

# **主な開発品の治験概要**

**2016年7月22日現在**

# List of abbreviations

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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

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# 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.	Aug-17  N=187	<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: MTD, DLT •Secondary endpoint: Objective tumor response rate	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> •Part 1 (Dose Escalation Phase) Increased iv doses of Arm 1 or Arm 2. •Part 2 (Cohort Expansion Phase) Patients will be treated with MTD established in Part 1	•Primary endpoint: AE, DLT	Jointly developed with AstraZeneca
Phase I  NCT02444793	U.S.	Dec-18  N=70	<u>KW-0761 + PF-05082566</u> •Part 1 (PF-05082566 dose escalation phase) Increased iv doses of PF-05082566 with KW-0761. •Part 2 Patients will be treated with MTD established in Part 1.	•Primary endpoint: DLT •Secondary endpoint: PK, Response, PFS	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	

# 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	

# KRN23

## XLH (pediatric)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02163577	U.S., Europe	Mar-17  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 (phosphorus), 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=10	<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

## XLH (adult)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02526160	North America, Europe, Japan, Korea	Mar-17 N=120	<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 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	Jan-17 N=10	<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

## 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, starting dose of 0.3 mg/kg (Week 0), 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=72	<u>Arm 1: RTA402</u> <u>Arm 2: Placebo</u> •QD, 16 weeks	•Primary endpoint: AE, change in GFR •Secondary endpoint: PK	

# KHK7580 (evocalcet)

## Secondary hyperparathyroidism

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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	

# BIW-8962

## Cancer (NSCLC, SCLC, Mesothelioma)

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I/IIa  NCT01898156	Korea	Apr-16  N=64	<u>BIW-8962</u> •Phase 1: iv, on day 1 of each 21 day cycle •Phase 2: recommended dose determined in Phase 1 until progression or unacceptable toxicity develops	•Primary endpoint: Phase 1: MTD, Safety and tolerability Phase 2 : ORR •Secondary endpoint: Phase 1: Tumor response, PK Phase 2 : Safety and tolerability	

# KHK4083

## Ulcerative Colitis

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02647866	U.S. Europe	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)

KYOWA KIRIN

## Asthma

Trial phase	Country/region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III CALIMA  NCT01914757	North America, Europe, Japan, others	Mar-16  N=2508	<u>Arm 1: Benralizumab</u> <u>Arm 2: Benralizumab</u> <u>Arm 4: Placebo</u> •sc, on Week 0 to 52  <u>Arm 3: Benralizumab</u> •sc, on Week 0 to 48	•Primary endpoint: Annual asthma exacerbation rate •Secondary endpoint: Pulmonary function (FEV <sub>1</sub> (Forced expiratory volume in one second)), asthma symptoms (PEF (Peak Expiratory Flow), ACQ-6(Asthma Control Questionnaire-6)), PK, AE and so on	Completed, Sponsored by AstraZeneca
Phase III SIROCCO  NCT01928771	U.S., Europe, Korea, others	Apr-16  N=2700	<u>Arm 1: Benralizumab</u> <u>Arm 2: Benralizumab</u> <u>Arm 3: Placebo</u> •sc, on Week 0 to 44	•Primary endpoint: Annual asthma exacerbation rate •Secondary endpoint: FEV <sub>1</sub> , PEF, ACQ-6, PK, AE and so on	Completed, Sponsored by AstraZeneca
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, PK, FEV <sub>1</sub> 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.	

# 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

## Aplastic Anemia

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
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	
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)	

# Z-206 (mesalazine)

KYOWA KIRIN

## Ulcerative Colitis (new dose regimen)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III  JapicCTI- 132135	Japan	Sep-16  N=600	<u>Z-206 2.4g/day</u> •QD or TID	•Primary endpoint: The proportion of patients without relapse •Secondary endpoint: The time to relapse	Jointly developed with Zeria Pharma