) infusion, intravenously, once on Day 1 of each 21-days treatment cycle (Q3W), for up to 1 year
Primary endpoint and key secondary endpoint(s)	**Primary:** • Safety and tolerability, overall response rate (ORR). **Secondary:** • PK parameters, progression free survival (PFS), overall survival (OS).
Study start date	April 2022

TAK-186:
T-CELL ENGAGER

Oncology

Study	NCT04844073
Indication	Solid tumors
Phase	**Phase I/II**
# of Patients	N = 210
Target Patients	Patients with unresectable, locally advanced or metastatic cancer
Arms/Intervention	Single-arm, open label, MVC-101 (also known as TAK-186) - An EGFR x CD3 Conditional Bispecific Redirected Activation (COBRA) Protein This Phase 1/2, open-label study will characterize safety, dose-limiting toxicities (DLTs), and maximum tolerated / recommended phase 2 dose (MTD/RP2D) of TAK-186. Dose escalation will occur in a 1+3 and then 3+3 design in patients with advanced solid tumors. Once the dose levels for expansion are determined, a Cohort Expansion Phase will be enrolled to further characterize safety and initial antitumor activity in patients with HNSCC, CRC or NSCLC.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Safety based upon incidence of treatment-emergent adverse events. **Secondary:** • Pharmacokinetics, Pharmacodynamics, Immunogenicity measured by plasma anti-drug antibodies, and Radiographic anti-tumor activity
Study start date	March 2021

TAK-280:
T-CELL ENGAGER

Oncology

Study	NCT05220098
Indication	Solid tumors
Phase	**Phase I/II**
# of Patients	N = 142-182
Target Patients	Patients with unresectable, locally advanced or metastatic cancer
Arms/Intervention	Single-arm, open label, TAK-280 - An B7-H3 x CD3 Conditional Bispecific Redirected Activation (COBRA) Protein This Phase 1/2, open-label study will characterize safety, dose-limiting toxicities (DLTs), and maximum tolerated/ recommended dose for the expansion phase into solid tumor indications Dose escalation will utilize a BOIN design in patients with advanced solid tumors. Once the recommended doses for expansion (RDEs) is determined, people living with metastatic NSCLC, mCRPC and cutaneous melanoma will be enrolled in the cohort expansion phase, to further characterize safety and initial antitumor activity.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Tolerability and Safety based upon incidence of treatment-emergent adverse events. **Secondary:** • Pharmacokinetics, Pharmacodynamics, Immunogenicity measured by incidence, titer and neutralizing potential of anti-drug antibodies, and radiographic anti-tumor activity.
Study start date	May 2022

TAK-012:
NON-ENGINEERED CELL THERAPY

Oncology

Study	NCT05886491
Indication	Relapsed/refractory acute myeloid leukemia (AML)
Phase	**Phase I/IIa**
# of Patients	N = 53
Target Patients	Adult patients with relapsed or refractory acute myeloid leukemia
Arms/Intervention	• During Phase 1 (sequential dose escalation), participants will be assigned to one of the following treatment groups each consisting of 3 to 6 participants to receive TAK-012 at one of the three dose levels: Dose 1, Dose 2, Dose 3. • Upon completion of Phase 1, 1 to 2 dose levels will be selected for Phase 2a of the study. At the completion of Phase 2a of the study, a single dose may be selected by the sponsor and investigators as the recommended phase 2 dose (RP2D) for future study.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Incidence of dose-limiting toxicities, treatment-emergent adverse events (AEs) and AEs of clinical interest
Study start date	July 2023

MIRVETUXIMAB SORAVTANSINE (TAK-853):
FOLATE RECEPTOR ALPHA (FRα) ANTIBODY DRUG CONJUGATE

Oncology

Study	NCT06390995
Indication	Folate Receptor Alpha (FRα)-Positive Platinum-Resistant Ovarian Cancer (PROC)
Phase	**Phase I/II**
# of Patients	Phase 1 part: At least 3 (up to 9) patients Phase 2 part: Approximately 22 patients
Target Patients	Phase 1 part: Patients with FRα-positive advanced ovarian cancer or other solid tumor Phase 2 part: Patients with platinum-resistant ovarian cancer with high FRα expression, who have received 1 to 3 prior lines of therapy
Arms/Intervention	Single arm study • **Dose Level(s):** Single-agent MIRV 6.0 mg/kg (adjusted ideal body weight) Q3W • **Route of Administration:** Intravenous • **Duration of Treatment:** Patients may receive study drug until disease progression, unacceptable toxicity, withdrawal of consent or permanent study discontinuation due to any other reasons specified in the study protocol.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Phase 1 part: The number and percentage of patients with dose-limiting toxicities (DLTs) in Cycle 1. • Phase 2 part: Objective response rate (ORR) assessed by investigator with RECIST 1.1. **Secondary:** Phase 1 part: • PK parameters including C_{max}, AUC, $t_{1/2}$, CL, V_{ss}, and t_{max}. Phase 2 part: • Duration of response (DOR) assessed by investigator with RECIST 1.1. • Observed plasma concentration. • The number of patients with immunogenicity of MIRV
Study start date	June 2024

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ADYNOVATE (TAK-660): *PEGYLATED RECOMBINANT FACTOR VIII*

Study	NCT02615691	NCT05707351
Indication	Hemophilia A	Hemophilia A
Phase	**Phase III**	**Phase III**
# of Patients	N = 120	N = At least 30 evaluable subjects aged 12 to 65 years
Target Patients	Previously untreated patients (PUPs) < 6 years with severe hemophilia A (FVIII < 1%)	Previously treated patients with severe hemophilia A (FVIII <1%) in the Chinese population
Arms/Intervention	Single group assignment	Single group assignment
Primary endpoint and key secondary endpoint(s)	**Primary:** Incidence of inhibitor development to FVIII (≥ 0.6 Bethesda unit (BU)/mL using the Nijmegen modification) **Key Secondary:** **Safety** 1. Binding IgG and IGM antibodies to FVIII, PEG-FVIII and PEG 2. Adverse events (AEs) and serious adverse events (SAEs) **Efficacy** 3. Annualized Bleeding Rate (ABR) for prophylactic and on demand treatment 4. Overall hemostatic efficacy rating at 24 hours after initiation of treatment and resolution of bleed 5. incremental recovery (IR) of Adynovate at baseline and over time **ITI** 6. Success rate of ITI therapy with BAX-855	**Primary:** Total Annualized Bleeding Rate (ABR) **Key Secondary:** **Efficacy** 1. Annualized bleeding rates based on bleed site and cause 2. Number of infusions and weight-adjusted consumption of Adynovate per week and month during the prophylactic treatment period **Safety** 3. Occurrence of AEs and SAEs, total incidence, by severity, and by causality **Pharmacokinetics** 4. Factor VIII activity (1-stage clotting assay) in PK samples collected for single-dose and steady-state PK assessments
Study start date	November 2015	April 2023

VONVENDI (TAK-577): *RECOMBINANT VON WILLEBRAND FACTOR*

Study	NCT02932618	NCT05582993
Indication	Pediatric On-demand and Surgery	Pediatric Prophylaxis
Phase	**Phase III**	**Phase III**
# of Patients	N = 23 (On-demand) N = 12 (Elective and Emergency surgery)	N =24
Target Patients	Severe von Willebrand Disease	Severe von Willebrand Disease
Arms/Intervention	• Arm A: On-demand • Arm B: Elective and emergency surgery	• Cohort 1 participants ≥12 to <18 years of age • Cohort 2 participants ≥6 to <12 years of age • Cohort 3 participants 0 to <6 years of age
Primary endpoint and key secondary endpoint(s)	**Primary:** • Hemostatic efficacy and safety of rVWF, with or without ADVATE, in the treatment and control of nonsurgical bleeding events **Key secondary:** • Hemostatic efficacy assessed after the last perioperative rVWF infusion	**Primary:** • Annualized bleeding rate (ABR) with intra-patient control (on-study compared to historical) for all (both spontaneous and traumatic) bleeding episodes classified by the investigator during prophylactic treatment with rVWF. **Key Secondary:** • Safety Endpoints • Overall Hemostatic Efficacy Rating of Breakthrough Bleed Treatment at Resolution of the Bleeding Episode
Study start date	October 2016	January 2024

LIVTENCITY (MARIBAVIR):
ORAL VIRAL PROTEIN KINASE INHIBITOR

Study	NCT05319353
Indication	Treatment of Cytomegalovirus (CMV) Infection in Children and Adolescents Who Have Received a Hematopoietic Stem Cell Transplant (HSCT) or a Solid Organ Transplant (SOT)
Phase	**Phase III**
# of Patients	N = 80
Target Patients	Treatment of Children and Teenage Transplant Recipients With CMV Infection
Arms/Intervention	Cohort 1: Maribavir 400mg BID (body weight ≥ 25kg) or 200mg BID (body weight 10-25 kg) participants 12 to <18 years of age Cohort 2: Maribavir 400mg BID (body weight ≥ 25kg) or 200mg BID (body weight 10-25 kg) participants ≥6 to <12 years of age Cohort 3: Maribavir participants 0 to <6 years of age
Primary endpoint and key secondary endpoint(s)	**Primary:** • Pharmacokinetic characterization of Maribavir in pediatric HSCT and SOT subjects from 0 years to <18 years of age • Safety and tolerability **Secondary:** • Confirmed clearance of plasma CMV DNA at week 8 • Maintenance of confirmed CMV viremia clearance achieved at the end of Study Week 8 through Week 12, Week 16 and Week 20
Study start date	November 2023

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HYQVIA (TAK-771): *IMMUNE GLOBULIN INFUSION 10% (HUMAN) WITH RECOMBINANT HUMAN HYALURONIDASE*

PDT

Study	NCT05150340	NCT05084053
Indication	Primary Immunodeficiency Diseases (PID)	Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Multifocal Motor Neuropathy (MMN)
Phase	**Phase III**	**Phase III**
# of Patients	N = 15	N = 21
Target Patients	Japanese persons ages 2 and older with primary immunodeficiency diseases	Japanese persons ages 18 and older with definite or probable CIDP or MMN
Arms/Intervention	• Experimental: Epoch 1: TAK-771 Ramp up Period Participants will receive subcutaneous infusion of rHuPH20 solution at a dose of 80 U/g IgG first, followed by SC infusion of 10% IGI within 10 minutes of completion of the infusion of rHuPH20 solution. The dose of 10% IGI will be increased from 1/3 of full dose to full dose in 3 weeks for participants who will receive TAK-771 once every 3 week, or from 1/4 of full dose to full dose in 6 weeks for participants who will receive TAK-771 once every 4 week. • Experimental: Epoch 2: TAK-771 Treatment Period Participants will receive subcutaneous infusion of rHuPH20 solution at a dose of 80 U/g IgG first, followed by SC infusion of 10% IGI within 10 minutes of completion of the infusion of rHuPH20 solution, every 3, or 4 weeks for up to Week 24.	• Cohort 1 (TAK-771 for CIDP Participants): - rHuPH20 SC dose of 80 U/g IgG followed by SC infusion of 10% IGI within 10 min of completion of infusion of rHuPH20 solution, every 2,3,4 weeks • Cohort 2 (TAK-771 for MMN Participants): - rHuPH20 SC dose of 80 U/g IgG followed by SC infusion of 10% IGI within 10 min of completion of infusion of rHuPH20 solution, every 2,3,4 weeks
Primary endpoint and key secondary endpoint(s)	**Primary**: Serum trough levels of total IgG antibodies after administration of TAK-771 **Secondary:** PK, safety and tolerability, efficacy, and disease activity and HRQoL.	**Primary:** % of participants with CIDP who experience relapse in 6 months; change in maximum grip strength in the more affected hand in 6 months for MMN participants **Secondary:** safety, and CIDP/MMN health-related metrics.
Study start date	March 2022	January 2022

HYQVIA (TAK-771): *IMMUNE GLOBULIN INFUSION 10% (HUMAN) WITH RECOMBINANT HUMAN HYALURONIDASE*

PDT

Study	NCT05513586
Indication	Primary Immunodeficiency Diseases (PID)
Phase	**Phase III**
# of Patients	N = 10
Target Patients	Japanese persons ages 2 and older with primary immunodeficiency diseases
Arms/Intervention	• This study is an extension study for participants with primary immunodeficiency disorders who were previously treated with TAK-771 in the TAK-771-3004 study. They must have completed that study or be about to complete it before joining this study. Participants will continue treatment with TAK-771 in this study. • The main aim of this study is to check for side effects from long-term treatment with TAK-771. This medicine is not yet licensed in Japan, so participants will be treated with TAK-771 until it becomes commercially available.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Percentage of Participants with Treatment-Emergent Adverse Events (TEAEs) [Time Frame: Up to 3 years] TEAEs are defined as AEs with onset after date-time of first dose of investigational drug or medical conditions present prior to the start of investigational drug but increased in severity or relationship after date-time of first dose of investigational drug. • Percentage of Participants who Develop Anti-rHuPH20 Binding Antibody Titers of Greater Than or Equal to 1:160 and who Develop Neutralizing Antibodies to rHuPH20 [Time Frame: Up to 3 years]
Study start date	September 2022

TAK-881 (FACILITATED SCIG 20%): *IMMUNE GLOBULIN SC (HUMAN), 20% SOLUTION WITH RECOMBINANT HUMAN HYALURONIDASE*

PDT

Study	NCT05755035
Indication	Primary Immunodeficiency Diseases (PIDD)
Phase	**Phase III**
# of Patients	N = 56
Target Patients	Participants aged 2 and older with PIDD
Arms/Intervention	Experimental: Randomized Crossover Treatment Epoch: TAK-881 followed by HYQVIA (Sequence 1) • Participants aged >=16 years will receive 6 or 8 full doses of TAK-881 followed by 6 or 8 full doses HYQVIA in sequence 1 Experimental: Randomized Crossover Treatment Epoch: HYQVIA followed by TAK-881 (Sequence 2) • Participants aged >=16 years will receive 6 or 8 full doses of HYQVIA followed by 6 or 8 full doses of TAK-881 in Sequence 2 Experimental: Non-Randomized Treatment Epoch: TAK-881 • Participants aged 2 to <16 years will receive 6 or 8 full doses of TAK-881.
Primary endpoint and key secondary endpoint(s)	**Primary:** • Area Under the Curve during the dosing Interval at steady-state (AUC0-tau;ss) of TAK-881 and HYQVIA based on total IgG levels **Key Secondary:** • Efficacy parameters including: (1) Annualized rate of all infections, (2) Annualized rate of acute serious bacterial infections (ASBIs), (3) Annualized rate of episodes of fever, (4) Time to first ASBI, and (5) Duration of infections • Healthcare resource utilization (HRU) parameters including: (1) Days not able to go to school, work, daycare, or to perform normal daily activities due to infection or other illnesses or treatment, (2) Days on antibiotics, (3) Number of hospitalizations, indication for the hospitalization (infection or other illnesses) and days hospitalized, (4) Number of acute physician visits (office and emergency room) due to infection or other illnesses. • PK parameters including: (1) Pharmacokinetics at steady-state including maximum concentration (Cmax), time of Cmax (Tmax), terminal half-life (t1/2), apparent clearance (CL/F), apparent volume of distribution (Vz/F), and AUC0-□,ss/week based on total IgG levels, (2) Trough level of total IgG, (3) Trough level of IgG subclasses and antigen-specific, and (4) IgG antibodies • Safety, tolerability and immunogenicity parameters including: (1) Occurrence of treatment-emergent adverse events (TEAEs), (2) Occurrence of infusion withdrawals, interruptions, and infusion rate reductions due to TAK-881-related TEAEs, and (3) Occurrence of positive binding (defined as titer ≥1:160) and neutralizing antibodies to rHuPH20
Study start date	November 2023

TAK-330: *PROTHROMPLEX*

PDT

Study	NCT05156983
Indication	Coagulation Disorder: Reversal of Direct Oral Factor Xa Inhibitor-induced Anticoagulation
Phase	**Phase III**
# of Patients	N = 328
Target Patients	Patients >18 years of age currently on Factor Xa inhibitor requiring urgent surgery/invasive procedure
Arms/Intervention	Adaptive parallel group sequential design Participants will receive PROTHROMPLEX TOTAL 25 international unit per kilogram (IU/kg) single intravenous infusion on Day 1 (prior to surgery). An additional dose of 25 IU/kg PROTHROMPLEX TOTAL can be administered during the surgery if deemed necessary by the surgeon. The total dose of PROTHROMPLEX TOTAL administered to the participant should not exceed 50 IU/kg or 5,000 IU, whichever is smaller. Active Comparator: 4F-PCC. Participants will receive 4F-PCC (excluding Prothromplex total and activated 4F-PCC) as SOC on Day 1 (prior to surgery). The dose and infusion speed of the SOC 4F-PCC will be based on local institutional protocols. An additional dose of SOC 4F-PCC not exceeding label specified limits can be given during the surgery if required. Intervention: Prothromplex total 25 IU/kg single IV on day 1 and an additional dose of 25 IU/kg if required
Primary endpoint and key secondary endpoint(s)	**Primary:** • Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the surgeon's assessment using the Four Point Intraoperative Hemostatic Efficacy Scale **Key Secondary:** • Occurrence of postoperative effective hemostasis assessed at 24 hours after the end of investigational product infusion (TAK-330 or comparator 4F-PCC) based on the surgeon's assessment using the Four Point Postoperative Hemostatic Efficacy Scale. • Occurrence of intraoperative effective hemostasis assessed at the end of the surgery/invasive procedure based on the surgeon's assessment using the Hemostatic Efficacy Rating Algorithm. • Safety/tolerability and other measures
Study start date	August 2022

GLOVENIN-I (TAK-961):
IMMUNE GLOBULIN INFUSION 5% (HUMAN)

PDT

Study	NCT05177939
Indication	Autoimmune Encephalitis (AE)
Phase	**Phase III**
# of Patients	N = 40
Target Patients	Japanese Subjects with Autoimmune Encephalitis Refractory to Steroid Pulse Therapy
Arms/Intervention	• Drug: NPB-01NPB-01 will be administered for the treatment of autoimmune encephalitis Other Name: Intravenous immunoglobulin • Drug: NPB-01-MENPB-01-ME will be administered for the treatment of autoimmune encephalitis Other Name: methylprednisolone sodium succinate
Primary endpoint and key secondary endpoint(s)	**Primary:** • The change in CASE score at each time point after the start of treatment with investigational product compared with that on Day 8 of the pretreatment period will be compared between the arms. Changes in CASE scores divided into three segments (0 -4: excellent, 5 -9: moderate, 10 -27: poor) will also be compared. In addition, the period until CASE score becomes 4 points or less after the start of treatment with investigational product will be checked. **Secondary:** • Changes in mRS at each time point after the start of investigational product treatment compared with Day 8 of the pretreatment period will be compared between the arms. • To compare the change in GCS at each time point after the start of investigational product with that on Day 8 of the pretreatment period between the arms. • The change in MMSE-J at each time point after the start of investigational product as compared with Day 8 of the pretreatment period will be compared between the arms. • The change in FAB at each time point after the start of investigational product as compared with Day 8 of the pretreatment period will be compared between the arms.
Study start date	April 2022

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QDENGA (TAK-003): *LIVE ATTENUATED TETRAVALENT VACCINE FOR PREVENTION OF DENGUE DISEASE*

Study	NCT02747927
Indication	The prevention of dengue fever of any severity caused by any dengue virus serotype in individuals 4 years to 60 years of age
Phase	**Phase III** ***Tetravalent Immunization against Dengue Efficacy Study (TIDES)***
# of Patients	N = 20,100
Target Patients	Healthy children aged 4 to 16-year-old in dengue-endemic countries in Latin America and Asia
Arms/Intervention	• Randomized 2:1 to receive either TAK-003 or placebo on Day 1 and Day 90
Primary endpoint and key secondary endpoint(s) to be met per Trial Protocol	**Primary:** • ≥70% efficacy against all symptomatic dengue fever caused by any strain **Secondary:** • ≥70% efficacy individual strains • ≥60% efficacy in seronegatives **Safety:** • Comparable to other live attenuated viral vaccines (e.g., MMR, YF, Varicella) • No disease enhancement in partially protected individuals
Study start date	September 2016
Publications	• Tricou V, et al. The Lancet Global Health. 2024. • López-Medina E, et al. The Journal of Infectious Diseases. 2020. • Biswal S, et al. Clinical Infectious Disease. 2021

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