

# Summary of late-stage clinical trials

**As of Jan. 24, 2017**

The document contains information available on the date indicated in its cover page. The public information of clinicaltrials.gov is continuously updated as the trials make progress. See the current information on our ongoing trials at the Website.

<https://clinicaltrials.gov/>

# List of abbreviations

AE	Adverse Events
BID	Twice daily
DLT	Dose Limiting Toxicity
GFR	Glomerular Filtration Rate
iv	Intravenous
MTD	Maximum Tolerated Dose
ORR	Overall Response Rate
OS	Overall Survival
PD	Pharmacodynamics
PFS	Progression Free Survival
PK	Pharmacokinetics
po	Peroral
PPK	Population Pharmacokinetics
Q2W	Every Two Weeks
Q3W	Every Three Weeks
Q4W	Every Four Weeks
QD	Once Daily
QW	Once Weekly
sc	Subcutaneous
TID	Three Times a Day

# Late-stage pipeline summary

**KYOWA KIRIN**

Phase II	Phase III
AMG531 (romiplostim) Aplastic Anemia	AMG531 (romiplostim) Aplastic Anemia
AMG531 (romiplostim) ITP	AMG531 (romiplostim) ITP
ASKP1240 (bleselumab) Organ transplant rejection	ARQ 197 (tivantinib) Hepatocellular cancer
KHK4083 Ulcerative colitis	KHK4563 (benralizumab) Asthma
KHK4563 (benralizumab) Eosinophilic chronic rhinosinusitis	KHK4563 (benralizumab) COPD
KRN23 TIO/ENS	KHK4827 (brodalumab) Psoriasis
KRN23 XLH (pediatric)	KHK7580 (evocalcet) Secondary hyperparathyroidism
KW-0761 (mogamulizumab) ATL	KRN23 XLH (adult)
KW-6356 Parkinson's disease	KRN23 XLH (pediatric)
RTA 402 (bardoxolone methyl) CKD in patients with type 2 diabetes	KW-0761 (mogamulizumab) CTCL
	KW-6002 (istradefylline) Parkinson's disease

# KW-0761 (mogamulizumab)

KYOWA KIRIN

## Hematological cancer - relapsed/refractory ATL

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT01626664	U.S., Europe, others	Nov-16  N=71	<u>Arm 1: KW-0761</u> •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression <u>Arm 2: Investigator's choice</u> -pralatrexate (30 mg/m <sup>2</sup> Q3W until progression) -gemcitabine plus oxaliplatin (gemcitabine 1000 mg/m <sup>2</sup> , oxaliplatin 100 mg/m <sup>2</sup> Q2W until progression) -DHAP (dexamethasone 40 mg on day 1-4, cisplatin 100 mg/m <sup>2</sup> , cytarabine 2000 mg/m <sup>2</sup> Q4W until progression)	•Primary endpoint: ORR •Secondary endpoint: PFS, OS	

# KW-0761 (mogamulizumab)

KYOWA KIRIN

Hematological cancer - relapsed/refractory CTCL

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III  NCT01728805	U.S., Europe, Japan, others	Feb-17  N=373	<u>Arm 1: KW-0761</u> •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression <u>Arm 2: Vorinostat</u> •400 mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: ORR	

# KW-0761 (mogamulizumab)

KYOWA KIRIN

## Solid tumor

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I/II NCT02705105	U.S.	Mar-18 N=188	<u>KW-0761 + Nivolumab</u> <ul style="list-style-type: none"><li>•Part 1 (Dose Escalation Phase) KW-0761 and nivolumab are administered (iv) in combination.</li><li>•Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1</li></ul>	<ul style="list-style-type: none"><li>•Primary endpoint: MTD, DLT</li><li>•Secondary endpoint: Objective tumor response rate</li></ul>	Jointly developed with Bristol-Myers Squibb
Phase I NCT02301130	U.S.	Nov-17 N=108	<u>Arm 1 : KW-0761 + MEDI4736</u> <u>Arm 2 : KW-0761 + Tremelimumab</u> <ul style="list-style-type: none"><li>•Part 1 (Dose Escalation Phase) Increased iv doses of Arm 1 or Arm 2.</li><li>•Part 2 (Cohort Expansion Phase) Patients will be treated with MTD established in Part 1</li></ul>	<ul style="list-style-type: none"><li>•Primary endpoint: AE, DLT</li></ul>	Jointly developed with AstraZeneca
Phase I NCT02444793	U.S.	Aug-19 N=70	<u>KW-0761 + PF-05082566</u> <ul style="list-style-type: none"><li>•Part 1 (PF-05082566 dose escalation phase) Increased iv doses of PF-05082566 with KW-0761.</li><li>•Part 2 Patients will be treated with MTD established in Part 1.</li></ul>	<ul style="list-style-type: none"><li>•Primary endpoint: DLT</li><li>•Secondary endpoint: PK, Response, PFS</li></ul>	Jointly developed with Pfizer

# KW-0761 (mogamulizumab)

KYOWA KIRIN

## Solid tumor – cont.

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I NCT02476123	Japan	Oct-17 N=108	<u>KW-0761 + Nivolumab</u> •Part 1 (Dose Escalation Phase) KW-0761 and Nivolumab are administered (iv) in combination •Part 2 (Expansion Phase) Patients will be treated with MTD established in Part 1	•Primary endpoint: AE, DLT	Jointly developed with Ono Pharmaceutical / Bristol-Myers Squibb
Phase I NCT02358473	U.S.	Dec-16 N=13	<u>KW-0761 + Docetaxel</u> KW-0761 will be given as monotherapy in a 4-week run-in period Then KW-0761 will be given in combination with docetaxel up to 6 cycles After that KW-0761 will be given at the same dose administered in Cycle 1, Q3W as monotherapy	•Primary endpoint: AE, DLT	Completed



# KW-0761 (mogamulizumab)

KYOWA KIRIN

## Solid tumor – cont.

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I  NCT02867007	U.S.	Aug-19  N=50	<u>KW-0761 + KHK2455</u> •Part 1 (Dose Escalation Phase) KHK2455 monotherapy [Cycle 0] followed by KHK2455 + KW-0761 combination [Cycle 1] •Part 2 (Expansion Phase) Patients will be treated with the recommended dose of KHK2455 established in Part 1 in combination with KW-0761	•Primary endpoint: AE, DLT	

# KW-6002 (istradefylline)

KYOWA KIRIN

## Parkinson's disease

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT01968031	North America, Europe, others	Nov-16 N=609	<u>Arm 1: KW-6002 20 mg/day and placebo</u> <u>Arm 2: KW-6002 40 mg/day and placebo</u> <u>Arm 3: Placebo</u> •po, 12 weeks, double-blind	•Primary endpoint: Change from Baseline in the total hours of awake time per day spent in the OFF state	Completed

# KRN23

## XLH (adult)

KYOWA KIRIN

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02526160	U.S., Europe, Japan, Korea	Mar-17  N=134	<u>Arm 1: KRN23 Q4W</u> •sc, 1mg/kg, double-blind <u>Arm 2: Placebo Q4W</u> •sc, double-blind •cross over to receive KRN23 treatment at Week 24	•Primary endpoint: Proportion of subjects achieving mean serum P (phosphorus) levels above the lower limit of normal •Secondary endpoint: BPI (Brief Pain Inventory) Q3 Pain, PD, Bone biomarker and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase III NCT02537431	North America, Europe, Japan, Korea	Aug-17  N=14	<u>KRN23 Q4W</u> •1.0 mg/kg, 28 days, rounded to the nearest 10 mg up to a maximum dose of 90 mg	•Primary endpoint: O.Th (Osteoid Thickness), OS/BS (Osteoid surface/Bone surface), MLt (Mineralization lag time), OV/BV (Osteoid volume/Bone volume) •Secondary endpoint: Proportion of subjects achieving mean serum P levels above the lower limit of normal, MAR, MS/BS/BFR and so on.	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02312687	U.S.	Sep-16  N=25	<u>KRN23 Q4W</u> •sc, 68 weeks (starting doses will be based on the subject's last dose in the previous study)	•Primary endpoint: AE •Secondary endpoint: Change from Baseline in serum FGF23, PD and so on	Jointly developed with Ultragenyx (U.S.)

# KRN23

## XLH (pediatric)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02915705	North America, Europe, Australia, Japan, Korea	Sep-18 N=60	<u>Arm 1: KRN23</u> •sc, Q2W, 0.8 mg/kg starting dose <u>Arm 2: Control (Phosphate and Active Vitamin D)</u> •po, multiple daily doses	•Primary endpoint: Improvement in rickets •Other endpoint: Change in Serum P, 1,25(OH) <sub>2</sub> D (1,25-dihydroxyvitamin D), Growth, Six Minute Walk Test and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02163577	U.S., Europe	Dec-18 N=50	<u>Arm 1: KRN23 Q4W</u> <u>Arm 2: KRN23 Q2W</u> •sc, 64 weeks (16-week individual dose Titration Period, followed by a 48-week Treatment Period)	•Primary endpoint: Serum P, AE •Other endpoint: Increasing in height, Healing of rickets and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02750618	U.S.	Dec-17 N=13	<u>KRN23</u> •sc, Q2W, 64 weeks	•Primary endpoint: AE, PD •Other endpoint: Change in rickets, lower extremity skeletal abnormalities, recumbent length/standing height and so on	Jointly developed with Ultragenyx (U.S.)

# KRN23

## TIO/ENS

KYOWA KIRIN

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT02304367	U.S.	Sep-16  N=15	<u>KRN23 Q4W</u> •sc, starting dose of 0.3 mg/kg (Week 0), 44 weeks	•Primary endpoint: AE •Secondary endpoint: PK, PD, Evaluate changes in skeletal disease/osteomalacia and so on	Jointly developed with Ultragenyx (U.S.)
Phase II  NCT02722798	Japan, Korea	Jul-17  N=6	<u>KRN23 Q4W</u> •sc, 44 weeks	•Primary endpoint: Serum P concentration •Secondary endpoint: PK, PD, Evaluate changes in skeletal disease/osteomalacia and so on	

# RTA 402 (bardoxolone methyl)

KYOWA KIRIN

## CKD in patients with type 2 diabetes

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT02316821	Japan	Dec-17  N=108	<u>Arm 1: RTA 402</u> <u>Arm 2: Placebo</u> •QD, 16 weeks	•Primary endpoint: AE, change in GFR •Secondary endpoint: Change in eGFR (estimated GFR) , PK	

# KHK7580 (evocalcet)

## Secondary hyperparathyroidism

KYOWA KIRIN

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02549391	Japan	Mar-17 N=600	<u>Arm 1: KHK7580</u> <u>Arm 2: KRN1493</u> •po, QD, 30 weeks	•Primary endpoint: Percentage of subjects achieving a mean intact PTH (parathyroid hormone) level of $\geq 60$ pg/mL and $\leq 240$ pg/mL	
Phase III NCT02549417	Japan	Sep-17 N=30	<u>KHK7580</u> •po, QD, 32 weeks, after that 20 weeks (extension period)	•Primary endpoint: Percentage of subjects achieving a mean intact PTH level of $\geq 60$ pg/mL and $\leq 240$ pg/mL	
Phase III NCT02549404	Japan	Jun-17 N=120	<u>KHK7580</u> •po, QD, 52 weeks	•Primary endpoint: AE •Secondary endpoint: Percentage of subjects achieving intact PTH level of $\geq 60$ pg/mL and $\leq 240$ pg/mL and so on	

# ARQ 197 (tivantinib)

KYOWA KIRIN

## Hepatocellular cancer

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III  NCT02029157	Japan	Dec-16  N=160	<u>Arm 1: ARQ 197</u> <u>Arm 2: Placebo</u> •po, BID	•Primary endpoint: PFS •Secondary endpoint: OS	



# KHK4083

## Ulcerative Colitis

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02647866	U.S. Europe, others	Sep-18  N=60	<u>Arm 1: KHK4083</u> <u>Arm 2: Placebo</u> •iv, multiple ascending doses from Baseline to Week 48	•Primary endpoint: AE, Improvement in the mucosa •Secondary endpoint: Antidrug antibody , Mucosal healing, mMES (modified Mayo endoscopy sub-score )	

# KHK4563 (benralizumab)

## Asthma

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III BORA  NCT02258542	North America, Europe, Japan, Korea, others	Jul-18  N=2200	<u>Arm 1: Benralizumab</u> <u>Arm 2: Benralizumab</u> •sc	•Primary endpoint: AE •Secondary endpoint: Annual asthma exacerbation rate , ACQ-6 (Asthma Control Questionnaire-6), PK, FEV <sub>1</sub> (Forced expiratory volume in one second) and so on	Sponsored by AstraZeneca

# KHK4563 (benralizumab)

KYOWA KIRIN

## Chronic Obstructive Pulmonary Disease (COPD)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III GALATHEA  NCT02138916	North America, Europe, Japan, Korea, others	May-18  N=1626	<u>Arm 1: Benralizumab</u> <u>Arm 2: Benralizumab</u> <u>Arm 3: Placebo</u> •sc, 48 weeks	•Primary endpoint: Annual COPD exacerbation rate. •Secondary endpoint: SGRQ (St. George's Respiratory Questionnaire), CAT (COPD assessment tool), FEV <sub>1</sub> , PK and so on	Sponsored by AstraZeneca

# KHK4563 (benralizumab)

KYOWA KIRIN

## Eosinophilic Chronic Rhinosinusitis (ECRS)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT02772419	Japan	Oct-17  N=50	<u>Arm 1: Benralizumab</u> <u>Arm 2: Benralizumab</u> <u>Arm 3: Placebo</u> •sc, 24 weeks	• Primary endpoint: Change from baseline in nasal polyp score at Week 12 • Secondary endpoint: Change from baseline in CT (Computed tomography) score, Blood eosinophil count, Nasal Airway Resistance and so on.	

# KHK4827 (brodalumab)

KYOWA KIRIN

## Psoriasis

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III  NCT02982005	Korea	Dec-18  N=60	<u>Arm 1: KHK4827</u> •sc, 12 weeks <u>Arm 2: Placebo</u> •sc, 12 weeks <u>Arm 1 and Arm 2 (from week 13 until week 62):</u> •sc, administered KHK4827	•Primary endpoint: PASI (Psoriasis area and severity index) 75 response, sPGA (Static physician's global assessment) 0 (clear) or 1 (almost clear)	

# ASKP1240 (bleselumab)

## Organ transplant rejection

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT01780844	U.S.	Feb-17  N=149	<u>Arm 1: CNI avoidance</u> •Basiliximab induction + ASKP1240 + MMF + Corticosteroids <u>Arm 2: CNI minimization-MMF avoidance</u> •Basiliximab induction + ASKP1240 + Tacrolimus + Corticosteroids <u>Arm 3 (Active Comparator): Standard of Care</u> •Basiliximab induction + Tacrolimus + MMF + Corticosteroids	•Primary endpoint: BPAR (Biopsy-proven acute rejection) •Secondary endpoint: GFR, Patient Survival, Graft Survival	Jointly developed with Astellas

# AMG531 (romiplostim)

KYOWA KIRIN

## Idiopathic (Immune) Thrombocytopenic Purpura (ITP)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02868099	China	Dec-17 N=200	<u>Arm 1: AMG531</u> <u>Arm 2: Placebo</u> •sc, QW	•Primary endpoint: Number of weeks in which the platelet response counts increase above 50 x 10 <sup>9</sup> /L	
Phase I/II NCT02868060	China	Dec-17 N=24	<u>Arm 1: AMG531 1 µg/kg</u> <u>Arm 2: AMG531 3 µg/kg</u> <u>Arm 3: AMG531 6 µg/kg</u> •sc, on Day 1 and 8	•Primary endpoint: AE, antidrug antibody status	

# AMG531 (romiplostim)

KYOWA KIRIN

## Aplastic Anemia

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II/III  NCT02773290	Japan, Korea	Aug-18  N=27	<u>AMG531</u> •sc, QW	•Primary endpoint: Proportion of subjects achieving a hematological response (any of the platelet response, erythroid response, and neutrophil response)	
Phase II  NCT02094417	Korea	Mar-18  N=32	<u>Arm 1: AMG531 (Dose 1)</u> <u>Arm 2: AMG531 (Dose 2)</u> <u>Arm 3: AMG531 (Dose 3)</u> <u>Arm 4: AMG531 (Dose 4)</u> •sc, QW	•Primary endpoint: The proportion of subjects achieving a platelet response	



# KW-6356

## Parkinson's Disease

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II  NCT02939391	Japan	Dec-18  N=150	<u>Arm 1: KW-6356 Low Dose</u> <u>Arm 2: KW-6356 High Dose</u> <u>Arm 3: Placebo</u> •po, 12 weeks	•Primary endpoint: Change from baseline in MDS-UPDRS (Movement disorder society-unified Parkinson's disease rating scale) part III score	