KYOWA KIRIN

主な開発品の治験概要

2017年12月31日現在

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本資料の内容は表紙に記載した時点における情報です。治験の進捗に伴い、治験データベース上の公開情報は随時更新されます。弊社が実施中の治験に関する最新情報につきましては、以下URLをご参照ください。
https://clinicaltrials.gov/

弊社の開発パイプラインの全体像は、以下URLよりご覧いただけます。
http://www.kyowa-kirin.co.jp/research_development_production/pipeline/index.html

List of abbreviations

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AE	Adverse Events
DLT	Dose Limiting Toxicity
iv	Intravenous
MTD	Maximum Tolerated Dose
ORR	Overall Response Rate
OS	Overall Survival
PD	Pharmacodynamics
PFS	Progression Free Survival
PK	Phamacokinetics
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

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Phase II	Phase III	
AMG531 (romiplostim) Aplastic Anemia	AMG531 (romiplostim) Aplastic Anemia	KW-0761 (mogamulizumab) HAM
ASKP1240 (bleselumab) Recurrence of focal segmental glomerulosclerosis in de novo kidney transplant recipients	KHK4563 (benralizumab) Asthma	
KHK2375 (entinostat) Breast cancer	KHK4563 (benralizumab) COPD	
KHK4083 Ulcerative colitis	KHK4827 (brodalumab) Psoriasis	
KHK4563 (benralizumab) Eosinophilic chronic rhinosinusitis	KHK4827 (brodalumab) axSpA	
KRN23 (burosumab) TIO/ENS	KHK7580 (evocalcet) Primary hyperparathyroidism	
KRN23 (burosumab) XLH (pediatric)	KRN23 (burosumab) XLH (adult)	
KW-0761 (mogamulizumab) ATL	KRN23 (burosumab) XLH (pediatric)	
KW-6356 Parkinson’s disease	KW-0761 (mogamulizumab) CTCL	

KW-0761 (mogamulizumab)

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Hematological cancer - relapsed/refractory ATL

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT01626664	U.S., Europe, others	Jan-18 N=71	Arm 1: KW-0761 •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression Arm 2: Investigator's choice -pralatrexate (30 mg/m^2 Q3W until progression) -gemcitabine plus oxaliplatin (gemcitabine 1000 mg/m^2, oxaliplatin 100 mg/m^2 Q2W until progression) -DHAP (dexamethasone 40 mg on day 1-4, cisplatin 100 mg/m^2, cytarabine 2000 mg/m^2 Q4W until progression)	•Primary endpoint: ORR •Secondary endpoint: PFS, OS	

KW-0761 (mogamulizumab)

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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	Dec-18 N=372	Arm 1: KW-0761 •1.0 mg/kg QW x 4 in cycle 1 then Q2W until progression Arm 2: Vorinostat •400 mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: ORR	

KW-0761 (mogamulizumab)

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Solid tumor

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase I/II NCT02705105	U.S.	Jul-18 N=188	KW-0761 + Nivolumab •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.	May-18 N=64	Arm 1 : KW-0761 + MEDI4736 Arm 2 : KW-0761 + Tremelimumab •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.	Oct-17 N=70	KW-0761 + PF-05082566 •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)

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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 Pharma-ceutical / Bristol-Myers Squibb
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	

KW-0761 (mogamulizumab)

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HTLV-1 Associated Myelopathy (HAM)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03191526	Japan	May-19 N=52	Arm 1: KW-0761 Q12W iv, 0.3mg/kg, double-blind, after that open study for 24 weeks Arm 2: Placebo Q12W Iv, double-blind, after that open study for 24 weeks	•Primary endpoint: Improvement in Osame's motor disability score •Secondary endpoint: HTLV-1 Proviral load in peripheral blood, Mean of twice 10 m walking time, Modified Ashworth Scale	

KRN23 (burosumab)

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XLH (adult)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02526160	U.S., Europe, Japan, Korea	Mar-18 N=134	Arm 1: KRN23 Q4W •sc, 1mg/kg, double-blind Arm 2: Placebo Q4W •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	KRN23 Q4W •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 (mineral apposition rate), MS/BS (mineralizing surface), BFR (bone formation rate) and so on.	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02312687	U.S.	Aug-18 N=25	KRN23 Q4W •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 (burosumab)

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XLH (pediatric)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02915705	North America, Europe, Australia, Japan, Korea	Oct-18 N=60	Arm 1: KRN23 •sc, Q2W, 64 weeks, 0.8 mg/kg starting dose Arm 2: Control (Phosphate and Active Vitamin D) •po, multiple daily doses, 64 weeks	•Primary endpoint: Improvement in rickets •Other endpoint: Change in Serum P, 1,25$(OH)_2$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	Arm 1: KRN23 Q4W Arm 2: KRN23 Q2W •sc, 64 weeks (16-week individual dose Titration Period, followed by a 48-week Treatment Period)	•Primary endpoint: Severity of rickets •Other endpoint: Change in Severity of Rickets, Growth, Walking Ability, Functional Disability and Pain and so on	Jointly developed with Ultragenyx (U.S., Europe)
Phase II NCT02750618	U.S.	Oct-19 N=13	KRN23 •sc, Q2W, 160 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 (burosumab)

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XLH (pediatric) – cont.

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03233126	Japan	Dec-19 N=10	KRN23 •sc, Q2W, 86 weeks	•Primary endpoint: AE •Secondary endpoint: Laboratory values, Change in Serum P, $1,25(OH)_2D$ (1,25-dihydroxyvitamin D), Rickets Severity Score (RSS) total score, Six Minute Walk Test, PK and so on	

KRN23 (burosumab)

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TIO/ENS

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02304367	U.S.	May-19 N=17	KRN23 Q4W •sc, starting dose of 0.3 mg/kg (Week 0), 140 weeks	•Primary endpoint: The proportion of subjects achieving mean serum P levels above the lower limit of normal, Percent change from baseline in excess osteoid based on analysis of iliac crest bone biopsies after 48 weeks of KRN23 treatment •Secondary endpoint: AE, PK, PD, bone turnover biomarkers (ex.BALP, CTx, P1NP), osteocalcin, BFI (Brief Fatigue Inventory), BPI and so on	Jointly developed with Ultragenyx (U.S.)
Phase II NCT02722798	Japan, Korea	Jun-19 N=6	KRN23 Q4W •sc, 44 weeks	•Primary endpoint: Serum P concentration •Secondary endpoint: PK, PD, Evaluate changes in skeletal disease/osteomalacia and so on	

KHK7580 (evocalcet)

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Primary hyperparathyroidism

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT03280264	Japan	Oct-19 N=10	KHK7580 •po, 24 weeks	•Primary endpoint: Percentage of subjects whose corrected serum calcium level is maintained ≤ 10.3 mg/dL for 2 weeks	

KHK2375 (entinostat)

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Breast cancer

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT03291886	Japan	Nov-21 N=124	Arm 1 : KHK2375 + Exemestane KHK2375: 5mg, po, QW Exemestane: 25mg, po, QD Arm 2 : Placebo + Exemestane Placebo: po, QW Exemestane: 25mg, po, QD	•Primary endpoint: PFS •Secondary endpoint: OS, Antitumor effect	

KHK4083

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Ulcerative Colitis

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02647866	U.S. Europe, others	Nov-18 N=60	Arm 1: KHK4083 Arm 2: Placebo •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) and so on	

KHK4563 (benralizumab)

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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=2133	Arm 1: Benralizumab Arm 2: Benralizumab •sc	•Primary endpoint: AE •Secondary endpoint: Annual asthma exacerbation rate , ACQ-6 (Asthma Control Questionnaire-6), PK, FEV_1 (Forced expiratory volume in one second) and so on	Sponsored by AstraZeneca

KHK4563 (benralizumab)

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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	Apr-18 N=1656	Arm 1: Benralizumab Arm 2: Benralizumab Arm 3: Placebo •sc, 48 weeks	•Primary endpoint: Annual COPD exacerbation rate. •Secondary endpoint: SGRQ (St. George's Respiratory Questionnaire), CAT (COPD assessment tool), FEV_1, PK and so on	Sponsored by AstraZeneca

KHK4563 (benralizumab)

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Eosinophilic Chronic Rhinosinusitis (ECRS)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02772419	Japan	Oct-17 N=64	Arm 1: Benralizumab Arm 2: Benralizumab Arm 3: Placebo •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)

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Psoriasis

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02982005	Korea	Dec-18 N=60	Arm 1: KHK4827 •sc, 12 weeks Arm 2: Placebo •sc, 12 weeks Arm 1 and Arm 2 (from week 13 until week 62): •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)	

KHK4827 (brodalumab)

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Axial Spondyloarthritis (axSpA)

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase III NCT02985983	Japan, Korea, Taiwan	Sep-19 N=120	Arm 1: KHK4827 •sc, 16 weeks Arm 2: Placebo •sc, 16 weeks Arm 1 and Arm 2 (from week 17 until week 66): •sc, administered KHK4827	•Primary endpoint: Percentage of ASAS (Assessment of SpondyloArthritis international Society) 40 in axSpA subjects	

ASKP1240 (bleselumab)

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Recurrence of focal segmental glomerulosclerosis (FSGS) in de novo kidney transplant recipients

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II NCT02921789	U.S.	May-20 N=60	Arm 1: ASKP1240 •Basiliximab + Methylprednisone + Prednisone + ASKP1240 + Tacrolimus Arm 2 (Active Comparator): Standard of Care •Basiliximab induction + Tacrolimus + Methylprednisone + Prednisone + MMF	•Primary endpoint: Recurrence of FSGS at 3 months post-transplant •Secondary endpoint: Recurrence of FSGS, BRAR, efficacy failure, and biopsy-proven rFSGS at 12 months post-transplant	Jointly developed with Astellas

AMG531 (romiplostim)

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Aplastic Anemia

Trial phase	Country/ region	Estimated study completion date / enrollment	Design	Endpoints	Remarks
Phase II/III NCT02773290	Japan, Korea	Dec-20 N=46	AMG531 •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	Arm 1: AMG531 (Dose 1) Arm 2: AMG531 (Dose 2) Arm 3: AMG531 (Dose 3) Arm 4: AMG531 (Dose 4) •sc, QW	•Primary endpoint: The proportion of subjects achieving a platelet response	

KW-6356

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Parkinson's Disease

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