CMB International Global Markets | Equity Research | Company Initiation

RemeGen (9995 HK)

A pioneer biopharma in innovative ADC and fusion protein medicines

BUY (Initiation)

Target Price	**HK$79.13**
Up/Downside	**+41.3%**
Current Price	**HK$56.00**

- **A pioneer biopharma with rich innovative pipelines.** RemeGen has developed a robust pipeline of more than 10 drugs/candidates, including 7 clinical-stage assets targeting over 20 indications. Since its inception in 2008, RemeGen has transformed from a biotech company into a fully integrated biopharma with two innovative biological drugs launched in China, telitacicept (RC18) and disitamab vedotin (RC48). The Company is one of the few Chinese biotech companies that have successfully marketed two internally developed innovative biological drugs.
- **RC18 is potentially best-in-class for SLE treatment**. RC18 was approved for the treatment of SLE in China in Mar 2021, becoming the second innovative biologic drug for SLE in China over the past 60 years. RC18's China Ph3 trial in SLE showed overwhelmingly strong efficacy, with the RC18 arm achieving 82.6% SRI-4 response rate, vs 38.1% in the control arm, indicating a significant response rate increase of 44.5% (P<0.001). A cross-trial comparison shows belimumab only had 9.4% increase in SRI-4 response rates in its China pivotal trial. Compared to other drugs or drug candidates at late-stage of development targeting SLE indication, RC18 demonstrated the best efficacy with a well-tolerated safety profile. RemeGen is evaluating RC18 in late-stage trials for multiple autoimmune diseases with limited treatment options, including SLE (Ph3 in China, the US and Europe), IgAN (Ph3 in China and Ph2 in the US), pSS, MG, RA, etc. We expect RemeGen to partner with an MNC pharma for the global development and commercialization of RC18.
- **RC48 is the first-to-market domestic ADC drug**. RC48, an anti-HER2 ADC, was approved in Jun 2021 for third-line or later treatment of GC in China, becoming the first-to-market domestic ADC. In Dec 2021, RC48 was further approved for UC treatment in China. RemeGen aims to bring RC48 to front-line treatment with multiple Ph3 trials for UC, BC and GC ongoing or planned in China and globally. Compared with other anti-HER2 ADC drugs like DS-8201 and T-DM1, RC48 distinguished itself by targeting differentiated indications, especially UC, and favorable safety profile. HER2-Low tumors, as observed in BC, GC, UC, BTC and NSCLC, generally do not respond to trastuzumab or T-DM1, and remain large underserved markets. RemeGen, partnered with Seagen, is strategically developing RC48 for HER2-low tumors, with a number of trials in both HER2-high and low UC/BC ongoing in China and the US.
- **Initiate at BUY with TP of HK$79.13**. Supported by the growing commercialization capabilities, we expect RemeGen's product sales to ramp up fast in the coming years, with RC18 and RC48 being the major revenue drivers due to the increasing patient demands and indication extensions. We derive our target price of HK$79.13 based on a DCF valuation (WACC: 10.25%, terminal growth rate: 3.0%).
- **Near-term catalysts:** Sales ramp-up; data readout of RC18 in SLE (China Ph3), IgAN (US Ph2) and pSS (China Ph2); NRDL indication extension of RC48; RC18 out licensing.

Earnings Summary

(YE 31 Dec)	FY20A	FY21A	FY22E	FY23E	FY24E
Revenue (RMB mn)	na	1,424	860	1,344	2,189
YoY growth (%)	na	na	(39.6)	56.4	62.9
Net profit (RMB mn)	(698)	276	(933)	(956)	(776)
EPS (Reported) (RMB)	(1.71)	0.57	(1.71)	(1.76)	(1.43)
R&D expenses (RMB mn)	(466)	(711)	(900)	(1,000)	(1,000)
Admin expenses (RMB mn)	(218)	(220)	(224)	(309)	(438)

Source: Company data, Bloomberg, CMBIGM estimates

China Healthcare Sector

Jill Wu, CFA
(852) 3900 0842
jillwu@cmbi.com.hk

Andy Wang
(852) 3657 6288
andywang@cmbi.com.hk

Stock Data

Mkt Cap (HK$ mn)	30,478.7
Avg 3mths t/o (HK$ mn)	43.8
52w High/Low (HK$)	109.30/26.00
Total Issued Shares (mn)	544.3

Source: FactSet

Shareholding Structure

HKSCC nominees limited	33.6%
Yantai Rongda	18.8%

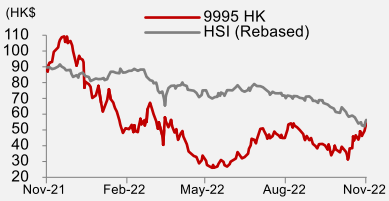
Source: Company data

Share Performance

	Absolute	Relative
1-mth	56.4%	74.2%
3-mth	25.3%	61.4%
6-mth	83.9%	153.0%

Source: FactSet

12-mth Price Performance



Source: FactSet

Auditor: Ernst & Young
Web-site: https://www.remegen.cn

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Investment Thesis

Incorporated in 2008, RemeGen has transformed from a biotech company into a fully integrated biopharma company with two internally developed innovative biological drugs launched in China. RemeGen was listed on HKEx in Nov 2020, and was listed on SSE STAR Market in Mar 2022.

Innovative pipelines with BIC/FIC potentials

RemeGen has discovered and developed a robust pipeline of more than 10 drug candidates, including 7 clinical-stage assets targeting over 20 indications. RemeGen is also evaluating its two commercial-stage drugs, telitacicept (RC18) and disitamab vedotin (RC48), in clinical trials targeting 14 indications in China and the US. Other clinical-stage assets include RC28 (VEGF/FGF fusion protein), RC88 (mesothelin ADC), RC108 (c-Met ADC), RC118 (Claudin18.2 ADC) and RC98 (PD-L1).

Telitacicept (RC18, a TACI-Fc fusion protein targeting BLyS/APRIL) was conditionally approved for the treatment of adult patients with moderate-to-severe SLE in China in Mar 2021, becoming the second innovative biologic drug approved for the treatment of SLE in China over the past 60 years, following the approval of GlaxoSmithKline's belimumab in Jul 2019 in China. RC18 was included in the NRDL in Jan 2022. We believe RC18 is potentially the best-in-class BLyS/APRIL dual-targeted therapy for SLE treatment, in comparison with other marketed and pipeline biologic therapies for SLE with single or different drug targets. RC18 has demonstrated strong efficacy and good safety profile in treating SLE. The China Ph3 trial in SLE demonstrated overwhelming results with the RC18 arm achieving 82.6% SRI-4 response rate, compared to 38.1% in the control arm, indicating a significant improvement of 44.5% in response rate ($P<0.001$). A cross-trial comparison shows that belimumab only achieved 9.4% increase in SRI-4 response rates in its China pivotal trial. While looking into other approved drugs or drug candidates at late stage of development targeting SLE indication, RC18 has demonstrated the best efficacy with a well-tolerated safety profile. Additionally, RemeGen is evaluating RC18 in late-stage clinical trials for multiple autoimmune diseases currently with limited treatment options, including SLE (Ph3 in China, the US and Europe), IgAN (Ph3 in China and Ph2 in the US), pSS, MG, RA, NMOSD, etc. We expect the Company to collaborate with MNC pharma companies for the global development and commercialization of RC18.

Disitamab vedotin (RC48, HER2 ADC) received conditional approval in Jun 2021 for third-line or later treatment of GC in China, becoming the first-to-market domestically-developed ADC. In Dec 2021, RC48 received conditional approval for the second-line or later treatment of UC in China. RemeGen targets to bring RC48 to earlier treatment settings for UC, BC and GC with multiple Ph3 trials ongoing or in plan in China and globally. Compared with other anti-HER2 ADC drugs like DS-8201 and T-DM1, RC48 distinguished itself with differentiated indications, especially UC, and a favorable safety profile. Low-level HER2 expression (IHC 2+/FISH- or IHC 1+) is observed in around 50% of BC cases, and is also observed in a number of other cancer types, such as GC, UC, BTC and NSCLC. Low HER2-expressing tumors generally do not respond to trastuzumab or T-DM1, indicating large unmet medical needs. Beyond HER2 high-expressing cancers, RemeGen is strategically developing RC48 to meet the needs of the underserved patients with HER2-low expressions, with a number of clinical trials in HER2 low-expressing UC/BC ongoing in China and the US. Worth mentioning, in a blockbuster deal, RemeGen out-licensed the rights of RC48 in certain overseas regions to Seagen, and is entitled to receive a total upfront and milestone payments of up to US$2.6bn and future sales royalties. The collaboration will facilitate RC48's global development and commercialization.

Proprietary R&D engine powered by three specialized platforms

The Company's fully-integrated capabilities are driven by a proprietary R&D engine, which consists of three specialized platforms, including (1) Antibody and fusion protein platform, which features the generation of novel mAbs and fusion proteins through internal studies. A number of mAbs and fusion proteins have been generated using this platform, including RC18 (BLyS/APRIL fusion protein), RC28

(VEGF/FGF fusion protein), RC98 (PD-L1 mAb), RC198 (confidential fusion protein), etc., with RC18 already been approved for SLE treatment. (2) ADC platform, which features fully integrated in-house capabilities covering the whole process of ADC development and manufacturing, including the syntheses of antibody, linker and chemotherapy payload. Leveraging this platform, the Company has discovered and is developing a number of ADC drugs, including RC48 (HER2 ADC), RC88 (mesothelin ADC), RC108 (c-MET ADC), RC118 (Claudin18.2 ADC), etc., with the leading ADC product RC48 already been approved in China for GC and UC treatment. (3) Bifunctional antibody (HiBody) platform, which focuses on R&D of next-generation bifunctional antibodies. Using this novel molecular format, a number of bifunctional antibodies have been constructed, i.e. RC138, RC148 and RC158.

Solid talent pool and abundant manufacturing capacity to support business growth

As of Jun 2022, RemeGen has 2,500 employees, among which 44% are research and development related employees. RemeGen's R&D team of over 500 employees (as of Aug 2022) is led by Dr. Fang Jianmin, the inventor of conbercept, an anti-VEGF fusion protein and the first domestic biologic drug approved for wet AMD in China. Leveraging Dr. Fang's experience in developing conbercept, the Company has designed one of its key assets RC28, a VEGF/FGF dual-targeting fusion protein. The in-house clinical development and registration team comprises 375 employees (as of Aug 2022). The team has intensive experience in bioinformatics and omics data analytics, and has designed and executed >30 clinical trials, including 7 phase II/III registrational trials. RemeGen is expanding its two independent commercial teams in the sales and marketing department. (1) The commercial team for autoimmune diseases is led by Wu Jingping, a seasoned leader previously in charge of 3SBio's overall sales of Yisaipu, a TNFR2-Fc fusion protein biosimilar for rheumatoid arthritis (RA), which shares the same hospital channel as SLE. The autoimmune disease commercial team has expanded from 130 employees as of end 2021 to ~470 employees as of Sep 2022. (2) The commercial team for oncology has expanded to 497 employees as of Sep 2022 from 180 employees as of the end of 2021. We expect the Company to further expand its two commercial teams in 2022.

RemeGen is expanding its manufacturing capability to meet the increasing product demand. The current manufacturing facility is capable of an annual output of up to 2.3mn vials of antibodies and up to 1.5mn vials of ADCs. The global GMP-compliant manufacturing facilities house six 2,000L disposable bag bioreactors for a total capacity of 12,000L for large-scale recombinant protein production. The manufacturing capacity has been expanded to 36,000L as of the end of 2021. RemeGen plans to further expand the total manufacturing capacity to 80,000L before 2025.

Initiate at BUY with TP of HK$79.13

We expect RemeGen's product sales to ramp up quickly and RC18 and RC48 will be the major revenue drivers of the Company. We estimate RemeGen's total risk-adjusted revenue of RMB860mn/ RMB1,344mn/ RMB2,189mn in FY22E/ 23E/ 24E, and net losses of RMB933mn/ RMB956mn/ RMB776mn in FY22E/ 23E/ 24E, respectively. We derive our target price of HK$79.13 based on a DCF valuation (WACC: 10.25%, terminal growth rate: 3.0%).

Investment risks

1) Failure of clinical development or regulatory approvals of drug candidates.

2) Competition of approved products both in China and overseas markets.

Pioneer biopharma in innovative ADC and other biological medicines

RemeGen is a commercial stage biopharma company committed to the development and commercialization of innovative biologics for the treatment of a variety of autoimmune, oncology and ophthalmology diseases. Founded in 2008, Remegen is headquartered in Yantai, Shandong, China, with research labs and offices also located in Beijing, Shanghai, San Francisco and Washington. Since its inception, RemeGen has transformed from a biotech company into a fully integrated biopharma company with two innovative biological drugs launched in China. The Company is one of the few Chinese biotech companies that have two internally developed innovative commercialized products. RemeGen was listed on HKEx in Nov 2020, and was listed on SSE STAR Market in Mar 2022.

Innovative pipelines with BIC/FIC potentials

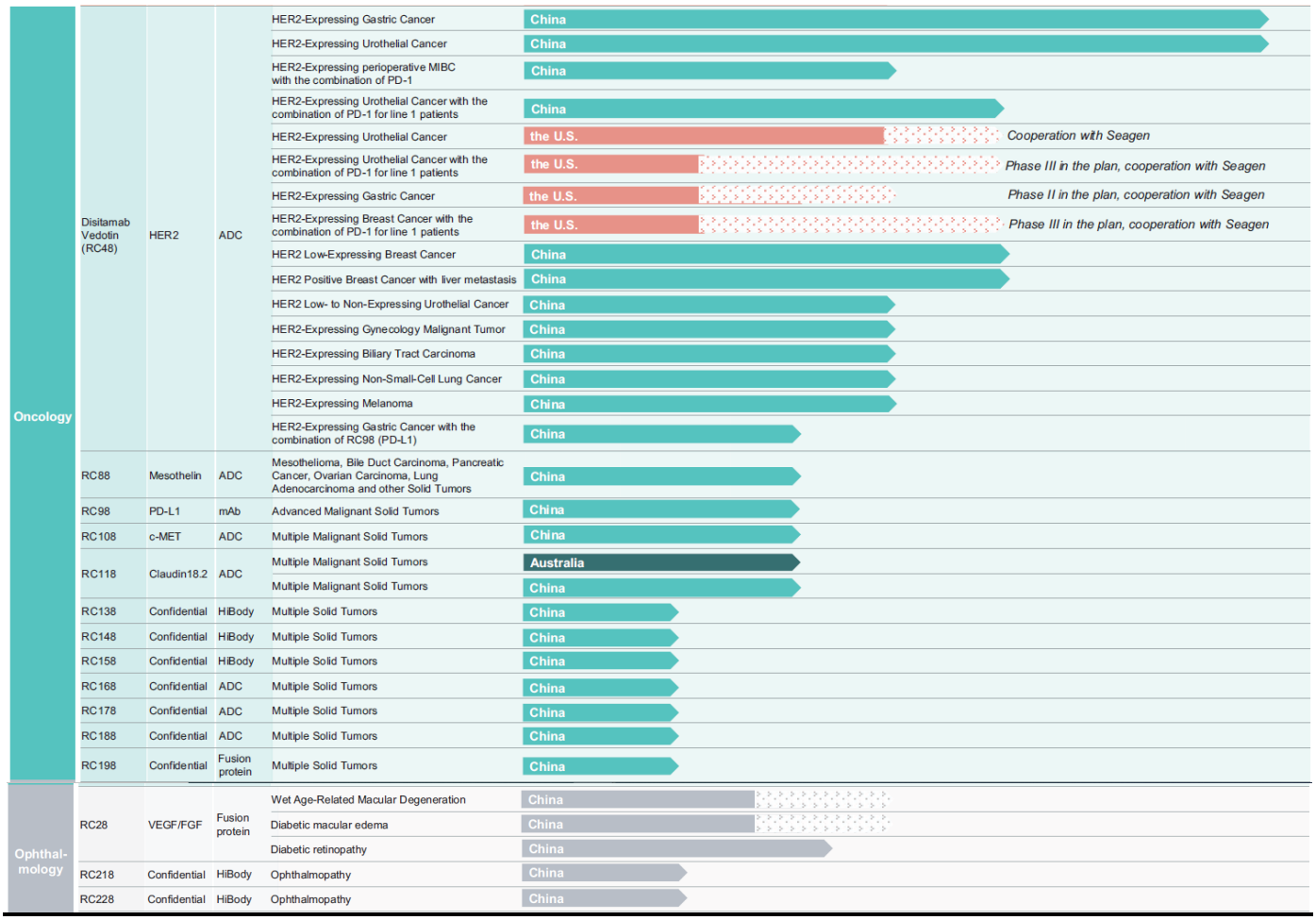
RemeGen has discovered and developed a robust pipeline of more than 10 drug candidates, including 7 clinical-stage assets targeting over 20 indications. RemeGen is also evaluating its two commercial-stage drugs, telitacicept (RC18) and disitamab vedotin (RC48), in clinical trials targeting 14 indications in China and the US. Other clinical-stage assets include RC28 (VEGF/FGF fusion protein), RC88 (mesothelin ADC), RC108 (c-Met ADC), RC118 (Claudin18.2 ADC) and RC98 (PD-L1).

RC18 was conditionally approved for the treatment of moderate-to-severe SLE in China in Mar 2021, becoming the second innovative biologic drug approved for treatment of SLE in China over the past 60 years.

RC48 received conditional approval in Jun 2021 for the treatment of GC, becoming the first-to-market domestic ADC. RC48 also received conditional approval for the treatment of UC in China in Dec 2021. In Aug 2021, the Company out-licensed the rights of RC48 in overseas regions except Asia (excluding Japan and Singapore) to Seagen (SGEN US), and is entitled to receive a total upfront and milestone payments of up to US$2.6bn and high single digit to mid-teens percentage of sales royalties.

Figure 1: Rich product pipeline across three therapeutic areas

	Drug Candidates	Target	Modality	Indication	Status (Clinical Sites Indicated on Status Bar)
					Pre-clinic. / IND / Ph I / Ph II / Pivotal/Ph III / NDA / Launched
Autoimmune Diseases	Telitacicept (RC18)	BLyS/ APRIL	Fusion protein	Systemic Lupus Erythematosus	China
				Systemic Lupus Erythematosus	the U.S.
				Neuromyelitis Optica Spectrum Disorder	China
				Rheumatoid Arthritis	China
				IgA Nephritis	China
				IgA Nephritis	the U.S.
				Primary Sjögren's Syndrome	China
				Multiple Sclerosis	China
				Myasthenia Gravis	China



Source: Company presentation in Aug 2022, CMBIGM

RC18: potential FIC dual-targeting fusion protein with impressive efficacy in B cell-mediated autoimmune diseases

Telitacicept (RC18), a TACI-Fc fusion protein, targets two cell-signaling molecules critical for B-lymphocyte development: B-cell lymphocyte stimulator (BLyS) and a proliferation inducing ligand (APRIL), which allows it to effectively reduce B-cell mediated autoimmune responses that are implicated in several autoimmune diseases. Telitacicept's fundamental differentiation in comparison with competing drugs (especially biologics) lie in: (i) its dual-targeting mechanism and bioinformatics-optimized structure design, which enhances its biological activity, promotes molecular stability, and facilitates production; and (ii) its full human amino acid sequence, which minimizes undesired potential immunogenicity.

SLE, currently the lead indication of telitacicept, is a hard-to-treat systemic autoimmune disorder that causes widespread immune attack in the human body, which inflicts tissue damage in multiple organs, and has one of the highest mortality and disability rates among autoimmune diseases. To date, there is no effective cure for SLE, and the currently available treatments other than telitacicept are either limited in efficacy or can cause severe side effects. Telitacicept is potentially the best-in-class BLyS/APRIL dual targeted therapy for SLE, in comparison with other marketed and pipeline biologic therapies for SLE with single or different drug targets.

In Mar 2021, the NMPA granted conditional approval of telitacicept for the treatment of adult patients with moderate-to-severe SLE in China, which made telitacicept the second innovative biologics drug approved for treatment of SLE in China over the past 60 years, following the approval of GlaxoSmithKline's belimumab in Jul 2019 in China. Telitacicept was included in the NRDL in Jan 2022.

Telitacicept has demonstrated a strong efficacy and good safety profile in treating SLE, supporting its best-in-class potential. In the China registrational Ph2b trial, telitacicept treatment groups at multiple dose levels had significantly higher SRI-4 response rates (68.3% ~ 75.8%) than the placebo group (33.9%), with the difference ranging from 34.4% to 41.9%, indicating significant reduction in SLE disease activity after the treatment with telitacicept. The confirmatory Ph3 trial demonstrated even better results with the telitacicept 160mg treatment group achieving 82.6% SRI-4 response rate, compared to 38.1% in the control arm, showing significant improvement of 44.5% in response rate (P<0.001). Cross-trial comparison shows that belimumab only achieved 9.4% increase in SRI-4 response rates as observed in its China pivotal trial. While looking into other approved drugs or drug candidates at late stage of development, RC18 has demonstrated the best efficacy with well-tolerated safety profile.

RemeGen is currently evaluating telitacicept in late-stage clinical trials for multiple autoimmune diseases currently with limited treatment options, including SLE (Ph3 in China, the US and Europe), IgAN (Ph3 in China and Ph2 in the US), pSS, MG, RA, NMOSD, etc. We expect the Company to collaborate with global leading biopharma companies for the potential co-development or out-license of telitacicept.

RC48: first-to-market domestic anti-HER2 ADC with differentiated targeted indications

Disitamab vedotin (RC48), a novel anti-HER2 ADC, is the first-to-market domestically-developed ADC drug in China. RC48 has demonstrated promising efficacy in patients with HER2-expressing advanced or metastatic GC and UC, and has also proved its potential as treatment for HER2-expressing (including low-expressing) BC. Conditionally approved in China for the third-line or later treatment of HER2 over-expressing GC in Jun 2021 and for second-line or later treatment of HER2 over-expressing UC in Dec 2021, RC48 is the first-to-market domestic ADC in China and is well-positioned to capture the largely unmet medical needs. RemeGen targets to bring RC48 to front-line treatment for UC, BC and GC with multiple Ph3 trials ongoing or in plan in China and globally. Compared with other anti-HER2 ADC drugs like DS-8201 and T-DM1, RC48 distinguished itself by targeting differentiated indications, especially UC, and having a favorable safety profile to support its potential front-line applications in combo with other I/O drugs.

Unlike the conjugation of trastuzumab and a tubulin inhibitor emtansine in T-DM1 or the conjugation of trastuzumab and a topoisomerase I inhibitor payload in DS-8201, RC48 is composed of hertuzumab and the microtubule inhibitor monomethyl auristatin E (MMAE) via a cleavable. Compared with trastuzumab, hertuzumab has a higher affinity to HER2 and capacity of ADCC in vitro. After conjugation with MMAE, the cytotoxicity of hertuzumab was significantly enhanced, whereas the binding specificity for HER2 was not affected. Furthermore, unlike T-DM1 with minimal bystander effect due to non-cleavable linker and poor membrane permeability, RC48 has a strong bystander killing effect on surrounding tumor cells that can reverse T-DM1 resistance by acting on populations of cells not overexpressing HER2. Additionally, RC48 features a cleavable linker that does not rely on the activity of V-ATPase in lysosomes and has less lysosomal resistance.

While HER2 has emerged as one of the main targets for the ADCs, HER2-positive BC continues to be the most heavily investigated cancer type for the use of anti-HER2 ADC. Low-level HER2 expression (IHC 2+/FISH- or IHC 1+) is observed in around 50% of BC cases, indicating a large therapeutic potential and opportunity for anti-HER2 ADCs beyond HER2 high-expressing BC. Moreover, HER2-expression at various levels (including low expression levels) is also observed in a number of other cancer types, such as GC, UC, BTC and NSCLC. Various tumors with low HER2 expressions remain to be a largely unmet therapeutic market. RemeGen is strategically developing RC48 to meet the needs of an underserved market, and is currently conducting clinical trials in both HER2-high and low UC/BC in China and the US.

RC28: potential FIC VEGF/FGF dual-targeting fusion protein for treating ophthalmic diseases

RC28 is a fusion protein targeting both vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) with first-in-class potential, in comparison with other ophthalmology biologic therapies with

single target. RemeGen is developing RC28 for the treatment of hard-to-treat ocular diseases, including wet age-related macular degeneration (wet AMD), diabetic macular edema (DME) and diabetic retinophathy (DR).

The current biological treatments approved for wet AMD and DME in China or the US include ranibizumab, aflibercept, conbercept and brolucizumab, all of which are VEGF single-targeted biologics. The competitive advantages of RC28 lie in (i) dual-targeting mechanism that overcomes the major challenges faced by single-target VEGF antagonists, which is the upregulated expression of other pro-angiogenic factors when the VEGF pathway alone is inhibited; and (ii) potentially less frequent dosing schedule due to a long half-time pharmacokinetic profile that could translate to reduction in treatment costs and improved compliance. We believe RC28 has the potential to be a differentiated biologic therapy with a good efficacy and safety profile for these diseases by inhibiting VEGF and FGF pathways simultaneously. Additionally, the Co-Founder, CEO and CSO, Dr. Fang Jianmin, is the inventor of conbercept, an anti-VEGF fusion protein and the first domestically-developed biologic drug approved for wet AMD in China. Conbercept achieved RMB1.32bn in sales in 2021. Dr. Fang's successful experiences in conbercept will facilitate the development of RC28, in our view.

Early clinical-stage drug candidates

RemeGen's early stage pipeline assets mainly include clinical-stage RC88 (mesothelin ADC), RC98 (PD-L1 mAb), RC108 (c-Met ADC), and RC118 (Claudin18.2 ADC), and around a dozen preclinical assets.

RC88 is a novel mesothelin-targeting ADC for the treatment of solid tumors. It is currently being assessed in a PhI trial in patients with multiple advanced solid tumors, including pancreatic cancer, mesothelioma, bile duct carcinoma, ovarian carcinoma, gastric cancer, triple-negative breast cancer and lung adenocarcinoma. The trial has enrolled 49 patients as of 30 Jun 2022.

RC98 is an innovative PD-L1 mAb for the treatment of solid tumors. The Company has initiated a PhI trial of RC98 in patients with multiple advanced solid tumors, including but not limited to lung cancer and urothelial cancer. 49 patients had been enrolled as of 30 Jun 2022. In addition, the Company is exploring the possibility of RC48 in combination with RC98 for the treatment of HER2-expressing GC, with the IND of the Ph1 trial approved by CDE in Apr 2022.

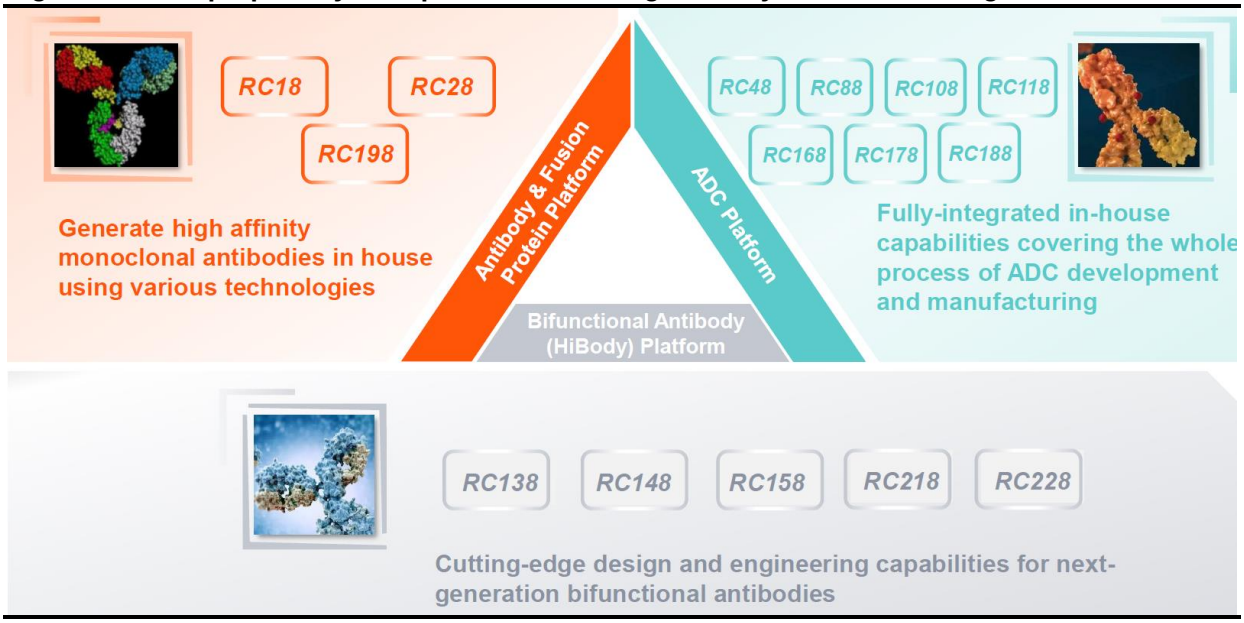
RC108, c-Met-targeted ADC, is Company's third ADC product developed in-house that has entered into clinical development stage. c-Met is a receptor tyrosine kinase that, after binding with its ligand, hepatocyte growth factor, activates a wide range of different cellular signaling pathways, including those involved in proliferation, motility, migration and invasion. It is a well-characterized oncogene that is associated with poor prognosis in many solid tumor types. RemeGen has started a PhI trial for RC108 in c-Met positive advanced solid tumors in China in 2020. 16 patients have been enrolled as of 30 Jun 2022.

RC118 is the Company's fourth clinical-stage ADC drug candidate, targeting Claudin18.2-positive solid tumors. RC118 conjugates the humanized anti-Claudin18.2 mAb and the small molecule MMAE via cathepsin-cleavable linkers, with optimized drug-to-antibody ratio. Currently, the Company is conducting a PhI trial in patients with Claudin18.2-positive solid tumors in Australia and China.

Proprietary R&D engine powered by three specialized platforms

The Company's fully-integrated capabilities are driven by a proprietary R&D engine, which consists of three specialized platforms, including: (i) an antibody and fusion protein platform, (ii) an ADC platform, and (iii) a bifunctional antibody (HiBody) platform.

Figure 2: Three proprietary R&D platforms enabling a variety of BIC/FIC biologics



Source: Company data, CMBIGM

The antibody and fusion protein platform features generation of novel mAbs and fusion proteins through internal studies. High affinity mAbs can be generated on the platform in-house using various technologies, including murine hybridoma, human B cell cDNA phage-display library and llama nanobody phage-display library. The platform has extensive capabilities in bioinformatics-aided protein design and engineering for Fc fusion proteins. The platform is well-established and includes the following main functionalities: (i) antibody/fusion protein screening and engineering; (ii) cell line/process development; and (iii) drug substance/drug product GMP manufacturing. A number of mAbs and fusion proteins have been generated using this platform, including RC18 (BLyS/APRIL fusion protein), RC28 (VEGF/FGF fusion protein), RC98 (PD-L1 mAb), RC198 (confidential fusion protein), etc. In the case of RC18, the recombinant TACI-Fc fusion protein is bioinformatics-optimized and incorporates the extracellular BLyS/APRIL-binding domain of human TACI to the maximum extent, which showcases the R&D capabilities of the platform.

The ADC platform features fully-integrated in-house capabilities covering the whole process of ADC development and manufacturing, including the syntheses of antibody, linker and chemotherapy payload. The key to ADC discovery and development is to get three distinct components to work together. Through many years of ADC research, the Company accumulated extensive expertise on choice of conjugation chemistry and linker and optimization of the conjugation reaction parameters. For each ADC drug candidate, RemeGen screens a large panel of combinations of conjugation methods, linkers and payloads to optimize molecular composition. A proprietary Thiel-bridge conjugation technology has been developed to yield more homogeneous ADC products that can improve pharmacodynamics and increase therapeutic window. The platform also has global GMP-compliant manufacturing facility for entire ADC manufacturing process, including antibody production, syntheses of payloads, linkers, and payload-linkers, ADC conjugation, and fill/finish. Leveraging this platform, the Company has discovered and is developing a number of ADC drugs, including RC48 (HER2 ADC), RC88 (mesothelin ADC), RC108 (c-MET ADC), RC118 (Claudin18.2 ADC), etc., with the leading ADC product RC48 already approved in China for GC and UC treatment.

The bifunctional antibody (HiBody) platform focuses on R&D of cutting-edge design and engineering capabilities for next-generation bifunctional antibodies. The HiBody technology is based on novel molecular format and is versatile in generating various bispecific antibodies. Using this novel molecular format, a number of bifunctional antibodies has been constructed, i.e. RC138, RC148 and RC158. For many bispecific platforms, manufacturability is a key issue that often results in project failure. The HiBody

products have shown high expression level and have constantly had product yield similar to conventional antibodies. The products from this HiBody platform is homogeneous and easy to adapt to the Company's manufacturing process.

Solid talent pool and abundant manufacturing capacity to support business growth

As of Jun 2022, RemeGen has 2,500 employees in total, among which 1,107 are research and development employees, accounting for 44% of the Company's total employee number.

RemeGen's R&D team of over 500 employees (as of Aug 2022) is led by Dr. Fang Jianmin, the inventor of conbercept, an anti-VEGF fusion protein and the first domestically-developed biologic drug approved for wet AMD in China. Leveraging Dr. Fang's successful experience in developing conbercept, the Company has designed one of its key assets RC28, a VEGF/FGF dual-targeting fusion protein. The Shanghai R&D center is the Company's main R&D hub in China. An early stage drug R&D center was set up in California, focusing on most cutting-edge innovative programs.

The in-house clinical development and registration team consists of 375 employees (as of Aug 2022), led by Dr. He Ruyi, a former FDA clinical review officer and former CDE chief scientist with ~20 years of regulatory experience. The clinical development team has intensive experience in bioinformatics and omics data analytics, and has designed and executed >30 clinical trials, including 7 phase II/III registrational trials. The team of regulatory affairs specialists has achieved remarkable results. For instance, the FDA has granted RC18 fast track designation for SLE in the US, provided clearance for Ph3 clinical trial of RC18 for SLE in the US, granted RC48 breakthrough therapy, fast track designations and provided clearance for clinical studies for UC in the US, etc.

The Company's sales and marketing department has two independent commercial teams in the area of autoimmune diseases and oncology, led by Mr. Wu Jingping and Mr. Tang Gang, respectively. (1) Commercial team for autoimmune diseases: Wu Jingping is a seasoned leader previously worked at 3SBio in charge of the overall sales of Yisaipu. Yisaipu is a TNFR2-Fc fusion protein biosimilar approved for the treatment of rheumatoid arthritis (RA), which shares the same hospital channel as SLE. The Company's commercial team for autoimmune diseases has expanded from 130 employees as of end 2021 to around 470 employees as of Sep 2022. (2) Commercial team for oncology: Previously worked for AstraZeneca, Pfizer, Roche, and BMS, Tang Gang has been deeply engaged in the Chinese pharmaceutical market for 20 years. As of Sep 2022, the sales team for oncology has expanded to around 500 employees from 310 employees at the end of 2021. We expect the Company to further expand its two commercial teams in 2022.

With RC18 and RC48 both covered by NRDL, the Company is leveraging its expertise and industry connections of the commercial teams through a physician-targeted marketing strategy to increase the accessibility of the two core products.

RemeGen is expanding its manufacturing capability to meet the increasing product demand. The manufacturing facilities of the Company are located in Yantai, Shandong province, where the headquarters are based. Current manufacturing facility is capable of an annual output of up to 2.3mn vials of antibodies and up to 1.5mn vials of ADCs. The global GMP-compliant manufacturing facilities house six 2,000L disposable bag bioreactors for a total capacity of 12,000L for large-scale recombinant protein production. The manufacturing capacity has reached 36,000L by the end of 2021. RemeGen plans to expand the total manufacturing capacity to 80,000L before 2025.

Telitacicept (RC18): innovative fusion protein for treating broad autoimmune diseases

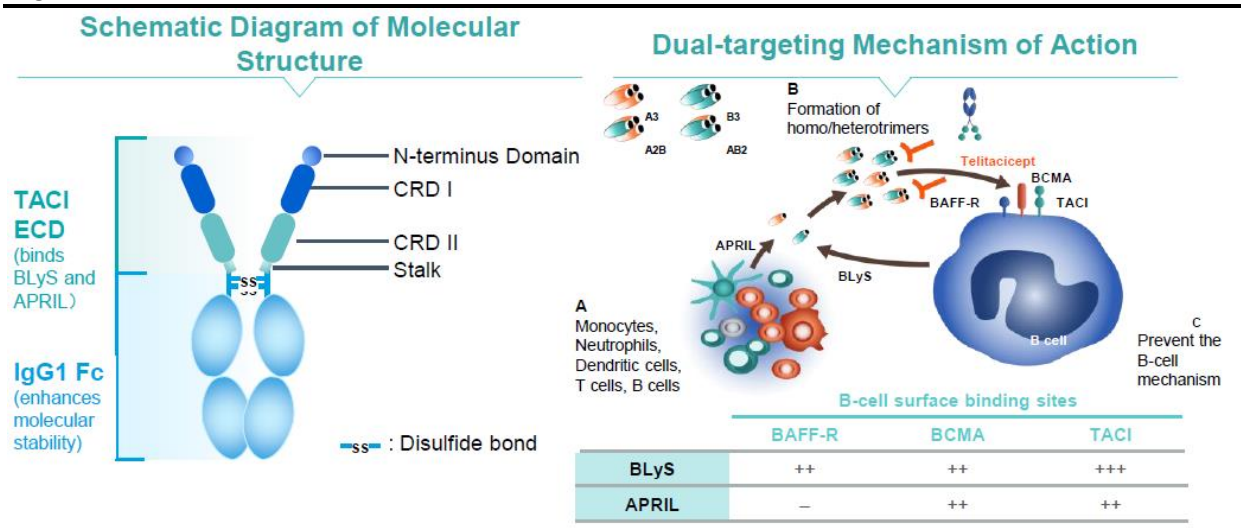
Novel fusion protein with BIC potential

Innovative structure design and MoA

Telitacicept (RC18) is the Company's proprietary first-in-class TACI-Fc fusion protein for treating autoimmune diseases. It is constructed with the extracellular domain of the human *transmembrane activator and calcium modulator and cyclophilin ligand interactor* (TACI) receptor and the *fragment crystallizable* (Fc) domain of human immunoglobulin G (IgG). Telitacicept targets two cell-signaling molecules critical for B-lymphocyte development: B-cell lymphocyte stimulator (BLyS) and a proliferation inducing ligand (APRIL). Telitacicept blocks the BLyS and APRIL from binding to B-cell activating factor receptor (BAFF-R), B-cell maturation antigen (BCMA) and TACI receptors expressed on B-cell surface, and inhibits the development and survival of mature B cells and plasma cells, which allows it to effectively reduce B-cell mediated autoimmune responses that are implicated in several autoimmune diseases.

The optimized structure design of telitacicept leads to improved biological activities and productivity. Compared with belimumab, a human IgG1λ mAb developed by GSK targeting only BLyS approved for treating SLE, telitacicept's dual blockade of both BLyS and APRIL can be more potent. The bioinformatics-optimized TACI fragment of telitacicept retains human TACI's high binding affinity and preserves its in vivo biological functions. The full human amino acid sequence structure of telitacicept will minimize potential immunogenicity as well.

Figure 3: Molecular structure and mechanism of action of RC18



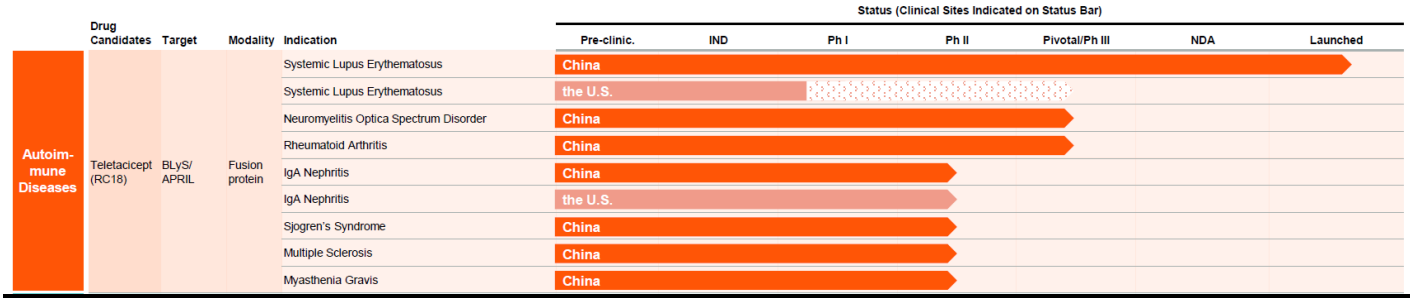
Source: Company data, CMBIGM

Broad application for autoimmune diseases with BIC potential

Telitacicept has the potential to become the best-in-class therapy in the global SLE market, with the existing other treatments limited in efficacy and safety. In Mar 2021, the NMPA officially granted conditional marketing approval of telitacicept for the treatment of adult patients with SLE, becoming the second innovative biologics drug approved to treat SLE in China over the past 60 years. In Dec 2021, telitacicept was included in the NRDL effective since Jan 2022. As of Sep 2022, the Company has established a commercial team of around 470 people in the area of autoimmune diseases, covering around 1,100 hospitals in 271 prefecture-level cities across China.

Besides SLE, RemeGen is currently evaluating telitacicept in late-stage clinical trials for six autoimmune diseases, in an attempt to address the unmet and underserved medical needs in this therapeutic area.

Figure 4: Clinical trials of telitacicept (as of Aug 2022)



Source: Company data, CMBIGM

(1) SLE.
   a. In China, RemeGen initiated a Ph3 confirmatory trial (NCT04082416) for SLE patients (18-65 years old) in Jul 2019, based on the encouraging results of its Ph2b registrational trial (NCT02885610). The Company has completed patient enrollment for the Ph3 trial as of Mar 2021. The follow-up of the Ph3 trial ended in 1H22 with encouraging top-line results released in Sep 2022. The detailed data of the Ph3 trial is expected to be released in Nov 2022 at the AACR meeting and the full approval application is expected in 4Q22.
   b. The IND of RC18 for the treatment of childhood SLE was approved by the CDE in Apr 2022.
   c. For global development, RemeGen launched a Ph3 trial (NCT05306574) of telitacicept for patients with SLE (12-70 years old) in Mar 2022, which will enroll patients from the US, Europe and China. The trial includes two stages, dose confirmation (160 or 240mg weekly) and efficacy confirmation. In Apr 2020, the FDA granted fast track designation to telitacicept, which will expedite the review and potential approval process in the US.

(2) Immunoglobulin A nephropathy (IgAN).
   a. In China, a randomized, double-blind, placebo-controlled Ph2 trial (NCT04291781) in IgAN has been completed with positive results. RemeGen is going to start a Ph3 trial in IgAN in China.
   b. In the US, a Ph2 trial (NCT04905212) for IgAN is ongoing with 10 of the 30 planned patients enrolled as of Jun 2022. A Ph3 study for IgAN is in plan in the US.

(3) Sjögren's syndrome (SS). The Company completed a randomized, double-blind, placebo-controlled Ph2 trial (NCT04078386) for SS in China with the results to be released in Nov 2022 at the AACR meeting. RemeGen is currently on track to start a Ph3 study of RC18 in pSS in China.

(4) Rheumatoid arthritis (RA). RemeGen is conducting a multi-center, double-blind, placebo-controlled Ph3 trial (NCT03016013) for RA in China, with the enrollment completed in Dec 2021 and the follow-up to be completed by end 2022. We expect RA to be the second indication of telitacicept to be approved in China following SLE. Although the RA market is crowded, RC18 could be a supplement of 2L treatment.

(5) Neuromyelitis optica spectrum disorder (NMOSD): A randomized, double-blind and placebo-controlled Ph3 trial (NCT03330418) for NMOSD is ongoing in China. The trial was initiated in Sep 2017 and has enrolled 133 patients as of Jun 2022.

(6) Myasthenia gravis (MG): A randomized, open-label Ph2 trial (NCT04302103) for MG in China has been completed in Feb 2022 with positive results. The Company plans to start a Ph3 trial in China. In Oct 2022, RC18 received the orphan drug designation from the US FDA for the treatment of MG.

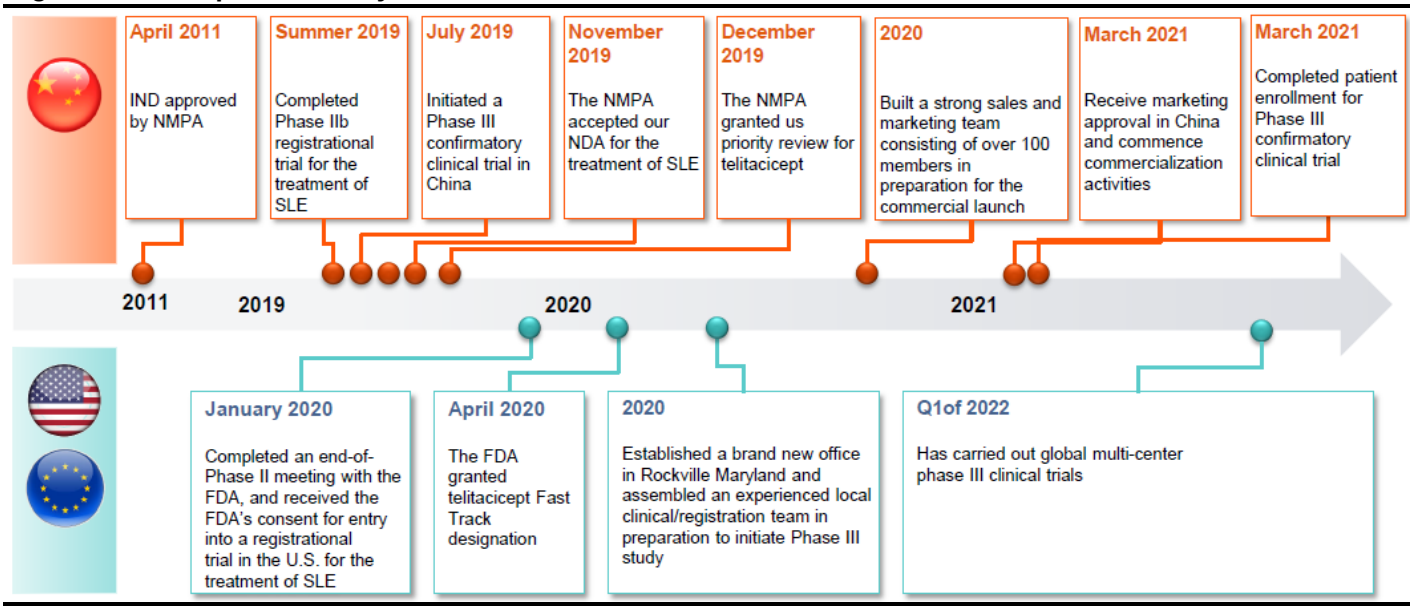
(7) Other indications: RemeGen is also evaluating telitacicept for other hard-to-treat autoimmune diseases, including multiple sclerosis (MS). The Company has enrolled 6 patients in Ph2 trial of MS as of Jun 2022.

The Company intends to prioritize the development of telitacicept for treatment of indications with highly unmet medical needs and sizeable addressable patient population in the global market, such as SLE,

IgAN, pSS and MG. Given telitacicept is internally developed by Remegen with global rights, we expect the Company to collaborate with global leading biopharma companies for the development and commercialization of telitacicept in overseas markets.

Potential best-in-class therapy in the global SLE market

Figure 5: Development history of RC18 for treatment of SLE



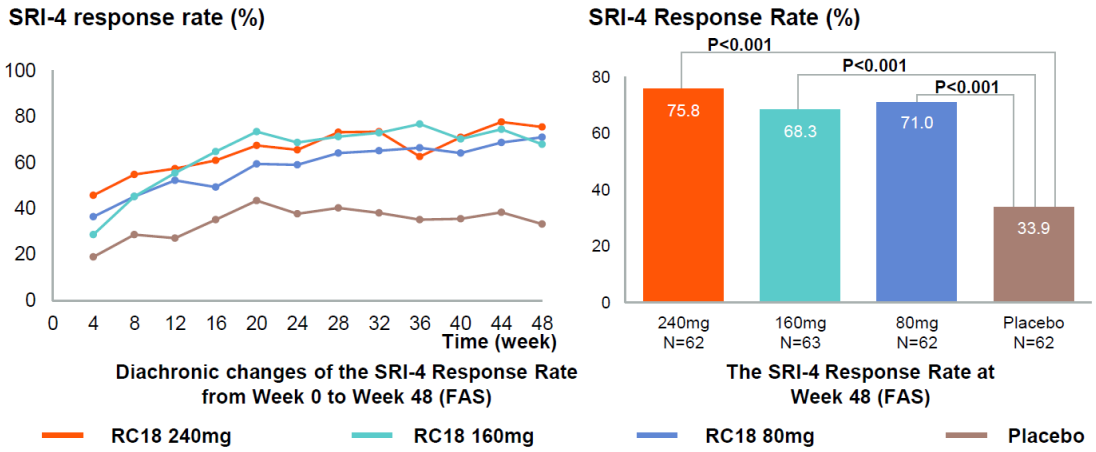
Source: Company data, CMBIGM

In Mar 2021, the NMPA granted conditional approval of telitacicept 160mg QW for the treatment of SLE based on the Ph2b registrational trial (NCT02885610). The trial was a multi-center, randomized, double-blinded and placebo-controlled study evaluating telitacicept vs placebo in combination with standard therapy for moderate to severe SLE patients. SLE patients with a SELENA-SLEDAI score ≥8 were randomized 1:1:1:1 to receive subcutaneous telitacicept at 240 mg, 160 mg, 80 mg or placebo once a week in combination with standard therapy for 48 weeks. The primary endpoint was the proportion of patients achieving SLE responder index-4 (SRI-4) response at week 48.

249 patients were randomized (link) to receiving telitacicept 240 mg (n=62), 160 mg (n=63), 80 mg (n=62) or placebo (n=62). In the 160 mg cohort (approved dosing regimen), 68.3% of patients achieved clinically meaningful disease activity improvement (SRI-4 rate), as compared to placebo (33.9%), indicating a 34.4% improvement of SRI-4 response rate ($p<0.001$). The proportion of patients with SRI-4 was also statistically significant at 240 mg (75.8%, $p<0.001$) and 80 mg (71.0%, $p<0.001$) as compared to placebo (33.9%).

Telitacicept was well tolerated in SLE patients. The incidences of SAEs were 12.9%, 15.9% and 12.9% in the 240mg, 160mg, 80mg group, respectively, lower than that of placebo group (16.1%). The incidence of AEs and SAEs was similar across groups ($P>0.05$).

Figure 6: Clinical results of the SLE Ph2b registrational trial



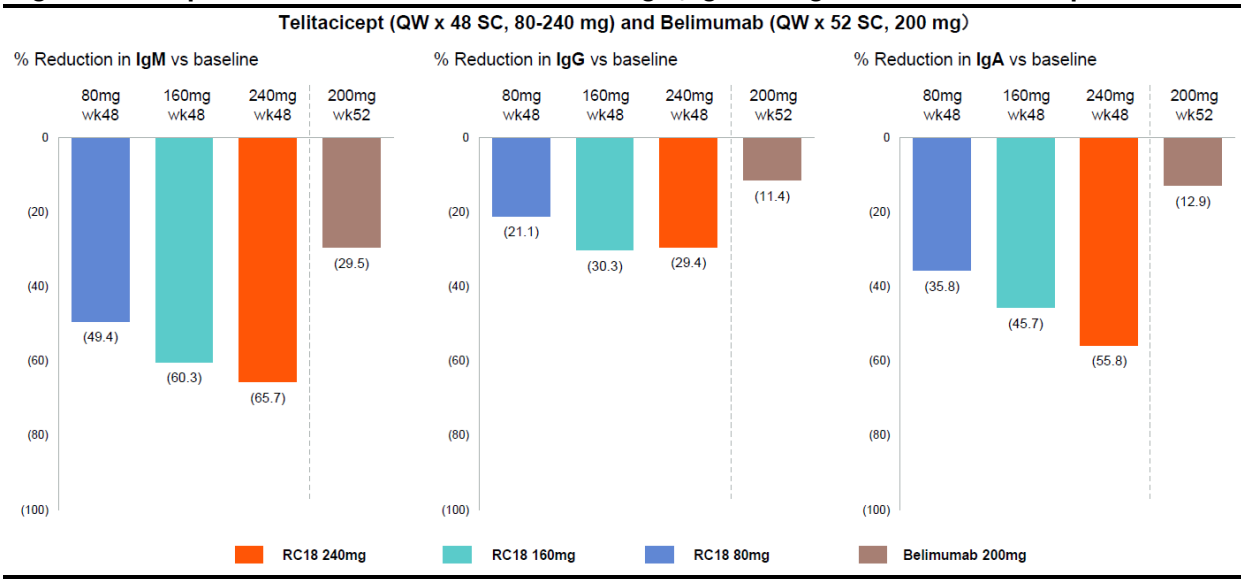
	240 mg (N=62), n (%)	160 mg (N=63), n (%)	80 mg (N=62), n (%)	Placebo (N=62), n (%)
AE	58(93.5)	58(92.1)	56(90.3)	51(82.3)
SAEs	8(12.9)	10(15.9)	8(12.9)	10(16.1)
SARs	3(4.8)	2(3.2)	3(4.8)	2(3.2)
AEs leading to dose reduction or suspension of treatment	39(62.9)	24(38.1)	25(40.3)	27(43.5)
ARs leading to dose reduction or suspension of treatment	30(48.4)	21(33.3)	20(32.3)	22(35.5)
AEs leading to permanent discontinuation	7(11.3)	8(12.7)	7(11.3)	8(12.9)
ARs leading to permanent discontinuation	2(3.2)	3(4.8)	2(3.2)	6(9.7)
AEs leading to death[1]	1(1.6)	0(0)	0(0)	0(0)
ARs leading to death	0(0)	0(0)	0(0)	0(0)
AEs at injection site	6(9.7)	12(19.0)	7(11.3)	4(6.5)
ARs at injection site	6(9.7)	11(17.5)	7(11.3)	4(6.5)

Source: Company data, CMBIGM. Note: clinical results were based on the full analysis set (FAS) of 249 patients. One non-drug-related death was reported in the telitacicept 240mg cohort.

The confirmatory Ph3 trial of RC18 in SLE demonstrated even better results (link) than its Ph2b registrational trial above. The Ph3 trial included 335 patients who were randomized to receive RC18 (160mg) or placebo subcutaneously once a week in combination with standard therapy for 52 weeks. Preliminary results from full analysis set showed a significantly higher response rate of SRI-4 in patients received RC18 than in patients received placebo (82.6% vs 38.1%; or 44.5% increase in response rate; p<0.001) at week 52. Results of all the sensitivity analyses showed a significantly higher response rate of SRI-4 in patients received telitacicept than in patients received placebo (p<0.001).

RC18 demonstrated superior clinical efficacy to belimumab in SLE patients based on cross-trial comparison. As illustrated bellow, RC18 achieved a dose dependent linear and robust effect on IgM, IgG and IgA reduction in SLE patients, compared to belimumab.

Figure 7: Comparison of RC18 and belimumab in IgM, IgG and IgA reduction in SLE patients



Sources: Company data, CMBIGM

In the pivotal Ph3 trial (BEL113750 /NCT01345253) supporting **belimumab**'s approval in China, 707 adult SLE patients from China, Japan and South Korea were randomized 1:2 to receive placebo or belimumab (10 mg/kg) (link1, link2). The modified intent-to-treat population included 677 patients (belimumab n=451, placebo n=226), with 517 patients (or 76.4%) enrolled from China. At week 52, the SRI-4 response rate was higher with belimumab vs placebo (53.8% vs 40.1%; P=0.0001). In the China sub-group, the SRI-4 response rate with belimumab was 54.8% compared to 45.5% with placebo, with a difference of 9.4% (P=0.0162), which was much lower than the 44.5% difference as observed in telitacicept's confirmatory Ph3 trial as a cross-trial comparison.

Figure 8: Efficacy results of belimumab's pivotal Ph3 trials

	BEL113750 (NCT01345253)				BEL110751 (NCT01914770)		BEL110752 (NCT01914770)	
	China group		Overall population					
	Placebo	Belimumab	Placebo	Belimumab	Placebo	Belimumab	Placebo	Belimumab
Total patient number	**171**	**346**	**226**	**451**	**275**	**273**	**287**	**290**
No. of pts with response	74/163	187/341	87/217	240/446	93	118	125	167
% of pts with SRI-4 response	45.4%	54.8%	40.1%	53.8%	33.8%	43.2%	43.6%	57.6%
Difference in % vs placebo	**9.4%**		**13.7%**		**9.4%**		**14.0%**	
P value	0.0162		0.0001		0.0207		0.0006	

Source: GSK data, CMBIGM. Notes: The three Ph3 trials in the table were conducted in different countries, with BEL113750 in China, Japan and South Korea; BEL110751 mainly in North America and Western Europe; and BEL110752 in South America, Eastern Europe, Asia and Australia.

Figure 9: Efficacy results of RC18's pivotal Ph2b trial and Ph3 trial

	Pivotal Ph2b trial (NCT02885610)				Ph3 confirmatory trial (NCT04082416)	
	Placebo	RC18 240mg	RC18 160mg	RC18 80mg	Placebo	RC18 160mg
Total patient number	62	62	63	62	335	
No. of pts with response	21	44	43	47	NA	
% of pts with SRI-4 response	33.9%	71.0%	68.3%	75.8%	38.1%	82.6%
Difference in % vs placebo	-	**37.1%**	**34.4%**	**41.9%**	-	**44.5%**
P value	-	<0.001	<0.001	<0.001	-	<0.001

Source: Company data, CMBIGM. RC18 (160mg dose) was approved in China for adult SLE treatment.

Anifrolumab, a type I interferon receptor antibody developed by AstraZeneca and BMS, was initially approved in the US in Aug 2021 for adult patients with moderate to severe SLE, followed by approvals in Japan, EU, etc. The approvals were based on the two Ph3 trials TULIP1 (NCT02446912) and TULIP2 (NCT02446899) and the MUSE (NCT01438489) Ph2 trial, while there were not without controversy about the approval. The TULIP1 trial did not meet its primary endpoint based on the SIR-4 measure - the proportion of patients at week 52 with an SRI-4 response was similar between anifrolumab 300mg and placebo (36% vs 40% in treatment and control groups, respectively; P=0.41; link).

Based on TULIP1 study, AstraZeneca shifted the primary endpoint of the second trial, TULIP2, midway from SRI-4 to another composite clinical measure called the BILAG-Based Composite Lupus Assessment (BICLA), which was used as a secondary endpoint in the previous TULIP1 trial. The TULIP2 trial met the primary endpoint - the percentage of patients who had a BICLA response was 47.8% in the anifrolumab group and 31.5% in the placebo group (16.3% difference; P=0.001; link). For key secondary endpoints, the results were mixed. Anifrolumab showed better outcomes on oral steroid use reduction, and offered improvements in disease severity measured by CLASI. However, it fell short of two other key secondary endpoints, i.e. the number of swollen or tender joints and the annualized flare rate. Additionally, as one of the secondary endpoints, SRI-4 response rate was 55.5% and 37.3% (18.2% difference; unadjusted P<0.001) in the treatment and control groups, respectively, in the TULIP2 trial.

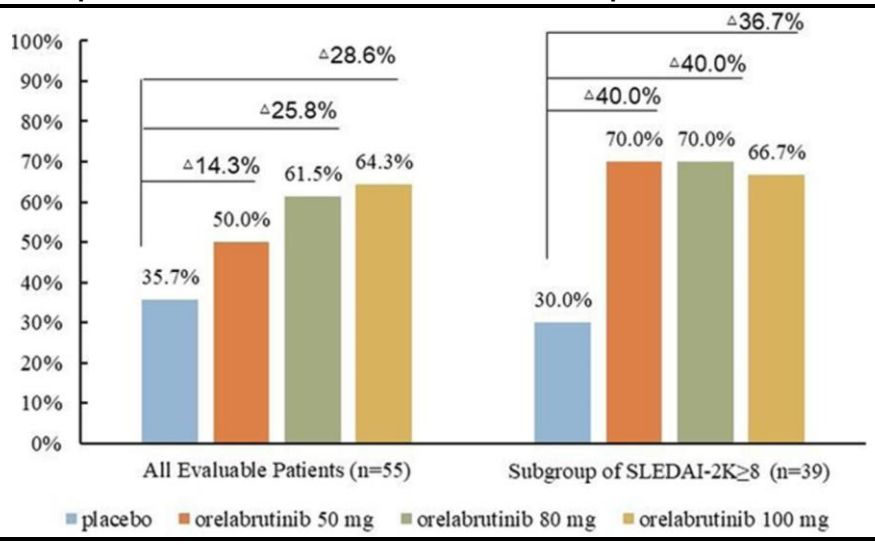
In some indications, the failure of one trial and success in another after mid-study changes could yield insufficient evidence to support approval. The approval of anifrolumab is an evidence of unmet medical need in SLE, in our view. Moreover, anifrolumab reached the best results in SRI-4 response rate improvement of 18.2%, which was far below that of RC18 of 34.4% (dose of 160mg weekly) as observed in its pivotal Ph2b trial and 44.5% in its confirmatory Ph3 study.

BTK inhibitors under investigation for SLE

Orelabrutinib (oral BTK inhibitor) developed by InnoCare Pharma (688428 CH, 9969 HK) is under investigation for the treatment of SLE. The PhIb/IIa trial (NCT04305197) enrolled 60 SLE patients who had a SLEDAI-2K score ≥5 at screening, and were autoantibody-positive. The patients were randomized 1:1:1:1 to receive oral orelabrutinib at 50mg, 80mg, 100mg or placebo once daily for 12 weeks, respectively.

55 patients completed 12-week treatment. In all evaluable patients, the SRI-4 response rates at week 12 were 50.0%, 61.5% and 64.3% in patients treated with orelabrutinib at 50mg (n=14), 80mg (n=13) and 100mg (n=14) respectively, compared with 35.7% in patients received placebo (n=14), which indicated the trend of dose-dependent improvement. Among the subgroup of patients with SLEDAI-2K ≥8 at screening, SRI-4 response occurred in 70.0%, 70.0% and 66.7% of patients treated with orelabrutinib at 50mg (n=10), 80mg (n=10) and 100mg (n=9), respectively, compared with 30.0% who received placebo (n=10). As of Oct 2022, InnoCare is in discussion with China CDE to initiate a Ph3 study of orelabrutinib for treatment of SLE.

Figure 10: SRI-4 response of orelabrutinib at week 12 for SLE patients



Source: Company data, CMBIGM.

Orelabrutinib is a potential oral treatment for mild-to-moderate SLE patients, whereas RC18 targets SLE patients with moderate-to-severe conditions. Instead of direct competition, the two medicines, as more efficacious than other available therapies for SLE patients, will together expand the market size of SLE in China, in our view.

Figure 11: Late-stage drugs or drug candidates with positive results in treating SLE

Drug	Company	Target	Latest status	Clinical results	Key efficacy results	SRI-4 ↑	P-value (SRI-4 ↑)	Data
RC18	RemeGen	BAFF, APRIL	Approved in China	Ph2 hit	SRI-4 response: 68.3% vs 33.9% (at the approved dosing of 160mg weekly)	34.4%	p<0.001	Link
				Ph3 hit	SRI-4 response: 82.6% vs 38.1% (confirmatory Ph3 trial with dosing of 160mg)	44.5%	p<0.001	Link
belimumab	GSK, AZ	BAFF	Approved in China, US, EU, etc	Ph3 hit	SRI-4 response: 54.8% vs 45.4% (China patients)	9.4%	p=0.0162	Link
anifrolumab	BMS, AZ	IFNAR-1	Approved in US, EU, etc	Ph3 hit	BICLA response: 47.8% vs 31.5% (SRI-4: 55.5% vs 37.3%, secondary endpoint)	18.2%	p<0.001 (unadjusted)	Link
orelabrutinib	InnoCare	BTK	Ph3 in planning	Ph2 hit	SRI-4 response: 64.3% vs 35.7%	28.6%	NA	Link
deucravacitinib	BMS	TYK2	Registration trial to start by end-2022	Ph2 hit	SRI-4 response: 58.2% vs 34.4%	23.8%	p=0.0006	Link
litifilimab	Biogen	BDCA2	Ph3 ongoing	Ph2 hit	absolute changes in total active joint count: -15.0 vs -11.6 (SRI-4: 56.77% vs 30.42%; secondary endpoint)	26.4%	p=0.003	Link
cenerimod	Idorsia, J&J	S1PR1	Ph3 in planning	Ph2 hit	mSLEDAI-2K difference: -2.420 (p=0.0306)	NA	NA	Link
iberdomide	BMS	IKZF3, IKZF1, CRBN	Ph2 completed	Ph2 hit	SRI-4 response: 54% vs 35%	19.4%	p=0.01	Link
RSLV-132	Resolve	Rnase	Ph2a completed	Ph2 hit	CLASI 50: 33% vs 23% (SRI-4: 21% vs 23%, secondary endpoint)	-2%	NA	Link

Source: Pharmcube, CMBIGM

The development of therapies for treatment of SLE is difficult due to the complexity of the disease. Many drug candidates have failed in their late-stage trials due to poor efficacy, safety concerns or other issues. Among the approved drugs or late-stage drug candidates with positive results in treating SLE, RC18 has demonstrated the best efficacy so far with well-tolerated safety profile. We see RC18 to become a potential global BIC biological therapy for SLE.

Figure 12: Major late-stage drug candidates discontinued/failed in SLE

Drug	Company	Target	Status	Highlights
rituximab	Biogen, Roche	CD20	Ph3 miss	during a safety review of studies U2970g and U2971g, the DMC recommended to terminate the enrollment
forigerimod	ImmuPharma	U1-70K	Ph3 miss	SRI-4 response: 52.5% vs 44.6% (p=0.2631)
tabalumab	Eli Lilly	BAFF	Ph3 miss	terminated (lack of efficacy)
epratuzumab	Gilead	CD22	Ph3 miss	BICLA response: 35.2% vs 33.5% (p=0.716)
blisibimod	Amgen	BAFF	Ph3 miss	SRI-6 response: 46.9% vs 42.3%
baricitinib	Eli Lilly, Incyte	JAK2, JAK1	Ph3 terminated	NA
ocrelizumab	Biogen, Roche	CD20	Ph3 terminated	terminated prematurely when the decision was made that ocrelizumab was not likely to benefit this patient population
ustekinumab	J&J, BMS, Mitsubishi	IL-12p40	Ph3 terminated	withdrawn (Pre-planned IA (global study) showed lack of efficacy)
infliximab	J&J, Mitsubishi	TNF-α	Ph3 terminated	terminated (failure to recruit patients with membranous lupus nephritis not previously treated with azathioprine)
sifalimumab	BMS, AZ	Interferon α (IFNα)	Ph2 hit, without further clinical study	SRI-4 response: 59.8% vs 45.4%
atacicept	Merck, BMS, Vera	TACI	Ph2b miss	SRI-4 response: 57.8% vs 44.0% (p=0.045)
fenebrutinib	Roche	BTK C481S mutation	Ph2 miss	SRI-4 response: 52% vs 44% (p=0.34)
abatacept	Ono, BMS, Simcere	CTLA4	Ph2 miss	primary end point: 79.7% vs 82.5%
dapirolizumab pegol	Biogen, Nektar, UCB	CD40L	Ph2 miss	BICLA response: 37.2% vs 54.5%
brentuximab vedotin	Takeda, Seagen	CD30 ADC	Ph2 terminated	terminated (sponsor decision based on portfolio prioritization)
PF-04236921	Pfizer	IL-6	Ph2 miss	SRI response: 59.9% vs 40.1% (p=0.076)

Source: Pharmcube, CMBIGM. Notes: not all late-stage drug candidates that failed in SLE trails are included in the table.

Rapid development progress in various autoimmune diseases

With promising data released, we see the potential of RC18 for the treatment of various autoimmune diseases besides SLE, including IgAN, pSS, MG, RA, etc.

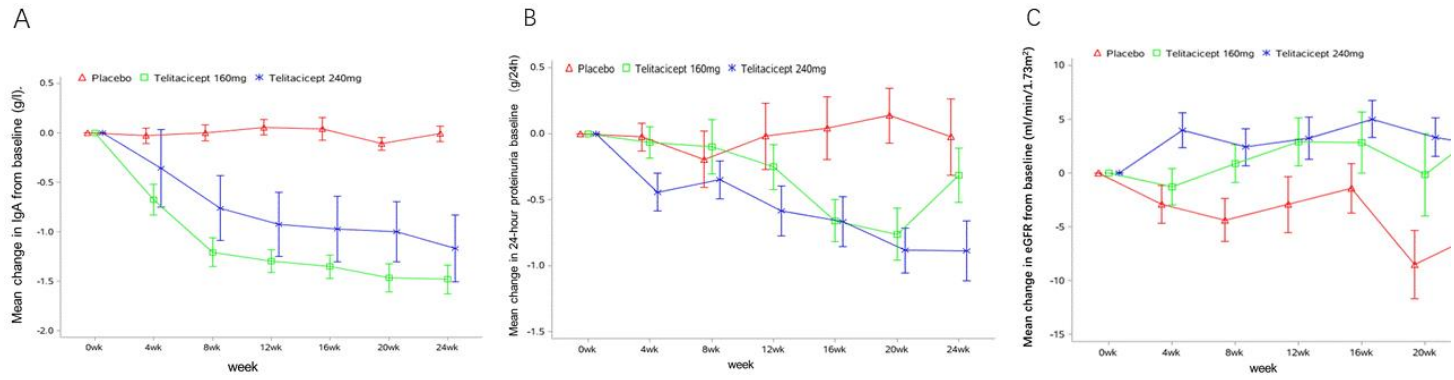
Immunoglobulin A nephropathy (IgAN)

A randomized, double-blind, placebo-controlled Ph2 trial of RC18 in IgAN patients in China has been completed with positive results. The Company is going to start a Ph3 study of RC18 in IgAN in China. In the US, a Ph2 trial for IgAN is currently ongoing with the interim data expected in 1H23, and a Ph3 study for IgAN is in plan.

The preliminary topline results of the Ph2 clinical study (NCT04291781) of telitacicept for treatment of IgAN patients in China was released in Aug 2021 (link) and in Nov 2021 (link). In this randomized, double-blind, placebo-controlled trial, 44 patients were randomized 1:1:1 to receive subcutaneous telitacicept at 160 mg, 240 mg or placebo weekly for 24 weeks. The primary endpoint was change in 24-hour proteinuria at week 24; key secondary endpoints included change in the evaluated glomerular filtration rate (eGFR).

Preliminary result showed that the reduction of proteinuria level of the treatment groups was significantly higher than the baseline compared with the placebo group. Telitacicept therapy achieved a 49% decrease from baseline in mean proteinuria (change in proteinuria vs placebo -0.88; p=0.013) in 240mg group, and a non-significantly 25% reduction in 160mg arm (-0.29; p=0.389) (see Figure B below). Estimated GFR remained stable over time (see Figure C below). TEAEs were similar in all groups and were mild or moderate in severity, with no severe TEAEs reported.

Figure 13: Mean change in IgA (A), proteinuria (B) and eGFR (C) of telitacicept's Ph2 trial in IgAN in China



Source: Company data, CMBIGM

IgAN is an immune-complex-mediated glomerulonephritis characterized by hematuria, proteinuria, and variable rates of progressive renal failure. While considered rare, IgAN is the most common cause of primary kidney disease worldwide. According to Frost & Sullivan, the number of IgAN patients globally increased from 8.8mn in 2015 to 9.3mn in 2020 (including 2.2mn in China). The total number of IgAN patients globally is forecasted to reach 9.7mn by 2025 (including 2.3mn in China), and to 10.2mn by 2030 (including 2.4mn in China).

Currently, there is limited specifically approved therapy for IgAN. The current standard of care is renin-angiotensin-aldosterone system (RAS) blockade with immunosuppression, which is also commonly used for patients with significant proteinuria or rapidly progressive glomerulonephritis. Tarpeyo (Nefecon, or Budosenide delayed-release capsules), a corticosteroid type medicine developed by Calliditas Therapeutics and Everest Medicines, has been approved in the US and EU to reduce proteinuria in IgAN adults who are at risk of rapid disease progression with a urine protein-to-creatinine ratio ≥1.5g/g.

Besides RC18, sparsentan, narsoplimab, iptacopan, and sibeprenlimab are currently under late stage of clinical investigation for IgAN treatment. With RC18 achieved 49% reduction in proteinuria from baseline after 24 weeks, in cross-trial comparisons, we see the potential of RC18 to become one of the most effective therapies for IgAN treatment.

The BLA of sparsentan, a dual endothelin angiotensin receptor antagonist developed by Travere Therapeutics/BMS/Ligand, is under the US FDA review for the treatment of IgAN with an original PDUFA target action date of 17 Nov 2022. However, as part of the late-cycle review, the FDA has recently requested Travere to update its proposed Risk Evaluation Mitigation Strategy (REMS) to include liver monitoring for sparsentan consistent with certain other approved products in the endothelin receptor antagonist class. As a result, the PDUFA target action date is expected to have a three-month extension.

Figure 14: Drug candidates under late clinical stage for treatment of IgAN

Drug	Company	Target	Latest global status	Latest China status	Key clinical results	Link
Budosenide (Tarpeyo)	Calliditas, Everest, STADA	Corticosteroid type medicine	Approved in US and EU, based on Ph3 trial (NCT03643965)	Ph3 (MRCT with China included)	31% reduction in proteinuria from baseline after 9 months	Link
Sparsentan	BMS, Ligand, Travere	ET_AR, AT_1R	Ph3 (NCT03762850); BLA filed in the US; PDUFA date delayed to Feb 2023 due to liver monitoring requirement	-	49.8% reduction in proteinuria from baseline after 36 weeks	Link
Narsoplimab	Omeros	MASP-2	Ph3 (NCT03608033)	-	38% reduction in proteinuria from baseline (sustained)	Link
Iptacopan	Novartis	Complement factor B	Ph3 (NCT04578834)	Ph3 (MRCT with China included)	23% reduction in proteinuria after 90 days	Link
Sibeprenlimab	Visterra (Otsuka)	APRIL	Ph3 (NCT05248646)	-	-	-

Dapagliflozin	AstraZeneca, BMS	SGLT2	Ph3 (NCT03036150) in pts with chronic kidney disease, 6% of pts are IgAN	Ph3 (MRCT with China included)	-	-
Telitacicept	**RemeGen**	**BLyS, APRIL**	**Ph2 (NCT04905212)**	**Ph2 completed (NCT04291781); Ph3 to start (NCT05596708)**	**49% reduction in proteinuria from baseline after 24 weeks**	**Link**
BION-1301	Chinook	APRIL	Ph2 (NCT04684745)	-	>50% proteinuria reduction	Link

Source: Pharmcube, CMBIGM

Sjögren's syndrome (SS)

In Jan 2022, The Company released positive results of a randomized, double-blind, placebo-controlled Ph2 trial (NCT04078386) of telitacicept for the treatment of primary Sjögren's syndrome (pSS) in China (link). A total of 42 patients were randomized to receive weekly subcutaneous injections of RC18 160mg, RC18 240mg, or placebo for six months. The 160 mg treatment group showed encouraging results versus the placebo group, as measured by better ESSDAI scores in the full set analysis (FAS). The per-protocol-set analysis (PPS), which removed data from patients who failed to comply with the treatment protocol, also uncovered a statistical difference for both 160mg and 240mg treatment groups compared with the placebo group.

Primary SS is a chronic, autoimmune condition characterized by lymphocytic infiltration of the exocrine glands, which leads to glandular dysfunction and eventual irreversible tissue damage. The primary clinical manifestations are ocular and oral dryness. According to Frost & Sullivan, the number of patients with SS worldwide has risen from 3.7mn in 2016 to 3.9 mn in 2020. In China, 0.29-0.77% of the population is affected by pSS, or 631,000 Chinese people were affected by SS in 2020 with the number expected to reach 641,800 in 2025 and 644,900 in 2030.

Currently, no drug effective for the treatment of Sjögren's syndrome has been approved. Current treatment strategies are largely empirical and offer only symptomatic relief for patients. Symptomatic therapies for SS include corticosteroids and immunosuppressants, yet they can result in extensive non-specific immunosuppression with serious side effects. Belimumab and VAY736, both targeting BAFF, have demonstrated improvement in ESSDAI for SS patients. Telitacicept, dual-targeting BAFF and APRIL, has demonstrated significant ESSDAI reduction vs placebo in its Ph2 trial. As the only biological drug under late-stage development in China, we see the FIC potential of telitacicept in China for SS treatment.

Figure 15: Late-stage drug candidates for SS treatment

Drug	Company	Target	Latest global status	Latest China status	Key clinical results	Link
Abatacept	Ono Pharma, BMS, Simcere	CTLA4-Fc fusion protein	Phase 3 (NCT02915159)	-	primary endpoint not met, no significant difference in ESSDAI at day 169 between abatacept and placebo	Link
			Phase 3 (NCT02067910)	-	primary endpoint not met, no significant difference in ESSDAI at week 24	Link
Belimumab	GSK, AstraZeneca	BAFF	Phase 2 (NCT01160666)	-	primary endpoint met. ESSDAI decreased from 8.8 to 6.3 at week 28	Link
			Phase 2 (NCT02631538)	-	ESSDAI reduction with belimumab plus rituximab was greater than placebo (-5.73 vs -1.75 at week 68), but were not differentiated from monotherapy	Link
VAY736	Novartis, MorphoSys	BAFF-R	Phase 3 (NCT05350072)	-	primary endpoint of Ph2 trial (NCT02962895) was met with placebo-adjusted change of ESSDAI at -1.92 points	Link
			Phase 3 (NCT05349214)	-		
CFZ533	Novartis	CD40	Phase 2 (NCT03905525)	-	-	-
			Phase 2 (NCT04541589)	-	-	-
			Phase 2 (NCT02291029)	-	significant ESSDAI reduction of 5.21 points of intravenous CFZ533 vs placebo	Link
Ravaglimab	AbbVie	CD40	Phase 2 in (NCT05217472)	-	study withdrawn	-
Rituximab	Roche, Idec	CD20	Phase 2/3 (NCT00740948)	-	primary endpoint not met	Link

			Phase 3 (TRACTISS)	-	primary endpoint not met	Link
SAR441344	Sanofi, ImmuNext	CD40L	Phase 2 (NCT04572841)	-	-	-
LY3090106	Eli Lilly	BAFF / IL17	Phase 2/3 (NCT04563195)	-	-	-
VIB4920	AstraZeneca	CD40L	Phase 2 (NCT04129164)	-	-	-
Telitacicept	**RemeGen**	**BAFF / APRIL**	**-**	**Phase 2 (NCT04078386)**	**significant ESSDAI reduction from baseline vs placebo**	**Link**

Source: Pharmcube, CMBIGM

Strong sales ramp up with NRDL inclusion

Wu Jingping, previously in charge of the commercialization of Yisaipu at 3SBio, leads RemeGen's sales team for autoimmune business. Yisaipu is a TNFR2-Fc fusion protein biosimilar approved for the treatment of rheumatoid arthritis (RA) in China, which shares the same hospital channel with SLE. The Company's commercial team for autoimmune diseases has expanded from around 130 members as of the end of 2021 to 293 employees as of Jul 2022, and further to around 470 employees as of Sep 2022. As of Sep 22, the commercial team for autoimmune diseases has covered around 1,100 hospitals in 271 prefecture-level cities of 31 provincial administrative units across China, and RC18 has been admitted to 436 hospitals. We expect the Company to further expand this team in 2022.

Since the approval in China for treatment of SLE in Mar 2021, telitacicept has realized approximately RMB47mn revenue in 2021. In 1H22, sales of telitacicept was approximately RMB141mn, demonstrating strong sales growth momentum. In 3Q22, the Company recorded around RMB100mn sales from telitacicept. Telitacicept was added into the NRDL since Jan 2022, with a 68% price cut from RMB2,586/ 80mg to RMB818.8/ 80mg. We believe the NRDL inclusion has expedited the channel penetration and sales volume ramp-up of telitacicept.

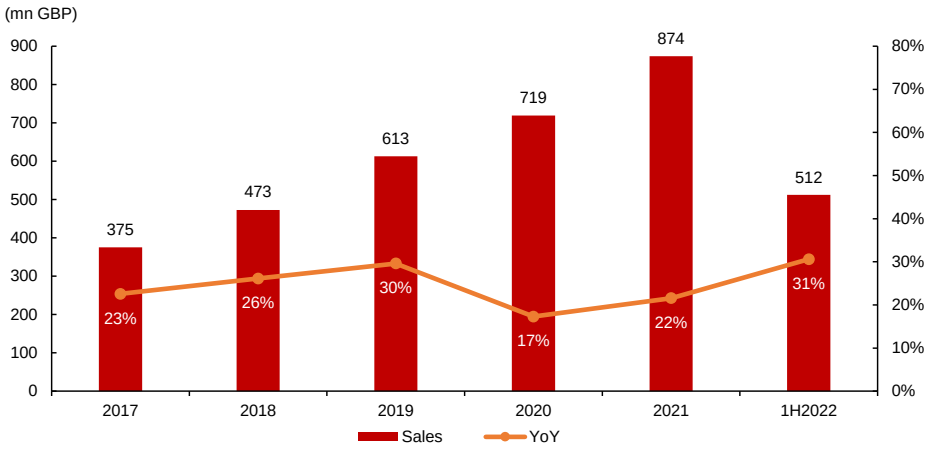
Figure 16: Treatment cost comparison of RC18 and belimumab

Drug	NRDL status	Retail price	Dose	Monthly cost	Annual cost
RC18	SLE (adult) covered by NRDL, valid period from 2022.01.01 to 2023.12.31	RMB818.8/ 80mg	160mg subcutaneous injection weekly	RMB7,096	RMB85,155
Belimumab	SLE (5+ years old) covered by NRDL, valid period from 2022.01.01 to 2023.12.31	RMB702/ 120mg	10 mg/kg intravenous injection at 2-week intervals for the first 3 doses and at 4-week intervals thereafter	RMB4,561	RMB54,738

Source: Company data, CMBIGM

Telitacicept is the second innovative biological drug approved in China to treat SLE over the past 60 years, following the approval of belimumab in Jul 2019. In the US, belimumab was initially approved for treatment of adult SLE patients in 2011, with the label expanded to 5+ years old SLE patients in 2019, and active lupus nephritis in 2020. In China, belimumab was approved as add-on treatment (combined with standard therapy) for adult SLE patients in Jul 2019 (NRDL inclusion since Mar 2021) and for children in Dec 2020 (NRDL inclusion since Jan 2022). Belimumab also received approval from the NMPA for the treatment of adult patients with active lupus nephritis in Feb 2022. The global sales of belimumab reached £874mn (or approximately US$1.0bn) in 2021 with a 22% YoY increase. In 1H22, belimumab relegalized £512mn (or approximately US$580mn; +31% YoY) sales globally. The steady sales growth of belimumab over the past years demonstrated the increasing demand of effective biological drug for SLE.

Figure 17: Global sales of belimumab



Source: GSK, CMBIGM

With effective biological drugs like telitacicept available and increasing patient awareness, the global SLE market will continue to expand, in our view. According to Frost & Sullivan, the global SLE prevalence was approximately 7.7mn in 2019, and is estimated to reach 8.6mn by 2030. In China, there were approximately 1.0mn SLE patients in 2019, and the prevalence is estimated to grow to approximately 1.1mn by 2030. The market size of global SLE biological therapeutics is estimated to grow at a CAGR of 26.8% from US$0.8bn in 2019 to US$10.8bn by 2030. With superior efficacy and safety, we believe telitacicept will potentially take a significant market share in the global SLE market.

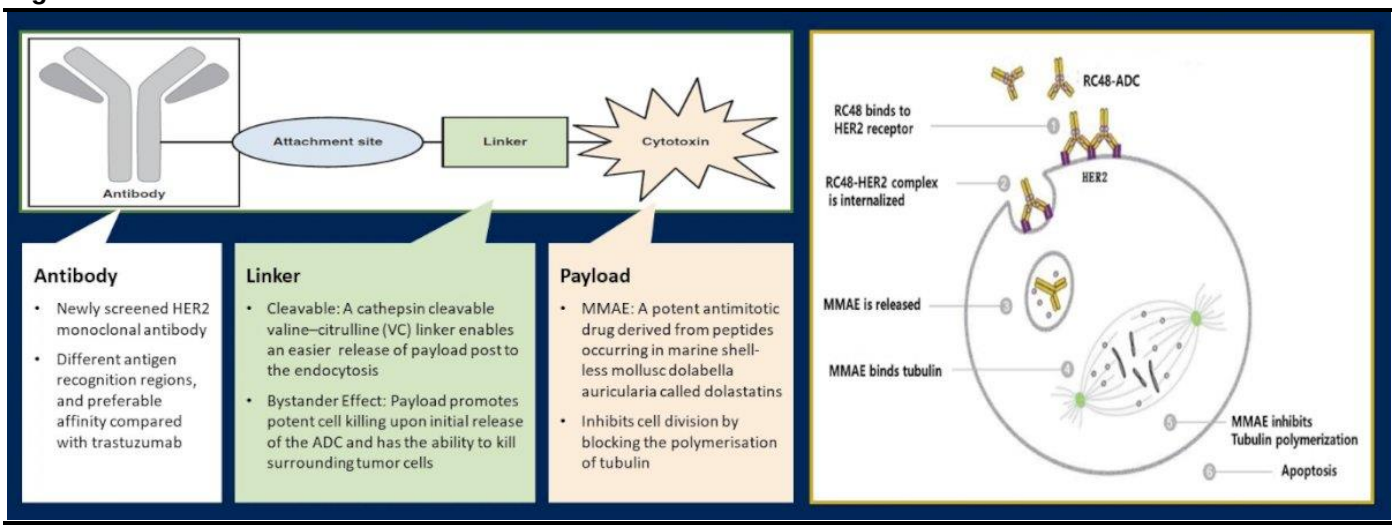
Disitamab vedotin (RC48): first-to-market domestic HER2 ADC

Novel HER2 ADC with broad potential in cancer treatment

Differentiated design of RC48

Disitamab vedotin (RC48) is RemeGen's leading antibody-drug conjugate (ADC) product and is the first ADC in China to have received IND approval for clinical trials. RC48 is a novel humanized antibody specific for human epidermal growth factor receptor 2 (HER2) in conjugation with the microtubule inhibitor monomethyl auristatin E (MMAE) via a cleavable linker. It is independently developed by the Company to treat HER2 expressing (including low-expressing) solid tumors.

Figure 18: Structure of RC48



Source: Company data, CMBIGM

Figure 19: Comparison of HER2 ADC drugs

RC48 vs. T-DM1 and DS-8201

	RC48	T-DM1	DS8201
Antibody	Novel monoclonal antibody with higher affinity	Trastuzumab	Trastuzumab
Cleavable linker	+	-	+
Bystander-killing effects	+	-	+

Source: Company data, CMBIGM

In the space of HER2 targeted therapies, several drugs have been approved. Trastuzumab is a first-to-market HER2 mAb that has been approved for the treatment of HER2-positive breast cancer (BC) and HER2-positive metastatic gastric cancer (GC). Trastuzumab emtansine (T-DM1), an ADC developed by Roche comprising trastuzumab and the tubulin inhibitor emtansine, has been approved for the treatment of HER2-positive metastatic BC patients who previously received trastuzumab and taxane and the adjuvant treatment of HER2-positive early breast cancer patients who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment. Trastuzumab deruxtecan (DS-8201), developed by AstraZeneca and Daiichi-Sankyo, is another HER2-ADC composed of trastuzumab and a topoisomerase I inhibitor payload (Dxd) that has been approved by the FDA for the treatment of HER2

positive BC patients who have received a prior anti-HER2-based regimen, HER2 low BC patients who have received a prior chemotherapy, HER2-positive GC patients who have received a prior trastuzumab-based regimen, and HER2 mutated NSCLC patients who have received a prior systemic therapy.

Unlike the conjugation of trastuzumab and a tubulin inhibitor emtansine for T-DM1 or the conjugation of trastuzumab and a topoisomerase I inhibitor payload for DS-8201, RC48 is composed of hertuzumab and MMAE. Compared with trastuzumab, hertuzumab has a higher affinity to HER2 and capacity of ADCC in vitro. After conjugation with MMAE, the cytotoxicity of hertuzumab was significantly enhanced, whereas the binding specificity for HER2 was not affected. As such, RC48 delivered enhanced cytotoxicity and high binding specificity. Furthermore, unlike T-DM1 with minimal bystander effect on nearby cells due to poor membrane permeability, RC48 has a strong bystander killing effect that can potentially overcome T-DM1 resistance by acting on populations of cells not overexpressing HER2. Additionally, RC48 features a cleavable linker that doesn't rely on the activity of V-ATPase in lysosomes and has less lysosomal resistance.

Broad targeted indications of RC48

RC48 is being evaluated in multiple late-stage clinical trials across a variety of HER2-expressing solid tumors, focusing on urothelial cancer (UC), gastric cancer (GC) and breast cancer (BC). In registrational trials in China, RC48 has demonstrated promising efficacy in HER2-expressing advanced or metastatic UC and HER2-expressing advanced or metastatic GC, and has also proved its potential as treatment for HER2-expressing (including HER2 low-expressing) BC. RemeGen targets to bring RC48 to earlier treatment settings for UC, GC and BC with multiple Ph3 trials ongoing or in plan in China and globally.

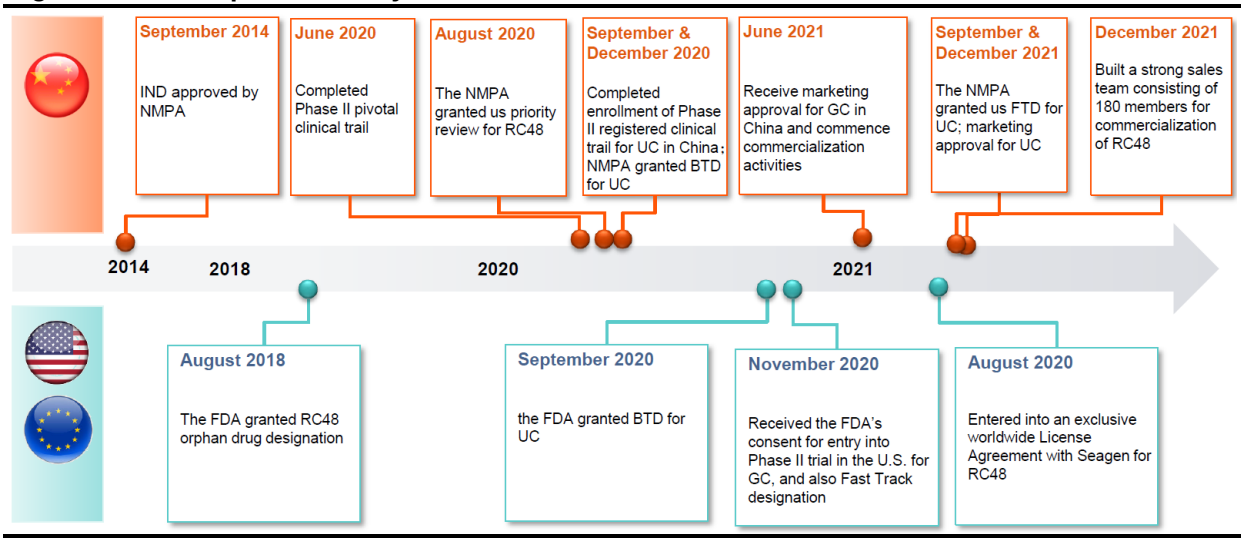
Compared with other HER2 ADC therapies like DS-8201 and T-DM1, RC48 distinguished itself by targeting differentiated indications, especially UC due to the superior efficacy. For the development of RC48 in the US and other overseas regions, Seagen currently focuses on indications such as UC and BC, and targets to further explore opportunities in other HER-2 expressing solid tumors, including GC. Besides the above-mentioned three tumor types (UC, BC and GC), RemeGen is also exploring the efficacy of RC48 in other prevalent cancer types with HER2 expression, such as NSCLC and biliary tract cancer (BTC).

Figure 20: Clinical trials of disitamab vedotin (as of Aug 2022)

Drug Candidates	Target	Modality	Indication	Status (Clinical Sites Indicated on Status Bar)
				Pre-clinic. / IND / Ph I / Ph II / Pivotal/Ph III / NDA / Launched
Disitamab Vedotin (RC48)	HER2	ADC	HER2-Expressing Gastric Cancer	China
			HER2-Expressing Urothelial Cancer	China
			HER2-Expressing perioperative MIBC with combination of PD-1	China
			HER2-Expressing Urothelial Cancer with the combination of PD-1 for line 1 patients	China
			HER2-Expressing Urothelial Cancer	the U.S. — *Cooperation with Seagen*
			HER2-Expressing Urothelial Cancer with the combination of PD-1 for first line patients	the U.S. — *Phase III in the plan, cooperation with Seagen*
			HER2-Expressing Gastric Cancer	the U.S. — *Cooperation with Seagen*
			HER2-Expressing Breast Cancer with the combination of PD-1 for first line patients	the U.S. — *Phase III in the plan, cooperation with Seagen*
			HER2 Low-Expressing Breast Cancer	China
			HER2 Postive Breast Cancer with Liver Metastasis	China
			HER2 Low- to Non-Expressing Urothelial Cancer	China
			HER2-Expressing Gynecology Malignant Tumor	China
			HER2-Expressing Biliary Tract Carcinoma	China
			HER2-Expressing Non-Small-Cell Lung Cancer	China
			HER2-Expressing Melanoma	China

Source: Company data, CMBIGM

Figure 21: Development history of RC48 in GC and UC



Source: Company data, CMBIGM

In Aug 2021, RemeGen granted Seagen an exclusive license to develop and commercialize RC48 in global regions excluding Asia (Japan and Singapore excluded). RemeGen received an upfront payment of US$200mn and is eligible to receive additional milestone payments of up to US$2.4bn and royalties of high single-digit to mid-teens of future net sales of RC48 by Seagen.

(1) GC:

a. RemeGen completed the Ph2 registrational trial of RC48 as monotherapy for the treatment of HER2 over-expressing (IHC 2+ or IHC 3+) GC in China in Nov 2019. Based on this study, RC48 was conditionally approved by the NMPA in Jun 2021 as a 3L+ therapy for HER2 over-expressing GC, becoming the first-to-market domestic ADC drug in China. RC48 has been included in the NRDL from Jan 2022. RC48 is included in 2022 CSCO Guidelines as a Class II recommendation for third-line or late-line treatment of HER2-expressing advanced metastatic GC.

b. A randomized Ph3 trial is ongoing in China to evaluate RC48 as a third-line treatment of HER2-overexpressing GC (NCT04714190).

c. The Company is also exploring the possibility of RC48 in combination with RC98 (PD-L1 antibody) for the treatment of HER2-expressing GC, with the IND of the Ph1 trial approved by CDE in Apr 2022.

d. Additionally, RemeGen is in discussions with CDE about the proposals of RC48 in 1L and adjuvant treatment for GC.

(2) UC:

a. RC48 received conditional approval from the NMPA in Dec 2021 for the 2L+ treatment of HER2 over-expressing UC patients who have previously received platinum-containing chemotherapy. The approval was based on a multi-center, single arm, open-label Ph2 registrational trial evaluating RC48 as a monotherapy in HER2 over-expressing UC in China. RC48 as a monotherapy was included in the 2022 CSCO Guidelines as a Class II recommendation for 2L and 3L treatment of UC. In combination with toripalimab, RC48 was included in the CSCO Guidelines as a Class III recommendations for 1L and 2L UC treatment.

b. In Jun 2019, the Company initiated a single-arm Ph2 study (NCT04073602) of RC48 in HER2-negative (IHC 1+ or IHC 0) UC in China. The enrollment of all the 18 patients was finished in Jul 2021 and the results of the study were released at the ASCO meeting in Jun 2022. The Company will continue to follow-up the study.

c. A Ph3 study (NCT05302284) of RC48 + toripalimab vs chemotherapy in 1L HER2-expressing UC in China is ongoing with 6 of the 452 planned patients enrolled as of Jun 2022.

d. A Ph2 study (NCT05297552) of RC48 + toripalimab for perioperative treatment of muscle-invasive bladder cancer (MIBC) in China is ongoing as well.
e. In the US, Seagen has initiated an open-label, pivotal Ph2 study (NCT04879329) of RC48 alone and with pembrolizumab in HER2-expressing UC patients. The trial has three cohorts, including cohort A – RC48 monotherapy for 2/3L HER2-positive UC patients, cohort B – RC48 monotherapy for 2/3L HER2-low UC patients, and cohort C – RC48 in combination with pembrolizumab for 1L HER2-expressing UC patients. RC48 was granted BTD by the US FDA for 2L treatment of HER2-expressing UC after chemotherapy.
f. Moreover, RemeGen and Seagen are in discussions with the US FDA to initiate a Ph3 MRCT study of RC48 in combination with pembrolizumab for 1L HER2-expressing UC.

(3) BC:
a. In Jun 2021, RC48 received BTD from the NMPA for the treatment of HER2-positive advanced BC patients with liver metastases who had previously received trastuzumab and taxane therapy. The Company is conducting a Ph3 trial (NCT03500380) in China in HER2-positive mBC with or without liver metastases with 56 patients enrolled as of Jun 2022.
b. RemeGen has initiated a Ph3 clinical trial (NCT04400695) of RC48 monotherapy vs chemotherapy in patients with HER2-low (IHC 2+ and FISH–) BC in China. As of Jun 2022, 212 patients have been enrolled in the study.
c. In the US, in collaboration with Seagen, RemeGen is in discussions with the US FDA regarding a Ph3 trial of RC48 in combination with pembrolizumab for 1L HER2-low BC.

(4) NSCLC: RemeGen is conducting an open-label Ph1b trial (NCT04311034) to evaluate RC48 as monotherapy for the 2L treatment of HER2 over-expressing (IHC 2+/3+) or HER2 mutant (HER2 exon 20 mutant) NSCLC in China.
(5) BTC: A multi-center, single-arm and open-label Ph2 trial evaluating RC48 as monotherapy in the patients with HER2 over-expressing BTC post the failure of first-line chemotherapy is currently ongoing in China.
(6) Other indications: RemeGen is also conducting trials for RC48 for the treatment of gynecology malignant tumor, melanoma, etc.

Promising data of RC48 in HER2-positive and HER2-low cancers

Encouraging results for urothelial carcinoma (UC) as monotherapy or combo with PD-1

For patients with metastatic UC, platinum-based chemotherapy remains as the SoC of first-line treatment. However, most patients will have disease progression following platinum-based chemotherapy. For second-line treatment, immunotherapy using single agent immune checkpoint inhibitors is recommended. We think RC48 is potentially an important option for second and later-line treatment of UC.

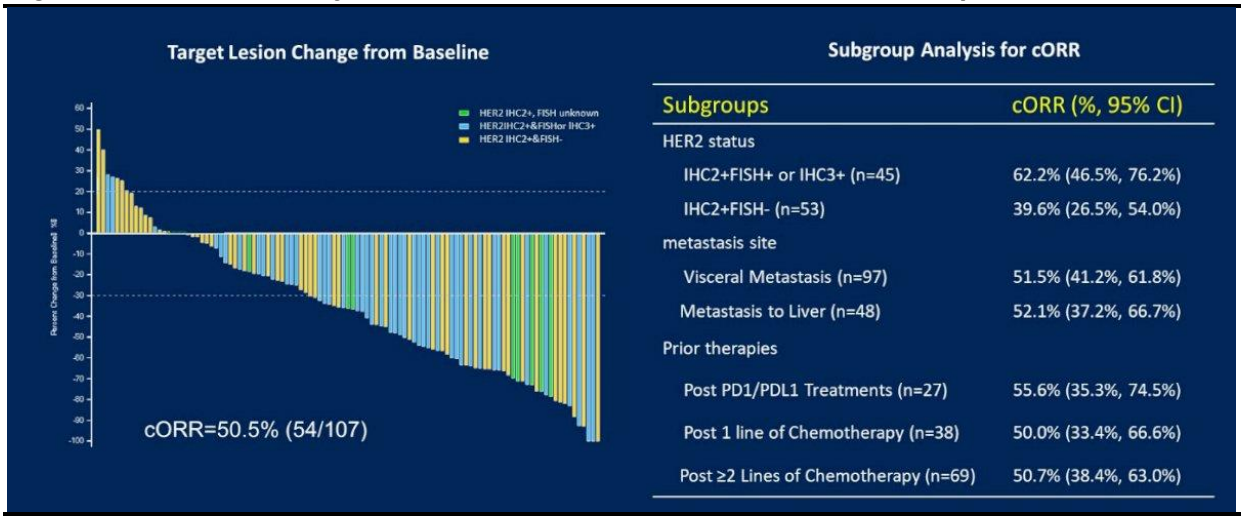
RemeGen completed a Ph2 trial (RC48-C005 /NCT03507166, link) of RC48 as a monotherapy in patients with HER2 overexpressing (IHC 2+ or IHC 3+) UC in China. Based on the positive results of this trial, the Company initiated a multi-center, single arm, open-label Ph2 registrational trial (RC48-C009 /NCT03809013, link). In Dec 2021, RC48 was conditionally approved for 2L+ treatment of UC patients who have previously received platinum-containing chemotherapy. RC48 received BTD and fast track designations from the US FDA for 2L treatment of HER2-positive UC in Sep 2020. In China, RC48 also received BTD in Dec 2020 for treatment of HER2 over-expressing UC post chemotherapy.

Superior efficacy of RC48 in HER2-positive UC

The combined analysis of two Ph2 trials RC48-C005 and RC48-C009 of RC48 in HER2-positive (IHC2+, 3+) metastatic UC was presented at the ASCO 2022 meeting (link1, link2). These two single-arm, multi-center, Ph2 trials enrolled 107 patients in total. The primary endpoints were ORR. Most (64.5%) patients

had received at least two lines systemic chemotherapy and the vast majority (90.7%) had visceral metastases. With a data cutoff of 4 Sep 2021, the confirmed ORR was 50.5%, and the DCR was 82.2%. In addition, the confirmed ORR was 62.2% (28/45) for IHC2+ & FISH+ or IHC3+ patients, 55.6% (5/9) for IHC2+ & FISH unknown patients, and 39.6% (21/53) for IHC2+ & FISH- patients, respectively. The mPFS was 5.9 months and the mOS was 14.2 months. Major grade≥3 TRAEs included hypoaesthesia (15.0%), neutropenia (12.1%) and r-GT increased (5.6%).

Figure 22: Combined analysis of RC48-C005 and RC48-C009 trials in HER2-positive UC



Source: Company data, CMBIGM

This combined analysis demonstrated an ORR of 39.6% for HER2 IHC2+ & FISH- patients, showing the benefit of RC48 in UC patients with low HER2 expression. As most (around 70%) patients with UC are HER2 expression low or negative, the Company is conducting a follow-up study (NCT04073602) of RC48 in HER2-negative (IHC 1+ or IHC 0) UC patients in an attempt to meet the large unmet medical needs.

Figure 23: Cross-trial comparison of drugs and drug candidates for 2/3L UC treatment

	RC48	Tislelizumab	Toripalimab	Pembrolizumab	Sacituzumab govitecan	Enfortumab vedotin	DS-8201	MRG002
Type of molecule	HER2 ADC	PD-1 mAb	PD-1 mAb	PD-1 mAb	TROP2 ADC	Nectin-4 ADC	HER2 ADC	HER2 ADC
Regimen	mono, single arm	mono, single arm	mono, single arm	mono, vs chemo	mono, single arm	mono, vs chemo	combo nivolumab, single arm	mono, single arm
Trial ID	RC48-C005, RC48-C009	NCT04004221	Polaris-03	KEYNOTE-045	TROPHY U-01, Cohort 1	EV-301	DS8201-A-U105	MRG002-006
Trial stage	Phase 2	Phase 2	Phase 2	Phase 3	Phase 2	Phase 3	Phase 1b	Phase 2
Primary endpoint	ORR	ORR	ORR	PFS, OS	ORR	OS	ORR	ORR
Treatment line	64.5% had ≥ 2 lines prior regimens	2L	2L	2L	median 3 prior regimens	87% had 1-2 prior regimens	61.8% had ≥1 prior regimens	80% had ≥ 2 lines prior regimens
Patient number	107	113	151	542	112	608	30 (cohort 3)	39
Biomarker status	HER2 ICH2+/3+	HER2 unknown, PD-L1+	-	-	-	-	HER2 IHC 2+/3+	HER2 IHC 2+/3+
ORR	**50.5%**	**24.0%**	**25.8%**	**21.1% vs 11.0%**	**27.7%**	**40.6% vs 17.9%**	**36.7%**	**65.2%**
CR	-	*9.6%*	*1.3%*	*9.3% vs 2.9%*	*5.4%*	*4.9% vs 2.7%*	*13.3%*	*8.7%*
PR	-	*14.4%*	*24.5%*	*11.9% vs 8.1%*	*22.3%*	*35.8% vs 15.2%*	*23.3%*	*56.5%*
mPFS (mo)	5.9	2.1	2.3	2.1 vs 3.3	-	5.55 vs 3.71	6.9	5.5
mOS (mo)	14.2	9.8	14.4	10.1 vs 7.3	-	12.88 vs 8.97	11.0	-
Grade ≥3 TRAEs/TEAEs	-	38%	20%	16.5% vs 50.2%	-	51.4% vs 49.8%	73.5%	-

Approval status in US and China	approved in China	approved in China for PD-L1+ patients	approved in China	approved in the US, not in China yet	approved in the US, not in China yet	approved in the US, not in China yet	not approved yet	not approved yet
Data source	Link	Link	Link	Link	Link	Link	Link	Link

Source: Company data, Pubmed, CSCO UC guidance, CMBIGM. Notes: Sacituzumab govitecan is a Trop2 targeted ADC developed by Gilead, and is approved for UC in the US with a boxed warning for severe or life-threatening neutropenia and severe diarrhea. Enfortumab vedotin is a nectin-4 targeted ADC developed by Astellas and Seagen, and is approved in the US with a box warning for serious skin reactions and a warning for pneumonitis. MRG002 is a HER2 ADC developed by Lepu Biopharma.

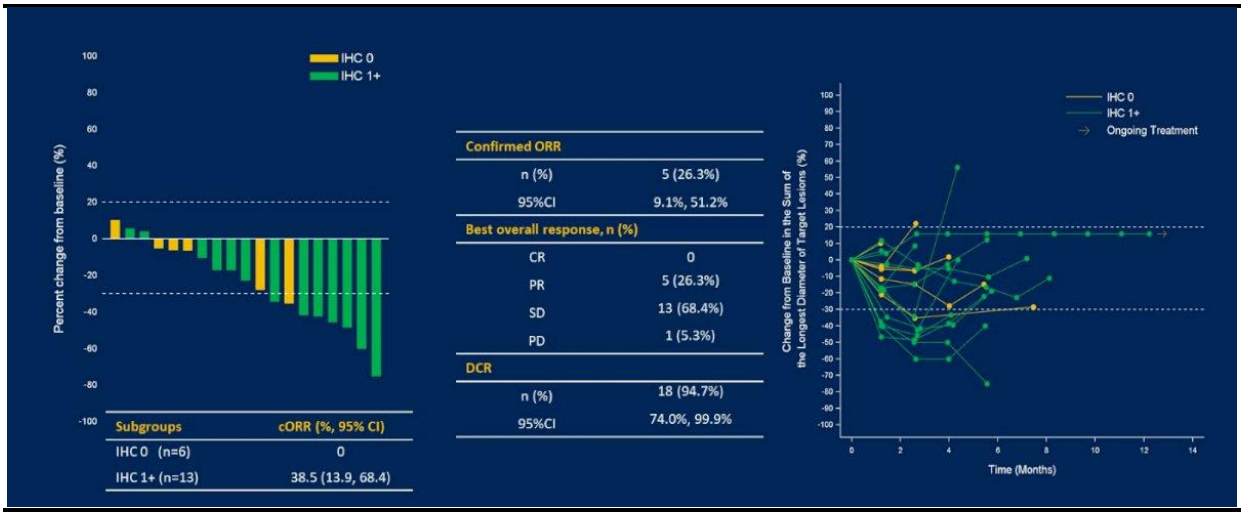
Globally there're so-far three approved ADC therapies for UC treatment, including RC48 (HER2 ADC), enfortumab vedotin (nectin-4 ADC, brand name PADCEV) and sacituzumab govitecan (TROP2 ADC, brand name TRODELVY). The combination therapy of DS-8201 with nivolumab (PD-1 mAb) realized an ORR of 36.7% in a Ph1b study. As cross-trial comparisons, RC48 had an encouraging ORR of 50.5% for 2L/3L UC treatment. It's worth noting that MRG002 (HER2 ADC developed by Lepu Biopharma) delivered a competitive ORR of 65.2% as a monotherapy in HER2-positive UC patients in a Ph2 study.

RC48 showed preliminary efficacy in HER2-negative UC

Remegen conducted a single-arm Ph2 study (NCT04073602) of RC48 in HER2-negative UC patients. As of May 2022 (link1, link2), 19 patients were enrolled, with 6 patients with HER2 IHC 0, and 13 patients with HER2 IHC 1+ at baseline. The confirmed ORR was 26.3% and the DCR was 94.7%. All of the 6 patients with HER2 0 reached SD in the study, while the ORR was 38.5% (5/13) in patients with HER2 IHC 1+. The mPFS and mOS were 5.5 and 16.4 months, respectively. This study demonstrated the activity of RC48 in HER-negative UC patients.

TRAEs of any grade were observed in all the patients with Grade 3/4 TRAEs in 3 patients (15.8%). Common TRAEs were leukopenia, hypoesthesia, alopecia, AST increase, ALT increase, neutropenia and fatigue. Most of these AEs were Grade 1 or 2. The most commonly reported grade 3/4 TRAEs were neutropenia (10.5%) and white blood cell count decreased (5.3%).

Figure 24: Results of a Ph2 trial of RC48 in HER2-negative UC patients



Source: Company data, CMBIGM

Preliminary results of RC48 + toripalimab (PD-1) for UC patients

Immunotherapy using single agent immune checkpoint inhibitors is a standard second line treatment for patients with metastatic UC. In a single-arm IIT trial, 41 UC patients were enrolled to assess if RC48 combined with PD-1 antibody may have a synergistic antitumor effect (NCT04264936, link). The majority of patients (61%) were systemic treatment naïve and most had visceral metastases (54%) including liver metastases (24%). HER2 expression was positive (IHC 2+ or 3+) in 59% patients, and PD-L1 was positive

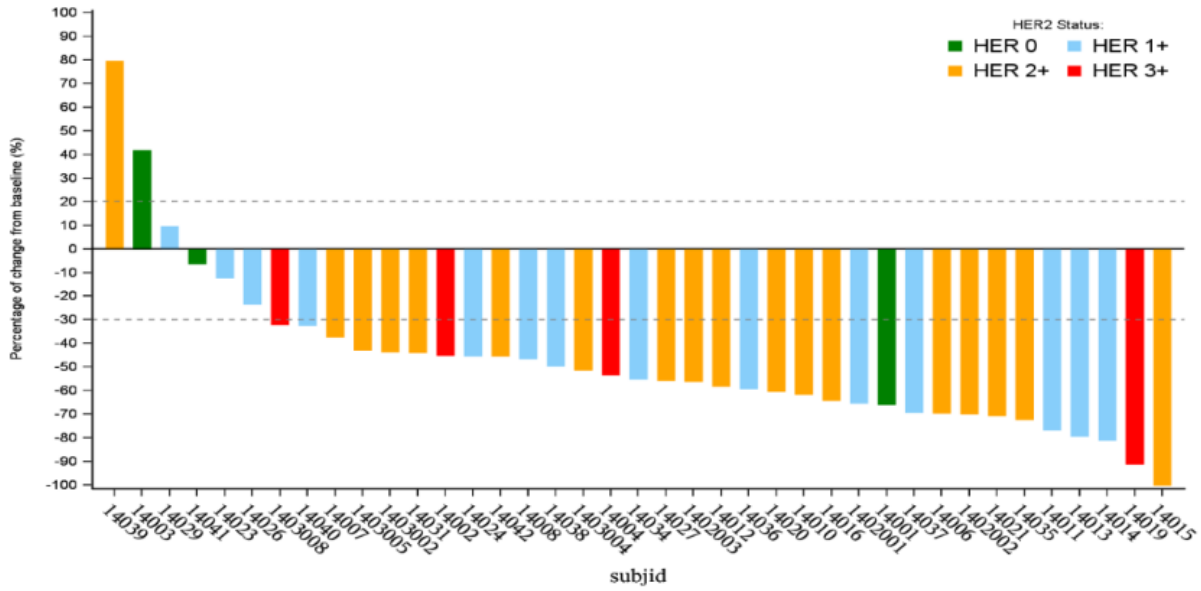
(CPS ≥ 10) in 32% patients. Patients received RC48 at 1.5 or 2 mg/kg, in combination with 3mg/kg toripalimab every two weeks. The recommended dose was RC48 2mg/kg + toripalimab 3mg/kg every 2 weeks.

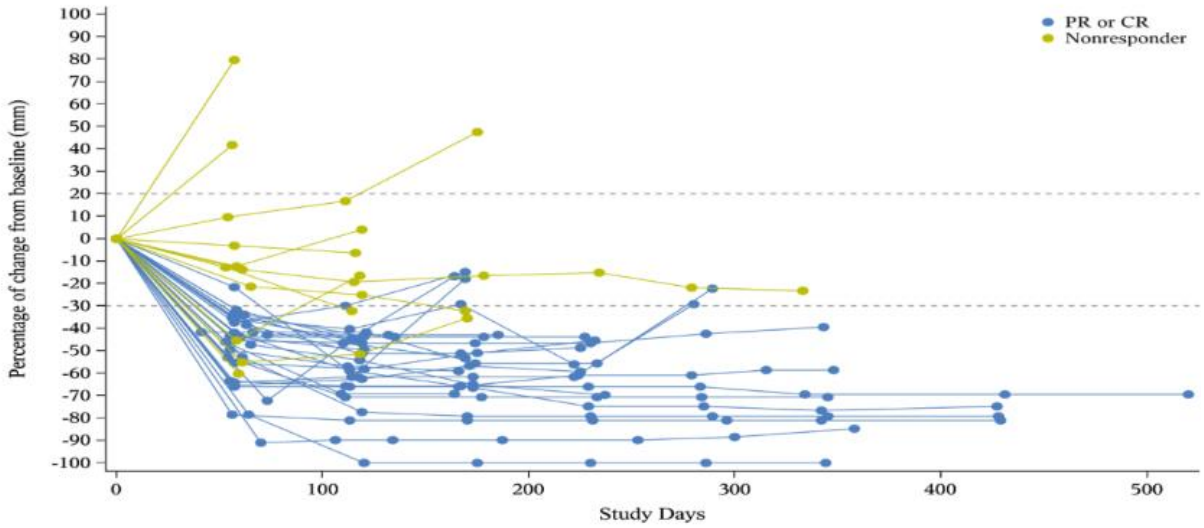
At a data cutoff of 22 Apr 2022, in the 39 patients who had at least two tumor assessments (link1, link2), the confirmed investigator assessed ORR was 71.8%, including 3 CR (7.7%) and 25 PR (64.1%). The DCR was 92.3%. The cORR was 73.9% for 1L patients who had not previously received systemic therapy. Furthermore, cORR differed according to HER2 and PD-L1 status (see table below). The mPFS was 9.2 months and the mOS was not reached. Grade ≥3 TRAEs included γ-glutamyl transferase increase (12.2%), ALT/AST increase (7.3%), asthenia (7.3%) and hypertriglyceridemia (7.3%).

RC48 in combination with toripalimab demonstrated promising early efficacy in UC patients and a manageable safety profile. A Ph3 study (NCT05302284) of RC48 and toripalimab vs platinum-based chemotherapy in previously untreated HER2-expressing (IHC 1+, 2+ or 3+) UC patients is currently ongoing in China.

Figure 25: Preliminary results of RC48 + toripalimab for UC patients

	No. of enrolled patients	No. of evaluable patients	No. of CR&PR	ORR
Overall	**41**	**39**	28	**71.8%**
Subgroups (by HER2 &PD-L1 expression)				
HER2 IHC(2+/3+), PD-L1(+)	8	7	6	85.7%
HER2 IHC(2+/3+), PD-L1(-)	16	15	13	86.7%
HER2 IHC(1+), PD-L1(+)	4	4	2	50.0%
HER2 IHC(1+), PD-L1(-)	10	10	6	60.0%
HER2 IHC(0), PD L1(+)	1	1	0	0.0%
HER2 IHC(0), PD-L1(-)	2	2	1	50.0%





Source: Company data, CMBIGM

As a cross-trial comparison, the 73.9% ORR of RC48 + toripalimab for 1L UC patients as mentioned above would be strongly competitive to enfortumab vedotin (nectin-4 ADC) as a front-line treatment for UC patients. In Cohort A of the EV-103 trial, the combination of enfortumab vedotin + pembrolizumab in first-line cisplatin-ineligible UC patients demonstrated an ORR of 73.3% (including 17.8% CR), DCR of 93.3%, and a mPFS of 12.3 months (link). At 2022 ESMO, Astellas Pharma and Seagen released the results of Cohort K of the EV-103 trial (link). The Cohort K investigated enfortumab vedotin + pembrolizumab and enfortumab vedotin alone as first-line treatment for mUC patients. In patients treated with enfortumab vedotin and pembrolizumab (n=76), the confirmed ORR was 64.5%, with 10.5% CR and 53.9% PR.

Promising efficacy for later-line gastric cancer (GC) treatment

RemeGen completed the single-arm Ph2 registrational trial (NCT03556345/ RC48-C008) of RC48 as a monotherapy in 2019 for the treatment of HER2 over-expressing (IHC 2+ or IHC 3+) GC. Based on this study, RC48 was conditionally approved in China in Jun 2021 as a third-line or later-line therapy in patients with HER2-overexpressing GC or GEJA, becoming the first domestic ADC drug approved for marketing in China. RC48 was included in the updated China NRDL for GC treatment effective from Jan 2022.

In the Ph2 trial (NCT03556345), 125 patients received RC48 treatment at 2.5mg/kg once every two weeks for six weeks (link). The ORR was 24.8%. The median PFS and OS were 4.1 months and 7.9 months, respectively. Among patients previously treated with trastuzumab, the ORR was 27.8% (20/72), demonstrating the potential of RC48 in trastuzumab-resistant patients. Among patients previously treated with taxane, the ORR was 22.4% (24/107), compared to 38.9% ORR for patients without prior taxane treatment. ORR was 26.3% (20/76) for HER2-positive patients. Furthermore, for patients with IHC2+/FISH-, which is normally defined as having low HER2 expression, the ORR was 16.7% (1/6), which in our view, shows the bystander effect of RC48. SAEs occurred in 45 (36.0%) patients, and RC48-related SAEs were mainly decreased neutrophil count (3.2%). Seven patients had adverse events that led to death were not RC48-related.

DS-8201 demonstrated very encouraging efficacy in response and OS among HER2-positive GC patients receiving at least two previous therapies in its Ph2 DESTINY-Gastric01 study. The study randomized patients 2:1 to receive DS-8201 (125 patients) or chemotherapy (62 patients). At a median follow-up of 12.3 months (link), the ORR was 51.3% in the DS-8201 group, compared to 14.3% in the chemotherapy group (P<0.001). The ORR of DS-8201 in patients with IHC3+ (58.2%, 53/91) was higher than that in patients with IHC2+/ISH+ (28.6%, 8/28). OS was longer with DS-8201 than with chemotherapy (12.5 vs

8.4 months; HR=0.59; P=0.01, which crossed the boundary of 0.0202). At the final OS analysis with a median follow-up of 18.5 months (link), ORR remained consistent of 51.3% (61/119; 11 CR; 50 PR) with DS-8201 vs 14.3% (8/56; all PR) with chemotherapy (P< 0.0001). OS was improved with DS-8201 vs chemotherapy (median OS 12.5 vs 8.9 months; HR=0.60; 95% CI, 0.42-0.86).

Nevertheless, T-DM1's Ph2/3 GATSBY study showed that T-DM1 was not superior to taxane in patients with previously treated HER2-positive GC, with the median OS of 7.9 months and 8.6 months in the T-DM1 and taxane group, respectively (link).

Following the completed single-arm registrational Ph2 trial, RemeGen is conducting a randomized controlled Ph3 trial (NCT04714190) to compare RC48 with standard treatment (taxane) in 3L+ HER2-overexpressing GC patients.

Figure 26: Cross-trial comparison of therapies for 2/3L GC treatment

	RC48	Apatinib	Nivolumab	DS-8201	T-DM1
Regimen	mono, single arm	mono, vs placebo	mono, vs placebo	mono, vs chemo	mono, vs chemo
Trial	RC48-C008	NCT01512745	ATTRACTION-2	DESTINY-Gastric01	GATSBY
Trial stage	Phase 2	Phase 3	Phase 3	Phase 2	Phase 2/3
Primary endpoint	ORR	OS, PFS	OS	ORR	OS
Treatment line	All pts had ≥2 lines prior regimens	All pts had ≥2 lines prior regimens	All pts had ≥2 lines prior regimens	All pts had ≥2 lines prior regimens	Progressed during or after first-line therapy
Patient number	125	267	493	187	345
Biomarker status	HER2 IHC2+/3+	-	-	HER2 IHC2+/ISH+ or IHC 3+	HER2-positive
ORR	**24.8%**	**2.8% vs 0%**	**11.9% vs 0%**	**51.3% vs 14.3%**	**20.6% vs 19.6%**
mPFS (mo)	**4.1**	2.6 vs 1.8	1.6 vs 1.5	**5.6** vs 3.5	2.7 vs 2.9
mOS (mo)	7.9	6.5 vs 4.7	5.3 vs 4.1	12.5 vs 8.4	7.9 vs 8.6 (not superior)
Grade ≥3 TRAEs/TEAEs	56.8%	69% vs 43%	11.8% vs 4.3%	85.6% vs 56.5%	60% vs 70%
Approval status in US and China	approved in China (3L+)	approved in China (3L+)	approved in China (mono for 3L+, +chemo for adj and 1L) and US (+chemo for adj and 1L)	approved in the US (2L+), not in China yet	not approved due to clinical trial failure
Data source	Link	Link	Link	Link	Link

Source: Company data, Pubmed, CSCO GC guideline, CMBIGM.

Exploring opportunities in both HER2-positive and HER2-low breast cancer (BC)

In Jun 2021, disitamab vedotin (RC48) received BTD from the NMPA for treatment of patients with HER2-positive advanced BC with liver metastases who had previously received trastuzumab and taxane therapy. The Company is currently conducting a Ph3 trial (NCT03500380) in China to evaluate the efficacy of RC48 versus capecitabine + lapatinib in HER2-positive mBC with or without liver metastases. Additionally, RemeGen is conducting a Ph3 clinical trial (NCT04400695) in patients with HER2 low-expressing (IHC 2+ and FISH-) BC.

Early efficacy of RC48 in HER2-positive BC with visceral metastasis

The combined outcomes of RC48 in the HER2-positive mBC of a Ph1 study (C001 CANCER, NCT02881138) and a Ph1b study (C003 CANCER, NCT03052634) were previously reported (link). Both studies enrolled patients with HER2-positive (IHC3+ or IHC2+ & FISH+) locally advanced or metastatic BC. C001 CANCER was a dose-escalation study (0.5, 1.0, 1.5, 2.0 and 2.5 mg/kg) with 3+3 design aiming to evaluate the maximum tolerated dose (MTD). C003 CANCER was an open-label, parallel designed study with 3 dose cohorts (1.5, 2.0 and 2.5 mg/kg, Q2W) aiming to determine the RP2D.

70 patients were included in the pooled analysis. At baseline, most patients had visceral metastasis (87.1%) and received no less than 2 lines of chemotherapy (78.6%). 47 patients (67.1%) had previously

received trastuzumab, 42.9% had previously received anti-HER2 tyrosine kinase inhibitor therapy and 24 patients (34.3%) had received ≥ 2 lines of anti-HER2 therapy.

RC48 demonstrated good tolerability and promising efficacy when administrated Q2W in the patients with HER2-positive mBC. Grade 3 or 4 TRAEs were reported in 29 patients (41.4%), mainly neutropenia (21.4%), asthenia (15.7%), and leukopenia (10.0%). The cORR was 31.4% (22/70). The clinical benefit rate was 38.6%. The mPFS was 5.8 months. For the 64 patients who received ≥ 1.5 mg/kg treatment, the cORR was 34.4% (22/64) with a median PFS of 6.2 months. Specifically, for the dose levels of 1.5, 2.0 and 2.5 mg/kg, the cORR was 22.2%, 42.9% and 36.0%, respectively; the mPFS was 6.2, 6.0 and 6.3 months, respectively. 2.0 mg/kg Q2W was selected as RP2D. These results remained steady with a longer follow-up at the data cutoff date of 31 Dec 2020 (link).

Figure 27: Cross-trial comparison of HER2 ADC therapies for 3L treatment of HER2-positive BC

	RC48	DS-8201		T-DM1	SYD985	
Regimen	mono, single arm	mono, single arm	mono, vs T-DM1	mono, vs lapatinib plus capecitabine	mono, vs chemo	mono, single arm
Trial	NCT02881138, NCT03052634	DESTINY-Breast01 (registrational)	DESTINY-Breast03 (head-to-head)	NCT00829166	NCT03262935 (registrational)	NCT02277717
Trial stage	Phase 1/1b	Phase 2	Phase 3	Phase 3	Phase 3	Phase 1
Primary endpoint	safety, RP2D	ORR	PFS	PFS, OS, safety	PFS	safety
Treatment line	78.6% pts received prior ≥2 lines of chemo	pts previously treated with T-DM1	pts previously treated with trastuzumab and taxane	pts previously treated with trastuzumab and a taxane	≥2 previous regimens or ≥1 treatment with T-DM1	heavily pretreated patients
Patient number	70	184	524	991	437	50
Biomarker status	HER2 IHC3+ or IHC2+&FISH+	HER2 IHC3+ (83.7%), IHC1+/2+&FISH+ (15.2%)	HER2 IHC3+ (88.9%), IHC2+&FISH+ (10.5%)	HER2 IHC3+ or FISH≥2	HER2-positive	HER2-positive (IHC 2+/3+/ISH+)
ORR	**42.9%**	**60.9%**	**79.7% vs 34.2%**	**43.60%**	No significant differences in ORR	**33%**
mPFS (mo)	6.0	16.4	not reached (18.5, NE) vs 6.8 (12mo PFS rate 75.8% vs 34.1%)	9.6 vs 6.4	7.0 vs 4.9 (met primary endpoint)	9.4
mOS (mo)	-	-	-	30.9 vs 25.1	20.4 vs 16.3	-
Grade ≥3 TRAEs	41.4%	48.4%	45.1% vs 39.8%	41% vs 57%	-	-
Approval status in US and China	not approved yet	approved for 2L in the US, BLA accepted in China in Mar 2022		approved in the US and China	BLA in the US accepted with PDUFA date in May 2023	
Data source	Link	Link	Link	Link	Link	Link

Source: Company data, Pubmed, CMBIGM. Notes: SYD985 is a HER2 ADC developed by Byondis. DS-8201 was approved in the US with a boxed warning for the risk of interstitial lung disease (ILD) and embryo-fetal toxicity.

We would also like to highlight that DS-8201 has demonstrated overwhelmingly strong efficacy in HER-2 positive BC, especially in patients resistant or refractory to T-DM1, while with a substantial safety risk on fatal interstitial lung disease (ILD). In a Ph2 study (DESTINY-Breast01/NCT03248492, link), 184 patients with HER2-positive mBC who were resistant or refractory to T-DM1 received DS-8201 at the recommended dose of 5.4mg/kg. The confirmed ORR on independent central review was 60.9%, including 6.0% had a complete response, and 54.9% had a partial response. The mPFS was 16.4 months among all patients and estimated overall survival was 93.9% at 6 months and 86.2% at 12 months. On the safety side, the results showed that DS-8201 was associated with interstitial lung disease (ILD) in 13.6% of the patients (grade 1 or 2, 10.9%; grade 3 or 4, 0.5%; and grade 5, 2.2%), and four deaths (2.2% of the patients) were attributed to ILD.

Additionally, in a head-to-head Ph3 trial evaluating DS-8201 vs T-DM1 in patients with HER2-positive mBC previously treated with trastuzumab and a taxane (link), among the 524 randomly assigned patients, the 12-month PFS rate was 75.8% with DS-8201 and 34.1% with T-DM1 (HR = 0.28). ORR was 79.7%

of the DS-8201 group and in 34.2% of the T-DM1 group. The study showed that treatment with DS-8201 was associated with ILD and pneumonitis, which occurred in 10.5% of the patients (grade 1, 2.7%; grade 2, 7.0%; grade 3, 0.8%; no grade 4 or 5 events) in the DS-8201 group vs 1.9% in the T-DM1 group.

Based on the above-mentioned encouraging efficacy data, DS-8201 was approved for the treatment of HER2-positive BC in the US in Dec 2019 (3L+) and May 2022 (2L+), but with a boxed warning of the risk of ILD and embryo-fetal toxicity. Without the concerns on ILD, the safety profile of RC48 would be a differentiated competitive standpoint in competing with DS-8201, in our view.

Preliminary efficacy of RC48 in HER2-low breast cancer

In contrast to HER2-positive (defined as HER2 IHC3+ or IHC2+/ISH+) breast cancer, HER2-low (IHC1+ or IHC2+/ISH-) breast cancer generally does not respond to trastuzumab or T-DM1. Nevertheless, new ADCs like DS-8201 and RC48 show potential in treating HER2-low breast cancer thanks to bystander killer effect by using cleavable linkers and higher drug-to-antibody ratio.

DS-8201 was approved in Aug 2022 in the US for the treatment of adult patients with HER2-low (IHC 1+ or IHC 2+/ISH-) BC who have received a prior chemotherapy, which has the potential to reshape how breast cancer is classified and treated. The approval was based on the results from the Ph3 study DESTINY-Breast04 (link1, link2). In this trial, at a median follow-up of 18.4 months, DS-8201 demonstrated a 50% reduction in the risk of progression and a 36% reduction in the risk of death compared to standard chemotherapy in BC patients with HER2-low expression. Among all 577 patients enrolled, the mPFS was 9.9 months in the DS-8201 group and 5.1 months in the chemo group (HR=0.50, P<0.001), and mOS was 23.4 months and 16.8 months, respectively (HR=0.64, P=0.001). DS-8201 showed meaningful benefits in PFS and OS compared to standard-of-care treatment, regardless of hormone receptor status.

Figure 28: Efficacy results of DS-8201's Ph3 trial DESTINY-Breast04 in HER2-low BC

Efficacy Measure	HR-Positive (n=494)[i]		All Patients (n=557)		HR-Negative (n=58)[i]	
	Enhertu (5.4 mg/kg) (n=331)	Chemotherapy (n=163)	*Enhertu* (5.4 mg/kg) (n=373)	Chemotherapy (n=184)	*Enhertu* (5.4 mg/kg) (n=40)	Chemotherapy (n=18)
PFS						
Median PFS (months)[ii]	10.1 (9.5-11.5)	5.4 (4.4-7.1)	9.9 (9.0-11.3)	5.1 (4.2-6.8)	8.5 (4.3-11.7)	2.9 (1.4-5.1)
Hazard Ratio (95% CI)	0.51 (0.40-0.64)		0.50 (0.40-0.63)		0.46 (0.24-0.89)	
p-value	p<0.001		p<0.001			
OS						
Median OS (months)	23.9 (20.8-24.8)	17.5 (15.2-22.4)	23.4 (20.0-24.8)	16.8 (14.5-20.0)	18.2 (13.6-NE)	8.3 (5.6-20.6)
Hazard Ratio (95% CI)	HR 0.64 (0.48-0.86)		HR 0.64 (0.49-0.84)		HR 0.48 (0.24-0.95)	
p-value	p=0.003		p=0.001			

Confirmed ORR (%) (95% CI)[ii,iii]	52.6% (47.0-58.0)	16.3% (11.0-22.8)	52.3% (47.1-57.4)	16.3% (11.3-22.5)	50.0% (33.8-66.2)	16.7% (3.6-41.4)
Complete Response (%)	3.6%	0.6%	3.5%	1.1%	2.5%	5.6%
Partial Response (%)	49.2%	15.7%	49.1%	15.2%	47.5%	11.1%
Stable Disease (%)	35.1%	50.0%	34.6%	49.5%	30.0%	44.4%
Progressive Disease (%) (95% CI)	7.8%	21.1%	8.3%	22.3%	12.5%	33.3%
Median DoR (months)[ii]	10.7	6.8	10.7	6.8	8.6	4.9
CBR (%)[ii,iv]	71.2%	34.3%	70.2%	33.7%	62.5%	27.8%
DCR (%)[iv,v]	88.0%	66.3%	87.1%	65.8%	80.0%	61.1%

Source: AstraZeneca, CMBIGM. Notes: the primary endpoint of the trial was PFS in the HR-positive cohort.

Approximately half of BC patients are HER2-low. The early approval of DS-8201 by the FDA ahead of its PDUFA date underscores the largely unmet-medical need of therapies for treating HER2-low patients. Based on the promising results of the DESTINY-Breast04 trial, clinicians start to redefine HER2-low patient population, previously defined as HER2-negative, which could benefit from HER2-based therapies.

As a potent HER2 ADC, RC48 is under evaluation for the treatment of HER2-low mBC as well, including a PhI/II trial (NCT03052634) and a Ph3 trial (NCT04400695). The preliminary data of the PhI/II trial was released at the ASCO 2021 meeting (link). In the HER2-low expressing (IHC2+/FISH- or IHC1+) subgroup, 48 patients received RC48 at a dose of 2.0 mg/kg dose Q2W. At the data cutoff of Dec 2020, the ORR and mPFS of HER-low mBC patients were 39.6% and 5.7 months, respectively. ORR and mPFS for IHC2+/FISH- mBC patients were 42.9% and 6.6 months, respectively. For IHC1+ patients, even though the COVID-19 pandemic led to treatment postpone for some patients, ORR and mPFS reached 30.8% and 5.5 months, respectively.

As a cross-trial comparison, the 39.6% ORR of RC48 in HER2-low mBC patients were comparable to the 37.0% ORR of DS-8201 in a Ph1b study in HER2-low mBC (link), while DS-8201 achieved a much longer mPFS of 11.1 months vs 5.7 months for RC48. We look forward to the further data readout of the Ph3 study of RC48 in HER2-low BC.

Figure 29: Cross-trial comparison of HER2 ADC therapies for late-line treatment of HER2-low BC

	RC48	DS-8201		SYD985	MRG002
Regimen	mono, single arm	mono, single arm	mono, vs chemo	mono, single arm	mono, single arm
Trial	NCT03052634	NCT02564900	DESTINY-Breast04	NCT02277717	NCT04742153
Trial stage	Phase 1b	Phase 1b	Phase 3	Phase 1	Phase 2
Primary endpoint	RP2D	ORR	PFS in HR-positive cohort	Safety	ORR
Treatment line	40% had received ≥3 prior chemo regimens (overall trial)	median 7.5 prior therapies	HR-positive pts received a median of 2 prior lines of endocrine therapy	heavily pretreated patients	median 3 lines of prior treatment
Patient number	48	54	557 (88.7% HR-positive)	49	56
HER2 expression level	IHC1+ or IHC2+/FISH-	IHC1+ or IHC2+/FISH-	IHC1+ or IHC2+/FISH-	HER2-low (IHC1+/2+/ISH-)/HR-positive, and TNBC	IHC1+ or IHC2+/FISH-
ORR	**39.6%**	**37.0%**	**52.3%** vs 16.3% (all pts)	**27%** in HER2-low/HR-positive; **40%** in TNBC	**34.7%**
mPFS (mo)	5.7	11.1	9.9 vs 5.1, HR=0.50, P<0.001 (all pts)	4.1 in HER2-low/HR-positive; 4.4 in TNBC	-

mOS (mo)	-	29.4	23.4 vs 16.8, HR=0.64, P=0.001 (all pts)	-	-
Safety	Neutrophil count decreased (16.9%), GGT increased (12.7%), and fatigue (11.9%) were the grade 3 and above TRAEs occurring in ≥ 10% of the overall pts	63% Grade ≥3 TEAEs; 3 pts suffered fatal events of drug–induced interstitial lung disease (ILD)/pneumonitis	52.6% vs 67.4% Grade ≥3 TEAEs; 12.1% pts in the DS-8201 arm had drug-related ILD or pneumonitis. 5 Gr3 ILD and 3 ILD-related deaths reported	The most common grade 3 TRAEs included neutropenia (6%), fatigue (3%), and conjunctivitis (3%). One death from drug-related pneumonitis reported	-
Approval status	not approved yet	sBLA for 3L HER2-low BC approved by US FDA in Aug 2022, ahead of the PDUFA date of 4Q22; BLA accepted in China in Aug 2022		not approved yet	not approved yet
Data source	Link	Link	Link	Link	Link

Source: Company data, Pubmed, CMBIGM. Notes: DS-8201 was approved with a boxed warning for the risk of ILD and embryo-fetal toxicity.

Large commercial potential in China and overseas

RemeGen has expanded its oncology commercial team from 180 employees as of the end of 2021 to 310 employees as of Jul 2022, and further to 497 employees as of Sep 2022. As of Sep 2022, the oncology commercial team has covered 1,487 hospitals in 276 prefecture-level cities across China, and RC48 has been admitted to 395 hospitals and 840 channel pharmacies. We expect the Company to further expand the oncology commercial team in the future.

Since the approval of RC48 in China for treatment of GC in Jun 2021, the Company realized approximately RMB84mn revenue from RC48 in 2021. RC48 was included in the updated China NRDL for GC treatment effective from Jan 2022, which largely boosts the sales volume of the drug. RC48 achieved revenue of approximately RMB187mn in 1H22 and roughly RMB100mn in 3Q22, indicating a strong sales growth momentum. The Company is seeking NRDL inclusion of RC48 for UC treatment in 4Q22.

We think competition of anti-HER2 ADC drugs in China is moderate while RC48 has advantages as a second-to-market anti-HER2 ADC in China. Meanwhile, DS-8201 is under NDA review by the China CDE for the treatment of HER2-positive and HER2-low BC. DS-8201 has been approved by the US FDA for treatment of multiple indications, including HER2-positive GC, HER2-positive and HER2-low BC, and HER2-mutated NSCLC.

We expect RC48 to face strong competitions from DS-8201 in breast cancer and gastric cancer upon its approvals in China. However, with differentiated indication coverage, such as UC and BC with liver metastases, and a favorable safety profile to support its potential use in earlier treatment settings, RC48 will take a meaningful share in the anti-HER2 ADC market in China and overseas, in our view.

Figure 30: Approved anti-HER2 ADCs in China (as of Nov 2022)

Drug	Approved indications	Initial China approval date	NRDL indications	Latest retail price	Dose	Monthly cost	Annual cost	NRDL valid period
RC48	3L+ GC, 2L+ UC	2021.06	GC included, UC not included yet	RMB3,800/60mg	2.5 mg/kg, Q2W (GC); 2.0 mg/kg, Q2W (UC)	RMB24,429 (GC); RMB16,286 (UC)	RMB293, 143 (GC); RMB195, 429 (UC)	2022.01.01-2023.12.31 (GC)
T-DM1	3L+ BC, Adjuvant therapy for early BC	2020.01	No	RMB8,340/100mg; RMB11,9522/160 mg	3.6 mg/kg, Q3W	RMB28,988	RMB347, 857	--

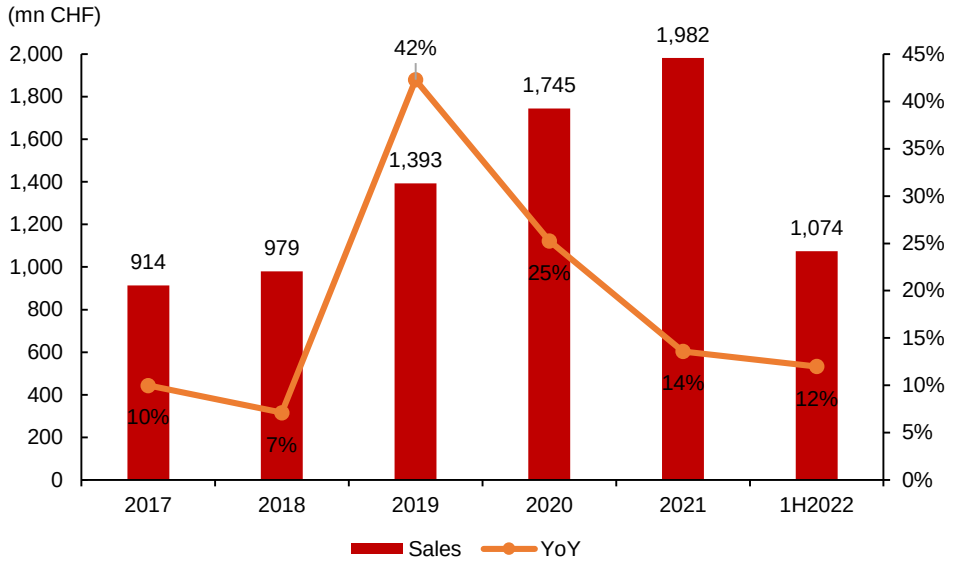
Source: Company data, CMBIGM. Notes: RemeGen is seeking NRDL inclusion of RC48 for UC treatment in 4Q22. Monthly cost of RC48 is estimated based on an average weight of patients of 60kg. Roche cut the price of T-DM1 twice in China in 1H22 (in Mar and Jun) with the current price 57% lower than the price prior Mar 2022, potentially in an attempt to prepare for the NRDL inclusion.

In the overseas market, T-DM1 was initially approved in the US in Feb 2013 for HER2-positive breast cancer after previous trastuzumab and a taxane treatment. In May 2019, T-DM1 was further approved by

FDA for the treatment of early HER2-positive breast cancer after surgery, which contributed its strong sales growth in 2019. T-DM1 realized global sales of CHF1,982mn (or US$1,993mn; +14% YoY) in 2021 and CHF1,074 (or US$1,080mn; +12% YoY) in 1H22. Even though the YoY sales growth of T-DM1 decelerated over the past years, the sales momentum of T-DM1 remained steady.

Nevertheless, we expect DS-8201 and RC48, as next generation HER2 ADC therapies, to strengthen their foothold in the global HER2 market in competing with T-DM1 and other HER2 therapies like trastuzumab. DS-8201's in-market sales in the global region except Japan reached US$397mn in 1H22 (+117% YoY, link). As predicted by analysts, DS-8201 could reach multiple billion USD peak sales. SVB Securities analyst Andrew Berens previously projected DS-8201 could reach US$4.6bn in sales in HER2-low patients by 2030, according to Fierce Pharma (link), while Peter Welford from Jefferies forecasted DS-8201 to reach US$5.8bn global sales at peak across all indications (link). The multiple billion sales potential and the strong sales momentum of DS-8201 and T-DM1 highlight the market potential of HER2 ADC therapies.

Figure 31: Global sales of T-DM1 (2017-2022)



Source: Roche, CMBIGM. Notes: as of 18 Oct 2022, 1 CHF (Swiss Franc) = 1.01 USD. Significant YoY sales growth in 2019 was driven by the increased demand due to launch of new indication. YoY growth in 1H22 is based on the first half year sales in 2021 and 2022.

In Aug 2021, in a blockbuster deal, RemeGen granted Seagen an exclusive license to develop and commercialize RC48 in global regions excluding Asia (Japan and Singapore excluded). RemeGen received an upfront payment of US$200mn and is eligible to receive additional milestone payments of up to US$2.4bn and a high single-digit to mid-teens royalties on future net sales.

HER2 ADC is a hot space with multiple blockbuster deals

ADC drugs, especially HER ADC drugs, have become a hot area with many blockbuster BD deals in recent years. Besides the partnership between RemeGen and Seagen, in Aug 2022, GSK paid Mersana Therapeutics US$100mn to obtain an option to in-license XMT-2056, Mersana's preclinical HER2 ADC asset. If GSK exercises the option, Mersana could receive up to US$1.36bn milestone payments and additional tiered royalties. It is particularly worth mentioning that, in 2019, AstraZeneca in-licensed DS-8201, a HER2 ADC candidate, from Daiichi Sankyo with a total deal size up to US$6.9bn.

Figure 32: Major deals in the HER2 ADC space in recent years

Licensor	Licensee	Date	Product	Deal size (US$ mn)	Upfront payment (US$ mn)	Milestone payment (US$ mn)	Additional payments
Mersana Therapeutics	GSK	2022-08	XMT-2056	1,460	100	1,360	Tiered double-digit royalties
Byondis	medac	2022-05	SYD985	undisclosed	undisclosed	undisclosed	undisclosed
LegoChem Biosciences	Iksuda Therapeutics	2021-12	LCB14	1,000	50	950	-
RemeGen	Seagen	2021-08	RC48	2,600	200	2,400	High single-digit to mid-teens royalties
Daiichi	AstraZeneca	2019-03	DS-8201	6,900	1,350	5,550	-

Source: Company news release, CMBIGM

Figure 33: Anti-HER2 ADC molecules at late clinical stage (as of Oct 2022)

Drug	Company	China development phase	Global development phase	Targeted indications
trastuzumab deruxtecan (DS-8201)	Daiichi Sankyo, AstraZeneca	BLA filed	Approved	HER2-positive BC (2L+)
		BLA filed	Approved	HER2-low BC (3L+ approved, 2L data readout in 2023)
		Phase III	Approved	HER2-positive GC (2L+)
		Phase III	Approved	HER2-mutated NSCLC (2L+)
		Phase III	Phase III	HER2-positive early BC
		Phase III	Phase III	HER2-mutated NSCLC (1L)
		--	Phase II	CRC, bladder cancer, osteosarcoma, BTC, TNBC, UC, OVC, cervical cancer, endometrial cancer, pancreatic cancer
trastuzumab emtansine (T-DM1)	ImmunoGen, Roche	Approved	Approved	HER2-positive BC (3L+ and adjuvant)
		Phase II/III	Phase II/III	HER2-positive GC, GEJC
		--	Phase II	Salivary gland cancer, OVC, lung cancer
disitamab vedotin (RC48)	RemeGen, Seagen	Approved	Phase II	HER2-expressing UC (2L+)
		Approved	--	HER2-positive GC, GEJC (3L+)
		Phase III	--	HER2-low BC
		Phase II/III	--	HER2-positive BC
		Phase II	--	BTC, melanoma, MIBC, NSCLC
trastuzumab duocarmazine (SYD985)	Byondis, medac	--	BLA filed	HER2-positive BC
		--	Phase II	HER2-expressing endometrial cancer
		--	Phase I	UC, OVC, bladder cancer, BC
BAT8001	Bio-Thera Solutions	Phase III	--	HER2-positive BC
		Phase I	--	GC
SHR-A1811	Hengrui	Phase III	--	HER2-positive BC
		Phase I/II	--	HER2-expressing NSCLC
		Phase I	Phase I	GC, GEJC, CRC
TAA013	TOT Biopharm	Phase III	--	HER2-positive BC
ARX788	Ambrx, Novocodex	Phase II/III	Phase II/III	HER2-positive BC, GC
		IND	Phase II/III	GEJC
		--	Phase II	NSCLC, BTC, CRC
A166	Levena, Kelun-biotech	Phase II	Phase II	BTC, tongue carcinoma, larynx cancer, OVC, skin cancer, GC, HER2 positive BC, GEJC, CRC, UC, NSCLC, etc.
DAC-001	DAC Biotech	Phase II	--	GC, UC, HER2 positive BC, GEJC
DP303c	CSPC	Phase II	--	OVC, GC, HER2 positive BC, GEJC
LCB14-0110	LegoChem, Iksuda, Fosun	Phase II	Phase II	HER2-positive GC, BC, GEJC, CRC, NSCLC
MRG002	Lepu Biopharma	Phase II	Phase II	BTC, GC, UC, HER2-low BC, HER2-positive BC,GEJC, NSCLC

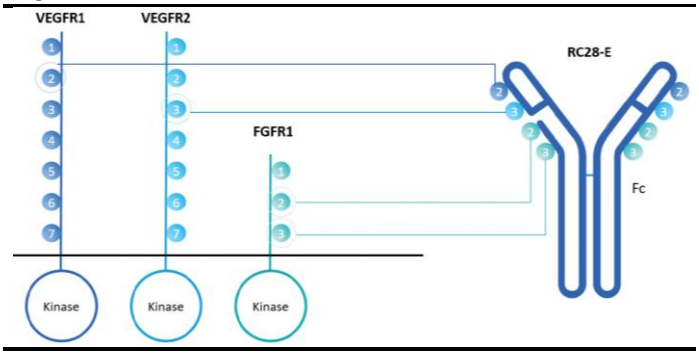
Source: PharmCube, CMBIGM

RC28: differentiated VEGF/FGF dual-targeting fusion protein targeting eye diseases

Differentiated dual-targeting MoA

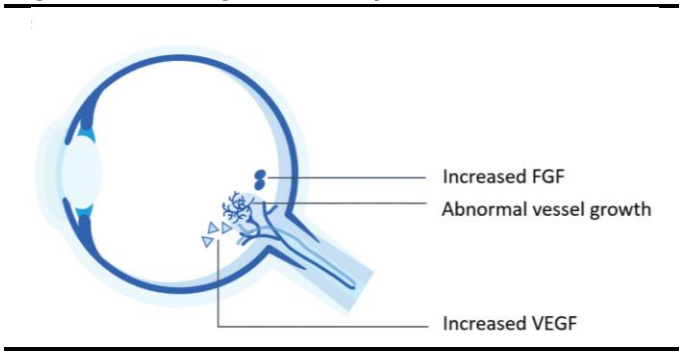
RC28 is a VEGF/FGF dual-targeting fusion protein for the treatment of eye diseases with best-in-class potential. RC28 is a recombinant dual decoy receptor IgG1 Fc-fusion protein, targeting both VEGF and FGF families simultaneously. VEGF and FGF are key pathway regulators in the formation of new blood vessels (angiogenesis), and are found in higher levels in patients with diabetes. Compared to single-target VEGF inhibitors, RC28 has the potential to more effectively inhibit the abnormal blood vessel growth implicated in various eye diseases through both VEGF and FGF pathways, and potentially allows for a better dosing profile.

Figure 34: Structure of RC28



Source: Company data, CMBIGM

Figure 35: Pathogenesis of ophthalmic diseases



Source: Company data, CMBIGM

Certain ophthalmic diseases, such as wet age-related macular degeneration (wet AMD), diabetic macular edema (DME) and diabetic retinopathy (DR), develop when blood vessels grow into the macula, causing fluid leaked from blood vessels into the eyes. These leak blood or fluid may lead to progressive vision loss and blindness. By binding to both of VEGF and FGF, RC28 can block angiogenesis factors in both VEGF and FGF families, thereby effectively slowing down the growth of new blood vessels and ultimately slowing the disease progression.

Dr. Fang Jianmin, R&D Head of RemeGen, is the inventor of conbercept, an anti-VEGF fusion protein and the first domestically-developed biologic drug approved for wet AMD in China. Conbercept achieved RMB1.32bn in sales in 2021. The successful experiences of Dr. Fang in developing conbercept will facilitate the clinical development and commercialization of RC28.

RemeGen is evaluating, and plans to evaluate, RC28 in clinical studies for several ophthalmic diseases, including wet AMD, DME and DR. Currently, the Company is conducting an open-label, single-arm Ph1/2 dose-expansion trial to evaluate RC28 in the patients with wet AMD with patient enrollment completed in Feb 2021. RemeGen is preparing to start a Ph3 study of RC28 for wet AMD. In addition, a Ph2 trial in DME and a Ph2 trial in DR are currently ongoing in China.

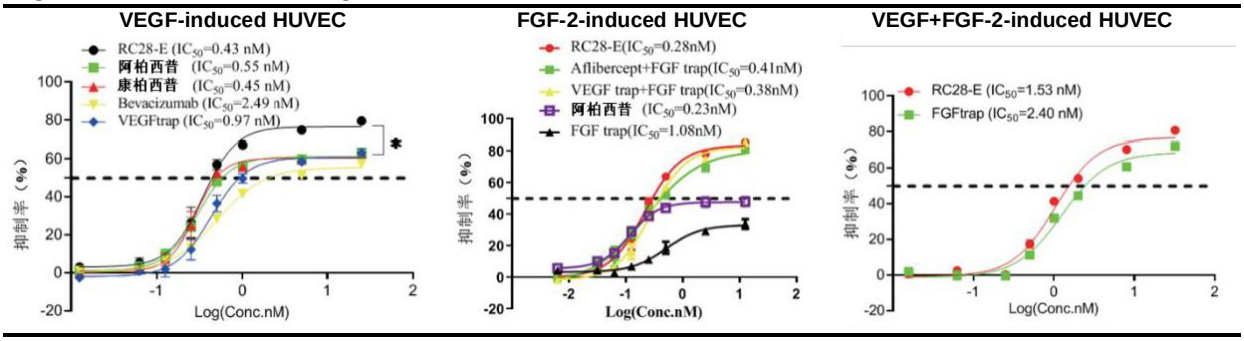
Promising efficacy demonstrated in pre-clinical studies

The dual-targeting mechanism of RC28 leads to effective inhibition of blood vessel growth. A major challenge faced by single-target anti-VEGF therapies is the upregulated expression of other pro-angiogenic factors, such as FGF-2, when the activation of VEGF is inhibited. With the dual-targeting mechanism, RC28 can block angiogenesis factors at both VEGF and FGF families simultaneously and therefore can inhibit the abnormal vessel growth more effectively.

RC28 potentially allows a less frequent dosing schedule due to a long half-time PK profile. RC28 is constructed as the extracellular domains of VEGFR1, VEGFR2, and FGFR1 fused with human IgG1 to achieve dual-blockade of VEGF and FGF, and to extend the half-life of the drug in serum. RC28 largely reduced neo-vascular nucleus number at the dosage of 0.5μg/eye as compared to other VEGF antagonists at the same dosage. Furthermore, as observed in a monkey choroidal neovascularization (CNV) model, traces of RC28 were detected as dispersing from eyeballs to the liver after 20 days, and a prolonged half-time PK profile was exhibited. Given the strong efficacy at low dose-level and an extended half-life, RC28 can potentially allow for a less frequent dosing profile and therefore reduce discomfort of the patients which is important as the drug is directly injected into the eyes.

RC28 demonstrated strong inhibition potential compared to other VEGF or FGF antagonists as observed in vitro. RC28 is able to inhibit proliferation of human umbilical vein endothelial cells (HUVEC) induced by either or both of VEGF and FGF-2 in a dose-dependent manner. While the anti-proliferative effect of RC28 induced by single factor binding was similar to that of VEGF or FGF antagonists as measured by IC50, the maximum relative inhibition rate of RC28 was higher than other antagonists. In particular, RC28's ability to block double factors (VEGF+FGF-2)-induced HUVEC proliferation was significantly stronger than other antagonists.

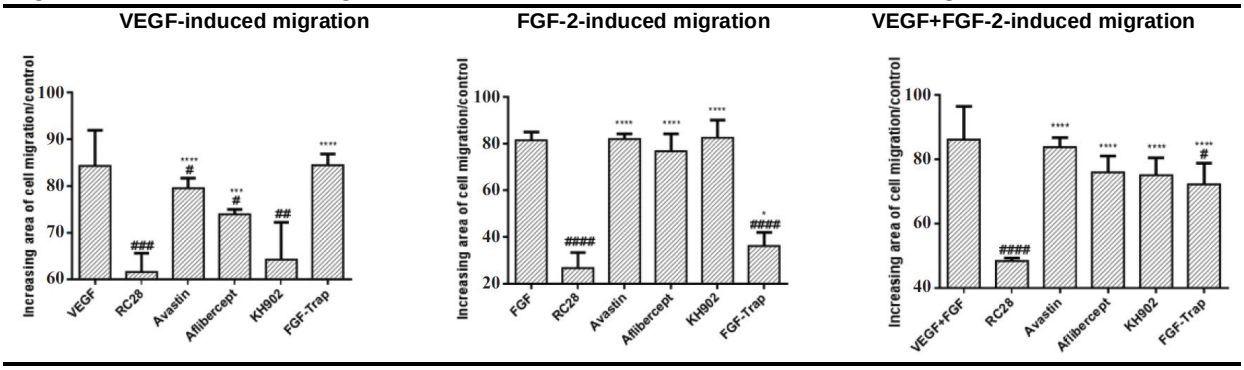
Figure 36: RC28 has stronger inhibition to VEGF and/or FGF-2 induced HUVEC



Source: Company data, CMBIGM

RC28 also exhibited stronger inhibition effects on VEGF-induced migration, compared to Avastin (bevacizumab) (P<0.001) and aflibercept (P<0.005) at the same concentration (1nM), and on FGF-2-induced migration compared to FGF-Trap (P<0.05). RC28 resulted in significant inhibition effects on VEGF+FGF-2-induced migration at the half concentration (1nM) among all the tested antagonists (2nM) (P<0.001).

Figure 37: RC28 has stronger inhibition to VEGF and/or FGF-2 induced migration



Source: Company data, CMBIGM

RC28 to compete with multiple existing biological therapeis

Wet AMD is a chronic eye disorder characterized by the abnormal growth of blood vessels and leakage of fluid and blood into the macula. Wet AMD and dry AMD are two types of age-related macular degeneration. While dry AMD leads to a gradual loss of vision, wet AMD, accounting for 10% of total AMD cases, leads to sudden and severe vision loss. In addition, a fraction of dry AMD patients eventually evolve into wet AMD. The most severe form of wet AMD is the leading cause of blindness among older Chinese and Americans.

DME is a complication of diabetes caused by fluid accumulation in the macula, or central portion of the eye, that leads the macula to swell. While diabetes is becoming increasingly common globally, its prevalence has been growing faster in China than the rest of the world in recent years and especially in the younger generation.

Several medicines have been approved in China and across the globe for the treatment of wet AMD and DME, including ranibizumab, aflibercept, conbercept, brolucizumab, etc. RC28 faces competitions from these marketed medicines. Additionally, bevacizumab was originally developed to treat various types of cancers, while it is commonly used "off-label" in patients with wet AMD and DME as a less expensive alternative. Moreover, with the patents of aflibercept to be expired in the coming years, several aflibercept biosimilars are under development. For instance, the aflibercept biosimilar developed by Qilu Pharmaceutical was filed for approval in Apr 2022 in China and three additional aflibercept biosimilar candidates are at clinical stage in China.

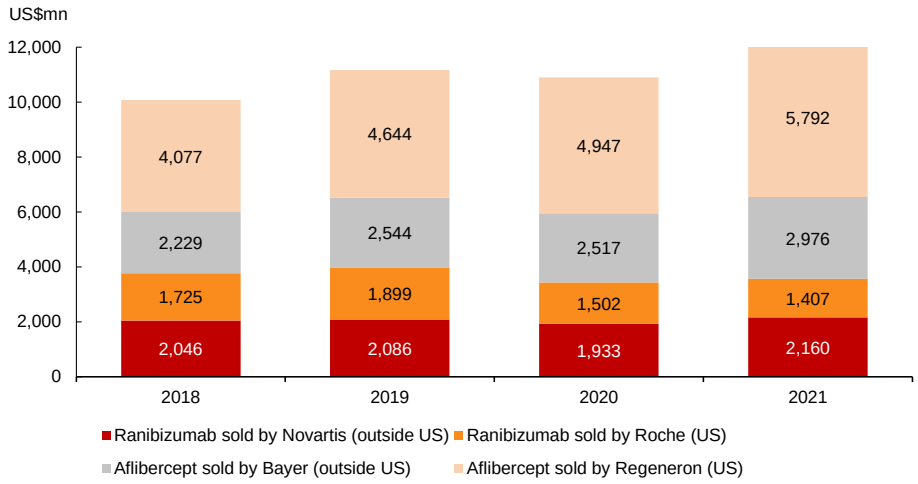
We see the large commercial potential of wAMD, DME and other eye diseases, despite fierce market competition. Regeneron and Bayer recorded a combined US$8.8bn sales from aflibercept in 2021 (+18% YoY). For ranibizumab, Novartis and Roche generated US$3.6bn (+4% YoY) revenue from the globe in 2021. The domestic VEGFR-Fc fusion protein conbercept recorded RMB1.3bn sales in China in 2021 (+13% YoY). The multiple billion sales of the marketed VEGF drugs indicate the enormous market size of eye disease therapies. With potentially better clinical profile, we expect RC28 to gain market share from the global eye disease market upon its approval.

Figure 38: Marketed medicines for w-AMD and DME

Drug	Company	Target	Major marketed regions	Initial China approval date	China NRDL period	Annual cost	Indications	Dose (post-initial period)	Price
Ranibizumab	Novartis, Roche	VEGF-A	China, US	2012.01	2022.01-2023.12	RMB 47,400	w-AMD, DME, etc.	0.5mg, Q4W	RMB 3,950/ 1.65mg
Aflibercept	Bayer, Regeneron	VEGFR	China, US, EU	2017.12	2022.01-2023.12	RMB 26,723	w-AMD, DME, etc.	2mg, Q8W*	RMB 4,100/ 4mg
Conbercept	Kanghong	VEGFR	China	2013.11	2022.01-2023.12	RMB 15,003	w-AMD, DME, etc.	0.5mg, Q12W	RMB 3,453/ 10mg
Brolucizumab	Apexigen, Alcon, Novartis	VEGF-A	US, EU	-	-	-	w-AMD, DME	-	-
Faricimab	Roche	VEGF-A / Ang2	US, EU, Japan	China BLA accepted in 2022.08	-	-	w-AMD, DME	-	-
Bevacizumab & biosimilars	Roche and biosimilar companies	VEGF-A	Worldwide	-	Included	-	off-label	-	-

Source: PharmCube, CMBIGM. Notes: longer dosing interval is preferred because of the discomfort of intravitreal injection. Aflibercept 8mg 12-week and 16-week dosing regimens achieved non-inferiority in Sep 2022 compared to the 8-week dosing regimen (*link*).

Figure 39: Sales of major VEGF-A biologics for eye diseases



Source: PuarmCube, CMBIGM

Financial Analysis

Produce sales to ramp up fast

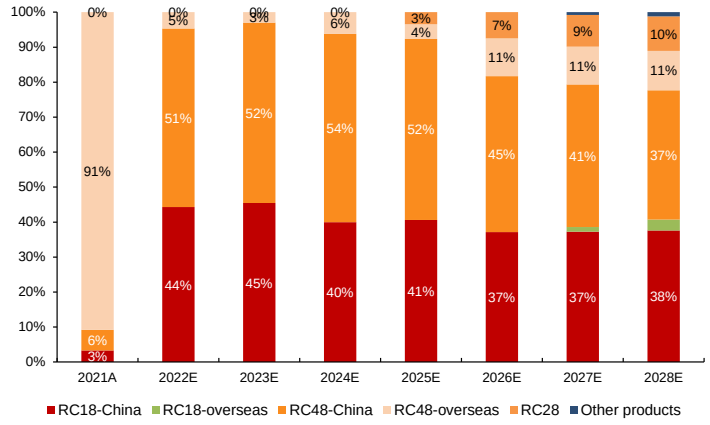
We expect RemeGen's product sales to ramp up quickly and RC18 and RC48 will be the major revenue drivers of the Company. We estimate RemeGen's total risk-adjusted revenue of RMB860mn/ RMB1,344mn/ RMB2,189mn in FY22E/ 23E/ 24E, respectively.

Figure 40: Risk-adjusted revenue forecasts

Revenue	2021A	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Sales of goods	**131**	**820**	**1,304**	**2,053**	**3,111**	**4,108**	**5,807**	**7,291**
YoY		*524%*	*59%*	*57%*	*52%*	*32%*	*41%*	*26%*
RC18-China	47	381	611	876	1,319	1,712	2,463	3,203
YoY		*705%*	*61%*	*43%*	*51%*	*30%*	*44%*	*30%*
RC48-China	84	439	693	1,177	1,680	2,051	2,693	3,149
YoY		*423%*	*58%*	*70%*	*43%*	*22%*	*31%*	*17%*
RC28					111	344	601	839
YoY						*209%*	*75%*	*40%*
Other products							50	100
YoY								*100%*
Licensing revenue & service income	**1,293**	**40**	**40**	**136**	**136**	**498**	**803**	**1,220**
YoY		*-97%*	*0%*	*241%*	*0%*	*265%*	*61%*	*52%*
RC18-overseas							89	261
YoY								*194%*
RC48-overseas	1,291	40	40	136	136	498	714	959
YoY			*0%*	*241%*	*0%*	*265%*	*43%*	*34%*
Total	**1,424**	**860**	**1,344**	**2,189**	**3,247**	**4,606**	**6,610**	**8,511**
YoY		*-40%*	*56%*	*63%*	*48%*	*42%*	*44%*	*29%*

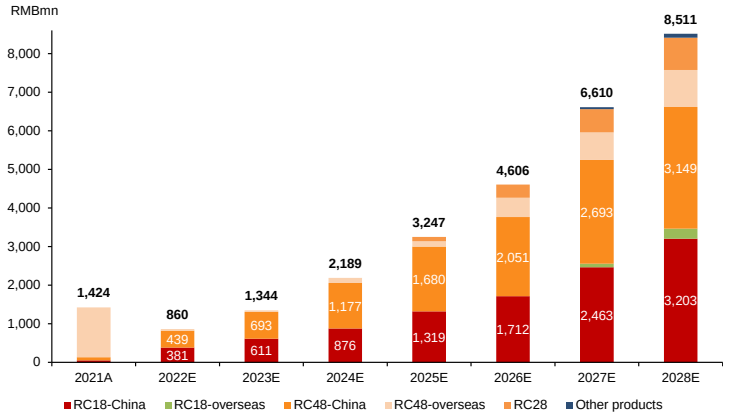
Source: Company data, CMBIGM estimates

Figure 41: Risk-adjusted revenue breakdown



Source: Company data, CMBIGM estimates

Figure 42: Risk-adjusted revenue forecasts



Source: Company data, CMBIGM estimates

RemeGen recorded net loss of RMB270mn/ RMB430mn/ RMB698mn in FY18A/ 19A/ 20A. In 2021, the Company recorded net profit of RMB276mn, mainly due to the RMB1.29bn upfront payment from Seagen. We expect the Company to incur net losses of RMB933mn/ RMB956mn/ RMB776mn in FY22E/ 23E/ 24E, and to turn profitable in FY26E, while the potential global out-license of RC18 could be a major variable of the breakeven timeline.

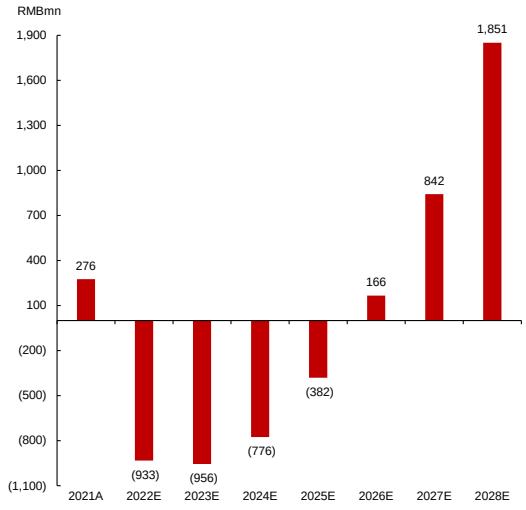
Figure 43: P&L forecasts

YE Dec 31 (RMB mn)	2021A	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Revenue	**1,424**	**860**	**1,344**	**2,189**	**3,247**	**4,606**	**6,610**	**8,511**
YoY								
Cost of sales	(67)	(279)	(313)	(452)	(653)	(842)	(1,161)	(1,422)
% of revenue	*5%*	*32%*	*23%*	*21%*	*20%*	*18%*	*18%*	*17%*
Gross profit	**1,357**	**581**	**1,031**	**1,738**	**2,594**	**3,764**	**5,448**	**7,090**
GPM	*95%*	*68%*	*77%*	*79%*	*80%*	*82%*	*82%*	*83%*

Selling and distribution expenses	(263)	(481)	(766)	(1,138)	(1,526)	(1,934)	(2,446)	(2,724)
% of revenue	*18%*	*56%*	*57%*	*52%*	*47%*	*42%*	*37%*	*32%*
Administrative expenses	(220)	(224)	(309)	(438)	(584)	(737)	(925)	(1,064)
% of revenue	*15%*	*26%*	*23%*	*20%*	*18%*	*16%*	*14%*	*13%*
R&D expenses	(711)	(900)	(1,000)	(1,000)	(900)	(921)	(1,124)	(1,192)
% of revenue	*50%*	*105%*	*74%*	*46%*	*28%*	*20%*	*17%*	*14%*
Finance costs	(5)	(4)	(4)	(14)	(34)	(44)	(34)	(14)
Others	13	35	0	0	39	20	99	119
Profit/(loss) before tax	**276**	**(933)**	**(956)**	**(776)**	**(382)**	**196**	**991**	**2,178**
% of revenue	*19%*	*-108%*	*-71%*	*-35%*	*-12%*	*4%*	*15%*	*26%*
Income tax benefit (expense)	0	0	0	0	0	(29)	(149)	(327)
Profit/(loss) for the year	**276**	**(933)**	**(956)**	**(776)**	**(382)**	**166**	**842**	**1,851**
Non-controlling interests	0	0	0	0	0	0	0	0
Attributable Net Profit/(loss)	**276**	**(933)**	**(956)**	**(776)**	**(382)**	**166**	**842**	**1,851**
NMP	*19%*	*-108%*	*-71%*	*-35%*	*-12%*	*4%*	*13%*	*22%*

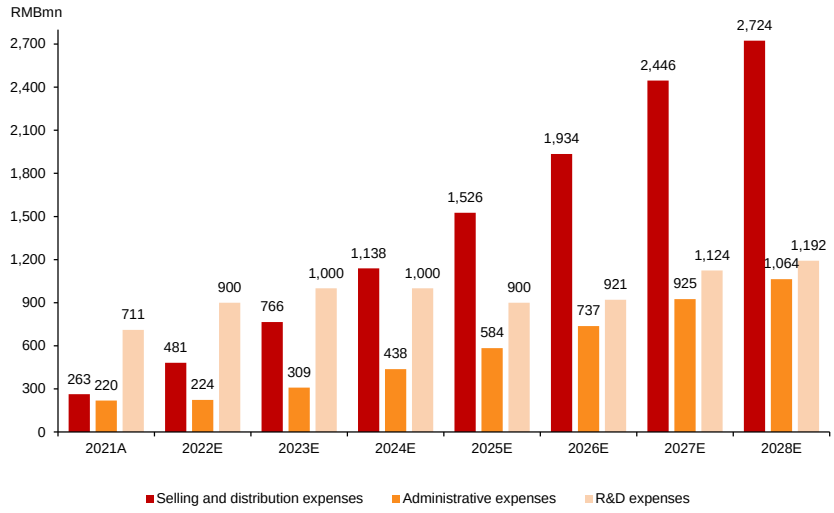
Source: Company data, CMBIGM estimates

Figure 44: Net profit (loss) forecasts



Source: Company data, CMBIGM estimates

Figure 45: Operating expenses forecasts



Source: Company data, CMBIGM estimates

Valuation

Initiate at BUY with TP of HK$79.13

We derive our target price of HK$79.13 based on a DCF valuation (WACC: 10.25%, terminal growth rate: 3.0%).

Figure 46: Risk-adjusted DCF valuation

DCF Valuation (RMB mn)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	**(929)**	**(951)**	**(762)**	**(347)**	**240**	**1,025**	**2,192**	**3,655**	**5,557**	**6,773**	**7,935**	**7,977**	**7,617**	**7,675**
Tax rate	*0%*	*0%*	*0%*	*0%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
EBIT*(1-tax rate)	(929)	(951)	(762)	(347)	204	871	1,863	3,107	4,724	5,757	6,745	6,780	6,475	6,524
+ D&A	228	260	289	301	290	279	270	261	253	246	239	232	226	221
- Change in working capital	(13)	(75)	(131)	(159)	(204)	(296)	(275)	(308)	(350)	(273)	(253)	26	143	8
- Capex	(800)	(600)	(600)	(400)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)
FCFF	**(1,514)**	**(1,367)**	**(1,204)**	**(606)**	**190**	**754**	**1,758**	**2,961**	**4,526**	**5,629**	**6,630**	**6,938**	**6,744**	**6,653**
Terminal value														**94,546**
FCF + Terminal value	**(1,514)**	**(1,367)**	**(1,204)**	**(606)**	**190**	**754**	**1,758**	**2,961**	**4,526**	**5,629**	**6,630**	**6,938**	**6,744**	**101,199**

PV of enterprise (RMB mn)	35,117
Net debt (RMB mn)	(2,785)
Equity value (RMB mn)	**37,901**
No. of shares (mn)	544
DCF per shares (RMB)	**69.64**
DCF per share (HK$)	**79.13**
Terminal growth rate	**3.0%**
WACC	**10.25%**
Cost of Equity	13.0%
Cost of Debt	4.5%
Equity Beta	1.0
Risk Free Rate	3.0%
Market Risk Premium	10.0%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%

Source: CMBIGM estimates

Figure 47: Sensitivity analysis (HK$)

	WACC				
Terminal growth rate	**9.25%**	**9.75%**	**10.25%**	**10.75%**	**11.25%**
4.0%	111.57	98.57	87.76	78.66	70.91
3.5%	104.27	92.80	83.13	74.90	67.81
3.0%	98.15	87.88	**79.13**	71.61	65.09
2.5%	92.93	83.64	75.65	68.73	62.68
2.0%	88.43	79.95	72.60	66.18	60.54

Source: CMBIGM estimates

Financial Statements

INCOME STATEMENT	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Revenue	**0**	**0**	**1,424**	**860**	**1,344**	**2,189**
Cost of goods sold	0	0	(67)	(279)	(313)	(452)
Gross profit	**0**	**0**	**1,357**	**581**	**1,031**	**1,738**
Operating expenses	**(430)**	**(698)**	**(1,080)**	**(1,514)**	**(1,987)**	**(2,514)**
Selling expense	(1)	(24)	(263)	(481)	(766)	(1,138)
Admin expense	(68)	(218)	(220)	(224)	(309)	(438)
R&D expense	(352)	(466)	(711)	(900)	(1,000)	(1,000)
Others	(9)	10	113	91	89	62
Operating profit	**(386)**	**(669)**	**282**	**(929)**	**(951)**	**(762)**
Interest income	(44)	(29)	(5)	(4)	(4)	(14)
Pre-tax profit	**(430)**	**(698)**	**276**	**(933)**	**(956)**	**(776)**
Income tax	0	0	0	0	0	0
Minority interest	0	0	0	0	0	0
Net profit	**(430)**	**(698)**	**276**	**(933)**	**(956)**	**(776)**

BALANCE SHEET	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Current assets	**138**	**2,977**	**2,300**	**3,435**	**2,120**	**1,595**
Cash & equivalents	35	2,769	1,757	2,809	1,395	633
Account receivables	1	0	7	141	221	360
Inventories	31	66	280	229	249	346
Financial assets at FVTPL	0	0	0	0	0	0
Other current assets	71	143	256	256	256	256
Non-current assets	**552**	**1,140**	**1,859**	**2,493**	**2,896**	**3,269**
PP&E	460	803	1,578	2,202	2,594	2,957
Right-of-use assets	11	138	149	159	169	179
Intangibles	2	5	13	13	13	13
Financial assets at FVTPL	11	13	12	12	12	12
Other non-current assets	67	182	108	108	108	108
Total assets	**689**	**4,118**	**4,159**	**5,928**	**5,016**	**4,864**
Current liabilities	**857**	**431**	**616**	**686**	**710**	**816**
Short-term borrowings	60	108	0	0	0	0
Account payables	68	63	159	229	253	359
Other current liabilities	728	218	405	405	405	405
Lease liabilities	2	43	52	52	52	52
Non-current liabilities	**64**	**92**	**96**	**96**	**96**	**596**
Long-term borrowings	0	0	0	0	0	500
Deferred income	61	44	46	46	46	46
Other non-current liabilities	4	47	51	51	51	51
Total liabilities	**921**	**523**	**713**	**783**	**807**	**1,412**
Share capital	0	490	490	490	490	490
Other reserves	(232)	3,105	2,957	4,656	3,719	2,962
Total shareholders equity	**(232)**	**3,595**	**3,446**	**5,145**	**4,209**	**3,452**
Total equity and liabilities	**689**	**4,118**	**4,159**	**5,928**	**5,016**	**4,864**

CASH FLOW	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Operating						
Profit before taxation	**(430)**	**(698)**	**276**	**(933)**	**(956)**	**(776)**
Depreciation & amortization	40	49	65	176	208	237
Tax paid	0	0	0	0	0	0
Change in working capital	56	(117)	(168)	(13)	(75)	(131)
Others	52	105	90	75	75	85
Net cash from operations	**(283)**	**(660)**	**264**	**(694)**	**(748)**	**(585)**
Investing						
Capital expenditure	(65)	(443)	(615)	(800)	(600)	(600)
Acquisition of subsidiaries/ investments	0	(102)	0	0	0	0
Net proceeds from disposal of short-term investments	0	102	0	0	0	0
Others	(30)	(36)	(23)	(62)	(62)	(62)
Net cash from investing	**(95)**	**(479)**	**(638)**	**(862)**	**(662)**	**(662)**
Financing						
Dividend paid	0	0	0	0	0	0
Net borrowings	408	(498)	(108)	0	0	500
Proceeds from share issues	90	4,508	(14)	2,612	0	0
Share repurchases	0	0	(449)	0	0	0
Others	(91)	(105)	(55)	(4)	(4)	(14)
Net cash from financing	**407**	**3,904**	**(627)**	**2,608**	**(4)**	**486**
Net change in cash						
Cash at the beginning of the year	5	35	2,769	1,757	2,809	1,395
Exchange difference	0	(31)	(10)	0	0	0
Cash at the end of the year	**35**	**2,769**	**1,757**	**2,809**	**1,395**	**633**

GROWTH	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Revenue	na	na	na	(39.6%)	56.4%	62.9%
Gross profit	na	na	na	(57.2%)	77.5%	68.5%

PROFITABILITY	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Gross profit margin	na	na	95.3%	67.6%	76.7%	79.4%
Operating margin	na	na	19.8%	(108.0%)	(70.8%)	(34.8%)
Return on equity (ROE)	na	(41.5%)	7.8%	(21.7%)	(20.4%)	(20.3%)

GEARING/LIQUIDITY/ACTIVITIES	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Current ratio (x)	0.2	6.9	3.7	5.0	3.0	2.0

VALUATION	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
P/E	na	na	152.8	na	na	na

Source: Company data, CMBIGM estimates. Note: The calculation of net cash includes financial assets.

Investment Risks

1) Failure of clinical development or regulatory approvals of drug candidates.

2) Intense competition of approved products both in China and overseas markets.

Appendix: Company Profile

Figure 48: Major shareholders (as of 30 Sep 2022)

Shareholder	% of stake
HKSCC NOMINEES LIMITED	34.83%
Yantai Rongda	18.81%
FANG JIANMIN	4.82%
SDIC Venture Capital	4.54%
PAG Growth Prosperity Holding	2.77%
Shenzhen Capital Group	2.35%

Source: Company financial report, CMBIGM

Figure 49: Management profile

Name	Position
Wang Weidong	Chairman, Executive Director
Dr. Fang Jianmin	CEO, CSO, Executive Officer
Dr. Fu Daotian	President
Dr. He Ruyi	Executive Officer, CMO, Head of Clinical Research
Jason Li	CFO, Joint Company Secretary
Wu Jingping	Vice President, Commercial Head for Autoimmune Business Unit
Tang Gang	Vice President, Commercial Head for Oncology Business Unit
Marie Zhu	CTO
Kaisheng Huang	CQO

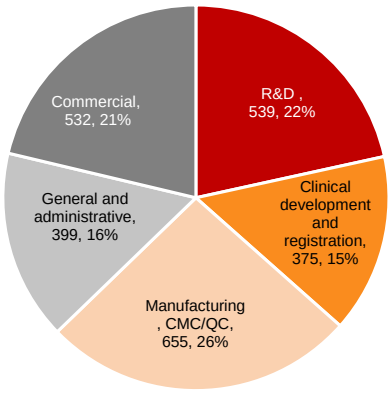
Source: Company data, CMBIGM

Figure 50: Employee structure

Function	# of staff	% of Total
R&D	539	11%
Clinical development and registration	375	42%
Manufacturing, CMC/QC	655	37%
General and administrative	399	10%
Commercial	532	21%
Total	**2,500**	**100%**

Source: Company report (as of Jun 2022), CMBIGM. Notes: as of 30 Sep 2022, the Commercial team has been expanded to around 960 employees.

Figure 51: Employee number breakdown



Source: Company annual report (as of Jun 2022), CMBIGM

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Address: 45/F, Champion Tower, 3 Garden Road, Hong Kong, Tel: (852) 3900 0888 Fax: (852) 3900 0800

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