Recbio Technology (2179 HK)

Leading innovative vaccine player with rich blockbuster pipelines

- **Recbio is a leading innovative vaccine company with rich pipeline assets.** Recbio has assembled a fruitful pipeline with 12 innovative vaccines, covered three of the top five global best-selling vaccines in 2020. The Core Product, REC603, is a recombinant HPV 9-valent vaccine candidate at Ph III trial. ReCOV is a recombinant COVID-19 vaccine adopting BFA03, which has initiated Ph II/III trial in Philippines. REC610 is an IND-enabling recombinant shingles vaccine candidate, with expected BLA submission in 2024E.

- **Comprehensive HPV franchise with early mover advantages.** Recbio has built a comprehensive HPV franchise with five highly differentiated assets, which aims to target different countries and populations. REC603 is a recombinant HPV 9-valent vaccine currently in Ph III study in China, aiming to file BLA by 2025E. Recbio is advancing clinical trials of two recombinant bivalent HPV vaccines, namely REC601 and REC602. Moreover, Recbio is employing a self-developed novel adjuvant benchmarking Adjuvant System 04 ("AS04") to develop two HPV vaccines, REC604a (HPV 4-valent vaccine) and REC604b (HPV 9-valent vaccine), which are designed to adopt fewer dose regimen compared with existing HPV vaccines.

- **Advanced technology platforms for developing best-in-class vaccines.** Recbio's technology platforms form a solid trifecta, creating synergies among the design and optimization of antigens, the development and production of adjuvants and the identification of the optimal combinations of antigens and adjuvants. Recbio is one of the few companies with ability to develop adjuvants, benchmarking all FDA-approved novel adjuvants (AS01, AS03, AS04, CpG1018 and MF59), which enables Rebio to develop new generation vaccines without relying on any particular adjuvant supplier.

- **Initiate at BUY with TP of HK$38.79.** We expect ReCOV to file EUA and contribute sales from 2022E, and forecast the Company to realize risk-adjusted revenue of RMB155mn/ RMB1,789mn/ RMB1,474mn in FY22E/ 23E/ 24E. To factor in the risks of vaccine development, we apply different probability of success (PoS) to the sales forecasts of pipeline assets. Recbio relies on future cash flows of vaccine sales. We derive TP of HK$38.79 based on a 14-year DCF model (WACC: 12.5%, terminal growth rate: 2.0%).

- **Risks:** Competition; Failures in clinical development activities.

Earnings Summary

(YE 31 Dec)	FY20A	FY21A	FY22E	FY23E	FY24E
Revenue (RMB mn)	0	0	155	1,789	1,474
YoY growth (%)	N/A	N/A	N/A	1052%	-18%
Net loss (RMB mn)	-179	-658	-752	-260	-284
EPS (RMB)	N/A	N/A	-1.56	-0.54	-0.59
R&D expenses (RMB mn)	-131	-473	-650	-600	-500
SG&A expenses (RMB mn)	-18	-147	-200	-788	-690
Capex (RMB mn)	-300	-300	-200	-200	-200
Current ratio (x)	12	9	39	6	6

Source: Company data, Bloomberg, CMBIGM estimates

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BUY (Initiation)

Target Price	**HK$38.79**
Up/Downside	**+59.63%**
Current Price	**HK$24.30**

China Healthcare Sector

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Stock Data

Mkt Cap (HK$mn)	11,736
Avg 3mths t/o (HK$mn)	N/A
52w High/Low (HK$)	28.30/22.00
Total Issued Shares (mn)	94

Source: Bloomberg

Shareholding Structure

Management	17.30%
Legend Capital	9.97%
Shanghai Chaorui	7.80%
LYFE Capital	7.20%
Oriental Fortune Capital	6.95%
Fer-Capital Investment	5.68%
Others	45.10%

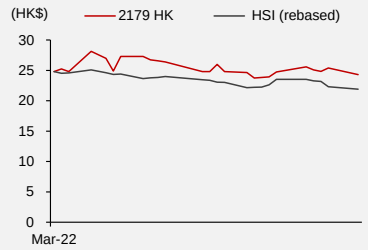
Source: Company data

Share Performance

	Absolute	Relative
1-mth	-7.0%	1.7%
3-mth	N/A	N/A
6-mth	N/A	N/A

Source: Bloomberg

12-mth Price Performance



Source: Bloomberg

Auditor: Ernst & Young

Web-site:
https://en.recbio.cn/about.html

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Investment Thesis

Founded in 2012, Recbio is an innovative vaccine company with a high-value vaccine portfolio. Leveraging in-depth technological accumulation, Recbio aims to further seize the massive growth in China's innovative vaccine market.

Rich innovative vaccine portforlio

Recbio has assembled a fruitful pipeline with 12 innovative vaccines, covered three of the top five global best-selling vaccines in 2020. Recbio's Core Product, REC603, is currently under Phase III clinical trial in China. With BLA application expected to be submitted to the NMPA by 2025E, REC603 has the potential to become one of the first approved domestic 9-valent HPV vaccine in China. ReCOV is a near-commercial adjuvanted recombinant COVID-19 vaccine, which is currently under Ph II/III trial in Philippines. Recbio has yet finished with subject enrollment and two-shot dosing of ReCOV for the Ph II trial. Moreover, the Company has recently received approval for Ph II/III trial in the UAE to evaluate ReCOV as a heterologous booster in adult subjects, as well as received clinical trial approval from the NMPA. REC610 is an IND-enabling recombinant shingles vaccine candidate, with expected IND submission in 2022E, and BLA submission in 2024E. Recbio's pipelines also cover large disease areas such as tuberculosis (TB), flu, and hand, foot and mouth disease (HFMD).

To further boost its vaccine franchise, the Company expanded into mRNA field. On Aug 28, 2021, Recbio entered into a shareholder collaboration agreement with Shenzhen Ruiji (深圳市瑞吉) and Wuhan Aiweige (武汉艾维格), to jointly establish Wuhan Ruikeji (武汉瑞科吉) which will be owned as to 55% by Recbio. The Wuhan JV will mainly focus on the R&D and commercialization of mRNA vaccines with its initial focus on SARS-CoV-2, shingles and influenza. Recbio also plans to expand its pipeline covering therapeutic vaccines for the treatment of cancers and latent infections. As first step of this collaboration, the Company is developing a pre-clinical stage Omicron-targeted mRNA COVID-19 vaccine candidate R520A. The IND application of this vaccine is expected to be submitted to the NMPA or other competent authorities overseas in 1H22.

Comprehensive HPV franchise with significant early mover advantages

Recbio has built one of the most comprehensive HPV franchises worldwide with five highly differentiated assets. The Company is currently in the process of conducting Ph III clinical trial in China for its core product REC603, which has completed 12,500 subject enrollments for the potency tests. The three-shot dosing is planned to be completed in 1H22, and to BLA application is expected to be submitted by 2025E. Targeting different countries and populations, the Company is also advancing clinical trials of two recombinant bivalent vaccines, REC601 (16/18) and REC602 (6/11). Employing a self-developed novel adjuvant benchmarking GSK's Adjuvant System 04 ("AS04"), Recbio is also developing REC604a (HPV 4-valent vaccine) and REC604b (HPV 9-valent vaccine) with a fewer dose regimen, in which the novel-adjuvanted 9-valent vaccine REC604b could possibly substitute the current available products. Recbio plans to submit the IND application to the NMPA for REC604a in 2022E and REC604b in 2023E.

Advanced technology platforms for developing best-in-class vaccines

Recbio's technology platforms form a solid trifecta, creating synergies among the design and optimization of antigens, the development and production of adjuvants and the identification of the optimal combinations of antigens and adjuvants. Leveraging its advanced technology platforms, Recbio is qualified with developing best-in-class vaccines. Exploring the opportunity to develop new immune potentiators, RecBio is also committed to continuously upgrading its technology platforms.

Recbio is one of the few companies with ability to independently develop and mass produce novel adjuvants benchmarking all FDA-approved novel adjuvants (AS01, AS03, AS04, CpG1018 and MF59). Adjuvants are compounds that enhances the immune response in vaccines. Application of novel

adjuvants can also reduce amount of antigen used, as well as lessen doses of vaccine shots. Novel adjuvant is manufactured through complex processes and quality control standards, so mass production is difficult. Leverage on its novel adjuvant platform, Recbio is able to discover and apply new adjuvants in new generation vaccine candidates without relying on any particular adjuvant supplier, thus may achieve the R&D and commercialization milestones of key product pipelines.

Recbio utilizes a structure-based immunogen design approach to provide antigen optimization solutions for innovative vaccines. In addition, the Company's protein engineering platform serves as a comprehensive toolbox to apply the most suitable expression systems in vaccine development. Recbio's protein engineering platform can elicit immune response in different expression systems (including E.coli, H. polymorpha, baculovirus, and CHO cell). Recbio's immunological evaluation platform provides the best alliance of optimal antigen and novel adjuvant. To elucidate the mechanism of immune protection for infectious diseases, immunological evaluation is a critical step in innovative vaccine discovery and development. With this platform, the Company is able to select the optimal antigen and adjuvant combination and in turn improve immunogenicity profile of its vaccine candidates.

Well prepared for commercialization

Recbio is led by a seasoned management and scientific team. The Company's R&D team was led by CEO, Dr. Liu Yong and vice president Dr. Chen Jianping, who have over 20 years of experience in vaccine development. Recbio's management also consists of industry-leading scientists and industry-leading experts who are familiar with bringing vaccine candidates from concept to market. Since 2021, Recbio has announced execution of several industry experts as management, including CMO Dr. Zhang Jianhui, CSO Dr. Hong Kunxue, CFO Ms. Chen Qingqing, and CBO Ms. Feng Yanfei.

Having started with constructing manufacturing capabilities, Recbio has completed with constructing GMP-standard manufacturing facility for ReCOV in 2021, which has an annual capacity of 300mn doses. The site has obtained a drug manufacturing license issued by Jiangsu Medical Products Administration, and can also be used for the manufacturing of recombinant shingles vaccine. Recbio is also constructing HPV vaccine manufacturing facility in Taizhou, Jiangsu, the first phase of which will be completed by the end of 2022. The manufacturing facility has a potential annual capacity of 5mn doses HPV 9-valent vaccines or 30mn doses HPV bivalent vaccines.

Recbio's commercialization will primarily focus on China market where the Company intends to build its own sales and marketing team and collaborate with other biotech companies with robust domestic sales network. Recbio is also gradually stepping into overseas markets. For developing countries, the Company's strategy is to cooperate with local pharmaceutical giants and major NGOs in regions such as Southeast Asia, South Asia, South America, and Africa through technology transfer and joint-ventures. For developed countries, Recbio plans to enter into strategic partnership on R&D and marketing with global-leading pharmaceutical companies in Europe and the US.

Net profit to breakeven in 2025E

We expect Recbio to file EUA of its first product, ReCOV, in 2022E. We forecast Recbio to submit BLA applications of its HPV vaccine candidates, REC603, REC601, and REC602, to the NMPA by 2025E.

We expect Recbio's vaccine sales to start from 2022E and estimate risk-adjusted revenue of RMB155mn/ RMB1,789mn/ RMB1,474mn in FY2022E/ 23E/ 24E. We expect Recbio to continue incur net losses of RMB752mn / RMB260mn/ RMB284mn in FY22E/ 23E/ 24E.

Initiate at BUY with TP of HK$38.79

As a pre-revenue company, Recbio relies on future cash flows of vaccine sales. We derive our target price of HK$38.79 based on a 14-year DCF model (WACC: 12.5%, terminal growth rate: 2.0%).

Investment risks

1) Facing fierce competition;

2) Failures in clinical development activities;

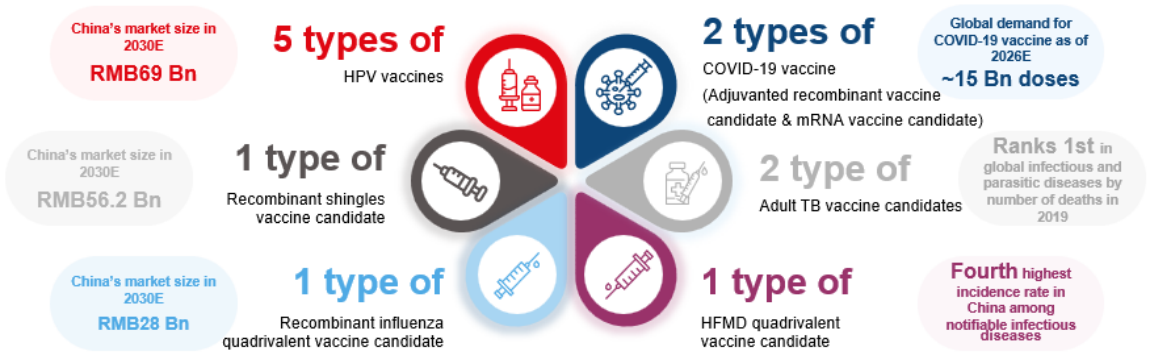
3) Risks relating to government regulation.

Recbio, growing into a leading innovative vaccine company

Recbio is an innovative vaccine company with a high-value vaccine portfolio. Date back to Mar 2011, the Company's first operating entity, Beijing ABZYMO, was founded by Dr. Liu in Beijing. In May 2012, Jiangsu Recbio, as predecessor of Recbio, was established in Taizhou, Jiangsu. The two companies were consolidated under the same corporate group in 2H18.

Recbio has assembled a vaccine portfolio of 12 candidates, covering a broad infectious disease spectrum spanning HPV, COVID-19, shingles, tuberculosis (TB), flu, and hand, foot and mouth disease (HFMD). Recbio's pipeline has been strategically extended to cover five of the ten diseases with greatest burden under the 2019 Global Burden of Diseases assessed by DALYs issued by the WHO and covering disease areas of three of the top five globally best-selling vaccine products in 2020.

Figure 1: Market potential of Recbio's core assets



Source: Company data, CMBIGM

Figure 2: Major milestones of Recbio

Time	Event
2011	Beijing ABZYMO, the first operating entity of Recbio Group, was established.
2012	Jiangsu Rec-Biotechnology Co., Ltd. was established and commenced operation in the Vaccine Engineering Center of China Medical City in Taizhou. In the same year, Jiangsu Recbio entered into a cooperation agreement with Beijing ABZYMO on HPV Preventive Vaccine (Recombinant H. polymorpha).
2015	Recbio submitted IND application for recombinant bivalent HPV-16/18 vaccine (H. polymorpha).
2016	Recbio initiated R&D of recombinant HZ vaccines and establishment of adjuvant platform, as well as submitted IND application for recombinant bivalent HPV-6/11 vaccine (H. polymorpha).
2017	Recbio obtained clinical trial approval for recombinant bivalent HPV-16/18 vaccine (H. polymorpha), as well as submitted IND application for recombinant 9-valent HPV vaccine (H. polymorpha).
2018	Recbio obtained clinical trial approval for recombinant bivalent HPV-6/11 vaccine (H. polymorpha), as well as obtained clinical trial approval for recombinant 9-valent HPV vaccine (H. polymorpha).
2019	Recbio acquired the entire equity interests in Beijing ABZYMO. The Company also initiated Ph I clinical trial for recombinant 9-valent HPV vaccine (Hansenula polymorpha). The Company completed Series A financing.
2020	Recbio commenced construction of HPV vaccine industrialization project manufacturing facilities and COVID-19 vaccine industrialization project. The Company completed Ph I clinical trial for recombinant 9-valent HPV vaccine (H. polymorpha) and initiated Ph I clinical trial for recombinant bivalent HPV-16/18 vaccine (H. polymorpha). The Company also completed Series B financing.
2021	Recbio initiated Ph III clinical trial for recombinant 9-valent HPV vaccine (H. polymorpha), as well as Ph I trial for recombinant COVID-19 vaccine in New Zealand. The Company completed Series B+ financing and Series C financing.
2022	Recbio obtained the clinical trial approval from the Philippines FDA to conduct the global Ph II/III trial for ReCOV.

Source: Company data, CMBIGM

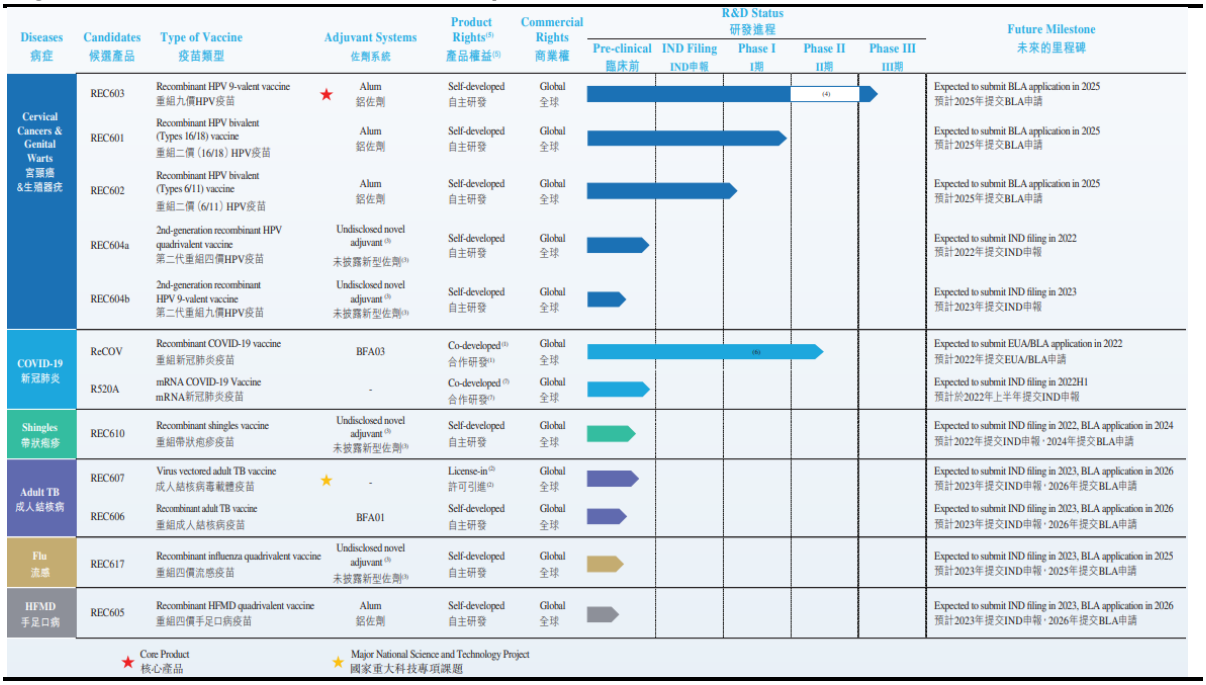
Based on extensive experiences in immunology studies and vaccine development, Recbio has built a solid technology platform with synergy. Leveraging its novel adjuvant platform, RecBio is able to self-produce all FDA-approved novel adjuvants, meaning independency from particular adjuvant supplier. The protein engineering platform serves as a comprehensive toolbox to provide antigen optimization

solutions. Not limited to structure-based immunogen design, its multiple expression systems are to guarantee the selection and application of the most suitable expression systems in vaccine development. Moreover, Recbio also owns a top-notch immunological evaluation platform, as providing the best alliance of optimal antigen and novel adjuvant. In addition to its technology platforms, Recbio's IPD ("Integrated Product Development") system has enhanced its effectiveness of simultaneously developing multiple vaccines.

In the 10 years since its inception, Recbio has assembled a fruitful pipeline with 12 innovative vaccines, featured by its unique HPV vaccine portfolio. In addressing the unmet global needs, Recbio has also built a comprehensive HPV franchise with 5 highly differentiated assets. The Company's core product, REC603, is a recombinant HPV 9-valent vaccine which is currently under Ph III trial in China. Targeting different countries and populations, the Company is advancing clinical trials of two recombinant bivalent vaccines, REC601 and REC602. Employing a self-developed novel adjuvant benchmarking Adjuvant System 04 ("AS04"), Recbio is also developing REC604a and REC604b, with a potential fewer dose regimen. Targeting the emerging COVID-19 market, Recbio also has a near-commercial recombinant COVID-19 vaccine (ReCOV), which is currently in Ph II/III trial in Philippines. Moreover, the Company also has a pre-clinical mRNA COVID-19 vaccine candidate, R520A, under collaboration.

Recbio is currently conducting a Ph III clinical trial for its 9-valent HPV vaccine (REC603) in China, and the Ph II/ III trial for ReCOV in Philippines. We expect Recbio to file BLAs for multiple of its vaccine candidates by end-2025E, including REC603, REC601, ReCOV, REC617, REC610, etc.

Figure 3: Recbio's innovative vaccine portfolio



Source: Company data, CMBIGM
Note:
1) ReCOV was co-developed with Jiangsu Province CDC and Prevention and the Management Committee of Taizhou Medical New & Hi-tech Industrial Development Zone.
2) REC607 was licensed in from Shanghai Public Health Clinical Center, ID Pharma Co., Ltd. and Shanghai Saimo Biotechnology Ltd.
3) "Undisclosed novel adjuvant" refers to a novel self-developed novel adjuvant to be adopted in the vaccine candidate.
4) REC603 obtained the umbrella IND approval from the NMPA in Jul 2018. The umbrella IND approval covers all three phases clinical trials of REC603. Based on communications with the CDE of the NMPA, the NMPA has no objection for Recbio to proceed Ph III clinical trial in China directly. Accordingly, the Company did not conduct any Ph II clinical trial for REC603.
5) All of Recbio's self-developed product candidates, including those developed prior to the acquisition of Beijing ABZYMO in Jan 2019 are co-developed and co-owned by Beijing ABZYMO and Recbio.
6) Recbio obtained the preliminary data for the Ph I New Zealand trial for ReCOV in Oct 2021 and are currently conducting data analysis for such trial. Based on the partial unblinded data from the Ph I trial, Recbio subsequently obtained the IND approval for ReCOV to conduct multicenter Ph II/III trial in Jan 2022.

7) R520A is a mRNA COVID-19 vaccine candidate developed by Wuhan Ruikeji, a joint venture established by Recbio and its business partners for the R&D and commercialization of mRNA vaccines. As of the Jan 11, 2022, Recbio owned 55% of the equity interest in Wuhan Ruikeji.

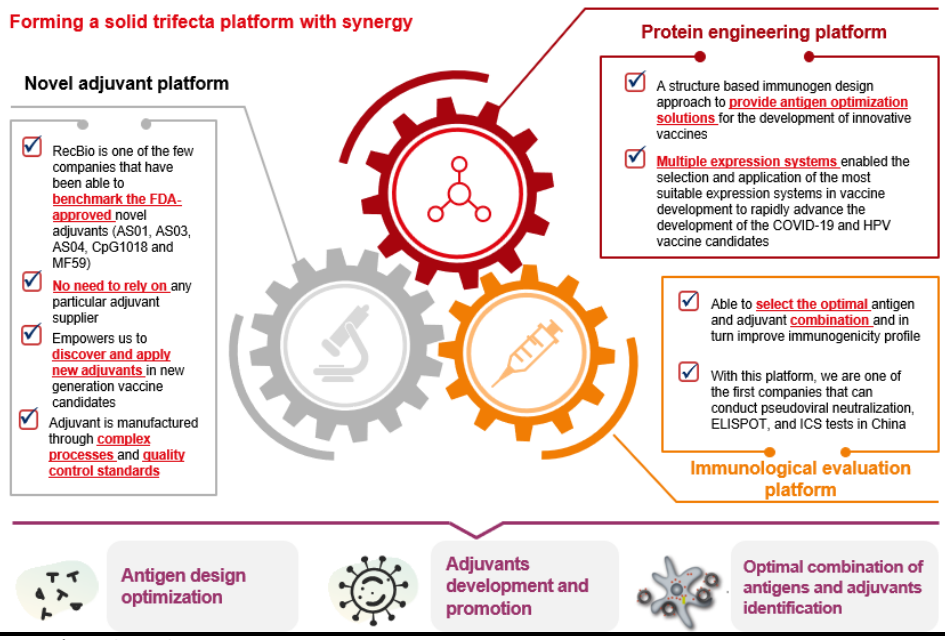
Self-developed platform via cutting-edge technology

Recbio's technology platforms have formed a solid trifecta, creating synergies in the antigen design optimization, the development and production of adjuvants, and the formulation of the optimal antigen-adjuvant combination. Leveraging the comprehensive technology platform, the Company has successfully developed a full suite of innovative vaccine candidates, and is able to continue to discover and develop innovative vaccines.

To further boost its vaccine franchise, the Company expanded into mRNA field. On Aug 28, 2021, Recbio entered into a shareholder collaboration agreement with Shenzhen Ruiji (深圳市瑞吉) and Wuhan Aiweige (武汉艾维格), to jointly establish a company in Wuhan named Wuhan Ruikeji, which will be owned as to 55% by Recbio, 40% by Shenzhen Ruiji and 5% by Wuhan Aiweige. The Wuhan JV will mainly focus on the research and development and commercialization of mRNA vaccines with its initial focus on the application of mRNA technology in SARS-CoV-2, shingles and influenza.

Moreover, Recbio plans to expand its pipeline covering therapeutic vaccines, for instance, those used in conjunction with other immunotherapies (such as PD-1 or siRNA) for the treatment of cancers and latent infections.

Figure 4: Recbio's vaccine development platform



Source: Company data, CMBIGM

Novel adjuvant platform

Adjuvants are used in conjunction with antigens to assist in antigen presentation and enhance immune responses. The conventional type of adjuvant, Alum, has been widely used in human vaccines for decades. Since the 21st century, novel adjuvants were subsequently discovered to enhance vaccine efficacy through stimulate higher and broader immune response. According to F&S, there are currently five novel adjuvants applied in FDA-approved human vaccines, namely AS01, AS03, AS04, CpG1018, and MF59, whose components have been in the public domain for over 20 years.

Recbio's novel adjuvant platform enables development and bulk manufacturing of novel adjuvants. Leveraging its novel adjuvant platform, Recbio has the capability of self-developing novel vaccine adjuvants, benchmarking all of these FDA-approved adjuvants. Moreover, the platform enables Recbio to continue developing innovative adjuvants for next generation vaccine candidates.

Protein engineering platform

Recbio's protein engineering platform utilizes a structure-based immunogen design approach to provide antigen optimization solutions for the development of innovative vaccines. Leveraging this platform, the Company may rapidly discover and identify potential antigens. The functions of the platform include to define the structural basis of antigenicity, to understand mechanisms of immune protection and to guide rational immunogen design. To date, the platform has already been applied to the design and selection of optimized recombinant protein in Recbio's vaccine developing process, including COVID-19 and HPV vaccines.

In addition, the protein engineering platform adopts multiple expression systems, including E. coli, H. polymorpha, baculovirus and CHO cell expression systems, among others. With this diversified expression system toolbox, Recbio has been able to select and apply the most suitable expression systems in the development of individual vaccines.

Figure 5: Protein expression systems adopted by innovative vaccines

Production system	Host	Manufacturer	Vaccine Name	Disease	Antigen	Vaccine type
Yeast	S. cerevisiae	Merck	Gardasil	HPV	L1 HPV 6, 11, 16, 18	VLP
	S. cerevisiae	Merck	Gardasil-9	HPV	L1 HPV 6, 11, 16, 18, 31, 33, 45, 52, 58	VLP
	S. cerevisiae	GSK	Mosquirix	Malaria	RTS, S	VLP
Baculovirus (Insect cell)	High Five	GSK	Cervarix	HPV	L1 HPV 16, 18	VLP
	ExpreSF+	Sanofi	FluBlok	Influenza	HA trivalent	Subunit
	ExpreSF+	Sanofi	Flublok Quadrivalent/ Supemtek	Influenza	HA quadrivalent	Subunit
	Sf9	Novavax	NVX-CoV2373	COVID-19	Full-length S Protein-Trimer	Subunit
	ExpreSF+	Sanofi/ GSK	VAT00002 VAT00008 (with adjuvant)	COVID-19	Full-length S protein	Subunit
	Sf9	West China Hospital	Recombinant COVID-19 vaccine	COVID-19	RBD	Subunit
Mammalian cells	CHO	GSK	Shingrix	Herpes zoster	gE	Subunit
	CHO	Clover	SCB-2019	COVID-19	Full-length S Protein-Trimer	Subunit
	CHO	Zhifei	ZF2001	COVID-19	RBD-Dimer	Subunit

Source: Cid R et al, Biomolecules 2021, CMBIGM

Immunological evaluation platform

Immunological evaluation is a critical step in vaccine R&D, as elucidate the mechanism of immune protection for diseases. Leveraging immunological evaluation platform, Recbio is able to select the optimal antigen and adjuvant combination and in turn improve immunogenicity profile of its candidates.

The immunological evaluation process involves multiple disciplines including immunology, biologics, molecular biology and clinical chemistry. Recbio's core scientific team began to build this immunological evaluation platform as early as 2004, so that the Company is one of the first companies that can conduct pseudoviral neutralization, ELISPOT (an immunoassay to determine cytokine-secreting cells), and ICS tests in China.

Comprehensive HPV franchises with five highly differentiated assets

HPV vaccines are one of the most commercially valuable vaccines worldwide. By end-2020, there are 110 countries which have included HPV vaccines into their routine national immunization schedule. By late 2021, 10 more countries planned to add HPV vaccines into their immunization schedule. Recbio features a comprehensive HPV franchise of five differentiated assets, which strategically target global markets of different affordability.

Leveraging its core product, REC603, Recbio is one of the front-runners in China's 9-valent HPV vaccine space, given 1) an overall favorable market landscape, with Merck's Gardasil 9 being the only 9-valent HPV vaccine approved in China with 48.5% market share in HPV vaccine market in 2020 (as per F&S), and 2) REC603 is leading the race of clinical development among peers.

Figure 6: Early mover advantage of REC603

Source: Company data, CMBIGM
Notes:
1) Recombinant human papillomavirus 14-valent Vaccine co-developed by The Sinocelltech Ltd. and Beijing Nuoning Biotechnology is currently at Ph I clinical trial;
2) Recombinant Human Papillomavirus 11-valent Vaccines (Hansenula polymorpha) developed by China National Pharmaceutical Group is currently at Ph I and II clinical trial

REC603 has significantly increased NAb GMT level against all of the target HPV types. At the same time, the incidence of adverse events in the vaccine group is 53.75%, with no statistical differences from placebo group. As comparison, in 2009, a non-inferior immunogenicity study of Gardasil 9 (by Merck) showed that the incidence of AEs in women aged 9-15 and 16-26 was as high as 86.6% and 90.1%, respectively.

Recbio obtained the umbrella IND approval for REC603 in Jul, 2018, which covers all three phases of clinical trials. In Jun, 2021, REC603 directly entered into Ph III evaluation in China, with Ph II trial waived approved by the NMPA. To date, Recbio has completed 12,500 subjects enrollment for the potency tests of Ph III trial of REC603, and plan to complete the three-shot dosing in 1H22. With BLA filing to the China NMPA expected in 2025E, REC603 has promising immunogenicity profile and favorable safety profile.

Figure 7: Clinical progress of REC603

Source: Company data, CMBIGM

Other than REC603, Recbio has two recombinant bivalent HPV vaccines, REC601 (Type16/18) and REC602 (Type 6/11), which are currently under Ph I clinical development. Leveraging cost advantage of bivalent vaccine, REC601 has the potential to become the mainstream vaccine for developing countries. Both of the vaccines are expected to submit BLA to NMPA in 2025E.

Moreover, the Company is also developing two next-generation HPV vaccines, namely REC604a (4-valent) and REC604b (9-valent), which are formulated with novel adjuvant benchmarking AS04 and potentially adopting a two-dose regimen. REC604a and REC604b are expected to file IND to NMPA in 2022/ 2023, respectively.

Figure 8: Competing advantages and marketing strategy of Recbio's HPV assets

REC601 / REC602 (HPV bivalent vaccine)	REC604a (Novel adjuvanted HPV quadrivalent vaccine)	REC603 / REC604b (HPV 9-valent / novel adjuvanted HPV 9-valent)
• **Key advantages**: cost advantages and scalable manufacturing potential • **Marketing strategy**: to cover low income group at a lower price, help developing countries with meeting immunization schedule	• **Key advantage**: high clinical value due to potential better cross-protection effectiveness • **Marketing strategy**: fulfill the unmet mid-to-high end demands of 9-valent vaccines	• **Key advantages**: more subtypes covered, favorable safety profile, REC604b has higher protection effectiveness (cross-protection) • **Marketing strategy**: REC603 as the first HPV vaccine of the Company to the mass market, REC604a as high-end iteration

Source: Company data, CMBIGM

Building integrated platform from discovery to commercialization

Recbio is led by an experienced management and scientific team, including industry-leading scientists with extensive experiences in immunology and vaccinology. The Company's CEO, Dr. Liu Yong, has over 23 years of experiences in innovative vaccines. Primarily served as a research professor at the China CDC, Dr. Liu has led the development of HIV DNA vaccine. Meanwhile, he also has work experiences in NIH Vaccine Research Center. Recbio's vice president, Dr. Chen Jianping has over 19 years' experiences in immunology and molecule biology research and over 10 years' experiences in vaccine development. He worked at the China CDC for 7 years and lead academic institutions including Harvard University and NIH Vaccine Research Center in the US.

Lead by Dr. Liu Yong and Dr. Chen Jianping, the Company's in-house R&D team consisted of over 100 talents, of which mostly held a doctoral or master's degree. The team is comprised of four different product development teams, namely the vaccine innovation core, process research core, comprehensive R&D core and R&D quality core. Aiming to develop potential best-in-class vaccine candidates for global market, the Company continues to invest heavily in R&D activities. In addition, Recbio has implemented the Integrated Product Development ("IPD") system to advance multiple vaccine development projects simultaneously and efficiently.

Under the relevant PRC laws, vaccine products can only be commercially manufactured by vaccine companies. To ensure smoothly transfer of vaccine candidates into commercial products, Recbio is constructing its vaccine manufacturing facility. Recbio's first phase of HPV vaccine manufacturing facility is expected to be completed by the end of 2022, and has a designed annual manufacturing capacity of 5mn doses of HPV 9-valent vaccines or 30mn doses of HPV bivalent vaccines, upper facility may be doubled in the future. As for ReCOV, the GMP-standard manufacturing facility can initially support the manufacturing of over 100mn doses per year by Nov 2021, which has the potential to eventually support manufacturing of over 300mn doses per year. The ReCOV capacity can also be used for the manufacturing of recombinant shingles vaccines. Recbio has a manufacturing and CMC team of 155 employees which is currently led by Mr. Zhang Kai, who has over 22 years' experiences in biopharmaceutical industry, including over 7 years' experiences in vaccine manufacturing at GSK.

Recbio has formulated a clear commercialization strategy on penetrating diversified markets. For China market, Recbio intends to build its own sales and marketing team and collaborate with other biotech companies with robust domestic sales network. Recbio also have plans on stepping into overseas markets. As for the developed market, Recbio targets on building collaborations with MNCs to commercialize vaccines candidates, as well as engaging local partners and set up local

manufacturing facilities. As for emerging countries, Recbio plans to collaborate with global reputable NGOs thus bring its products to larger populations.

Comprehensive HPV vaccine franchise

The Company features a strong HPV vaccine franchise, comprising of its core product, REC603, a recombinant 9-valent HPV vaccine candidate in Ph III trial in China, two recombinant bivalent HPV vaccines (REC601 and REC602) both in Ph I trials in China, as well as two 2nd generation, novel adjuvant formulated recombinant HPV vaccines, REC604a (quadrivalent) and REC604b (9-valent) under pre-clinical development in China.

Figure 9: Recbio's HPV vaccine franchise

Diseases	Candidates	Type of Vaccine	Adjuvant Systems	Product Rights	Commercial Rights	R&D status: Pre-clinical / IND Filing / Phase I / Phase II / Phase III
Cervical Cancers & Genital Warts	REC603 ★	Recombinant HPV 9-valent vaccine	Alum	Self-developed	Global	Expected to submit BLA application in 2025 (1)
	REC601	Recombinant HPV bivalent (Types 16/18) vaccine	Alum	Self-developed	Global	Expected to submit BLA application in 2025
	REC602	Recombinant HPV bivalent (Types 6/11) vaccine	Alum	Self-developed	Global	Expected to submit BLA application in 2025
	REC604a	2nd-generation recombinant HPV quadrivalent vaccine	Undisclosed novel adjuvant	Self-developed	Global	Expected to submit IND filing in 2022
	REC604b	2nd-generation recombinant HPV 9-valent vaccine	Undisclosed novel adjuvant	Self-developed	Global	Expected to submit IND filing in 2023

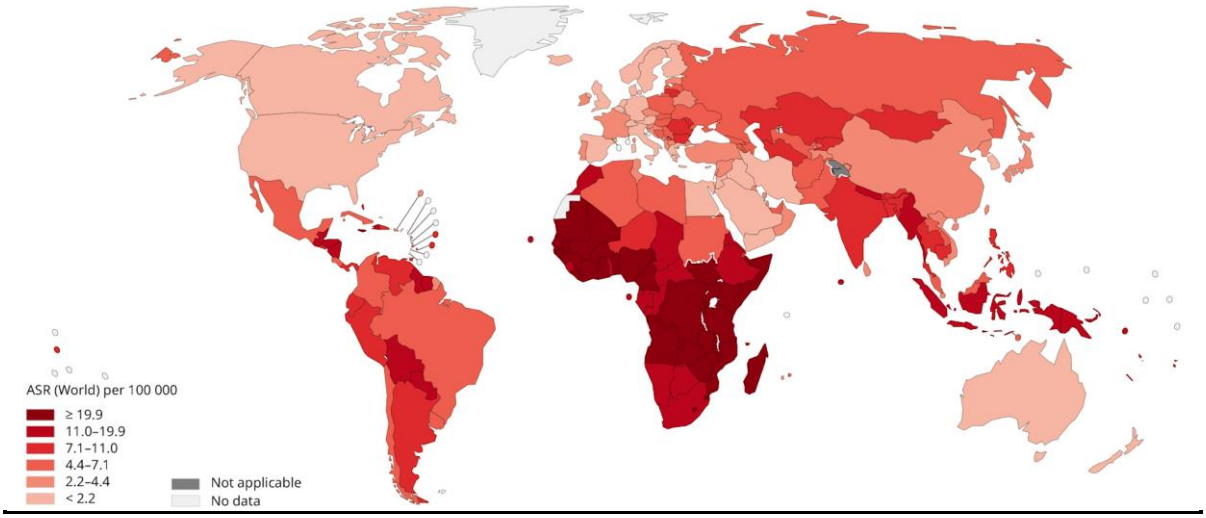
Source: Company data, CMBIGM

HPV infection is a global health issue

Human papillomavirus (HPV) is a group of more than 100 viruses, of which at least 14 types are cancer-causing and categorized as high-risk types. Although most of the HPV infections may clear up within a few months without any intervention, certain infections can persist and progress to cervical cancer. Naturally, the main high-risk HPV infections are caused by HPV types 16, 18, 31, 33, 45, 52 and 58, which account for approximately 90% of cervical cancer cases globally.

In 2020, cervical cancer has caused 4,290 deaths in the US and 59,060 deaths in China. Globally, two HPV strains (HPV-16 and HPV-18) cause about 71% of all cases of invasive cervical cancer, according to the World Health Organization (WHO).

Figure 10: Age-standardized mortality rate of cervical cancer per 100,000 females (2018)



Source: GLOBOCAN 2018, CMBIGM

Figure 11: Overview of HPV virus and vaccine design

Items	Detailed information
Characteristics of HPV	
Disease type	Anogenital & oral pharyngeal cancer
Structure & diversity	· 8 kb, double-stranded DNA papillomavirus, genome encodes 8 proteins · 55 nm particle of 72 capsomeres composed of major L1 & minor L2 capsid proteins · 12 High Risk oncogenic types (16,18, 31,33, 39,45, 51,52, 56,58 & 59), of which 70% of cancer caused by HPV types 16, 18
Life cycle & epidemiology	· Exclusively epithelial; no viraemia · Infection of basal epithelia mainly through sexual activity causing minor trauma · Productive infection linked to terminal differentiation of epithelium with particle release from uppermost apoptotic cells · Risk for cancer from persistent infection leading to viral E6 & E7 driven immortalization & genetic instability
Disease burden	· Premalignant cancers only apparent through screening · Cervical cancer is the second most common form of cancer in women living in less developed regions, with an estimated 570,000 new cases a year resulting in an estimated 311,000 deaths
Natural Immune control and escape	· Natural immune control and clearance most likely from T-cell immunity against viral early antigens E2, E6 & E7 · Neutralising antibodies develop against L1 but late after infection and only at low levels in 50% patients · Insufficient neutralising antibodies in cervico-vaginal secretions and local cellular immunity from lack of antigen-presenting cell activation/ inhibition of effector pathways leading to persistent infection
Vaccine design	
Vaccine strategy	· Vaccination to induce neutralizing antibodies to prevent infection prior to sexual debut in females can impact major disease burden
Antigen selection	· Recombinant HPV L1 can form a virus-like particle (VLP) mimicking key antigenic features of HPV types · L1 only made in terminally differentiated cells so cellular immunity not helpful for clearance of infection · Unknown if natural infection can necessarily boost a vaccinated individual's antibody response in a timely fashion to prevent infection · Animal studies established potential for antibody-mediated protection · Need neutralizing antibodies at sufficient levels to impact infection sites to maximize levels & longevity for sexual life protection; which can be optimized by the use of adjuvants
Immunogenicity	· HPV cannot easily be grown in vitro, nor is it cytopathic · Enzyme-linked immunosorbent assay, Competitive Luminex, pseudo-neutralization or cervicovaginal murine challenge assays of immunogenicity available are all surrogates for natural infection since there is no known immune correlate of protection · Immunization schedules in volunteers based on 2 or 3 vaccinations for both vaccines gave 100% sero-conversion and antibody levels many folds higher than natural levels
Future	· Therapeutic vaccines: for treatment of infections or early cancers by targeting E6 and E7 using a plethora of approaches. Recent DNA vaccine delivered by electroporation met primary clinical endpoint in CIN3

Source: Cunningham AL et al, Vaccine 2016, CMBIGM

According to the Lancet, the infection of HPV 6/11/16/18 was reduced by more than 90% in countries with high vaccination rates. The incidence of genital warts caused by HPV decreased by 90%, and the low-grade lesions of the cervix were reduced by 45%. However, there is a lack of supply of HPV vaccines globally. Crucially, vaccine coverage is <1% in many underdeveloped areas. By Oct 2014, the vaccination rate was 53.4% in North America, 36.4% in Europe, 41.1% in Oceania, 22.1% in South America, compared with only 1-2% for 10 to 20-year-old women in Africa and Asia.

In 2020, WHO issued "Global Strategy to Accelerate the Elimination of Cervical Cancer", which recommended 90% of girls to be fully vaccinated by HPV vaccine by age 15 by 2030.

Strong global demand in HPV vaccines

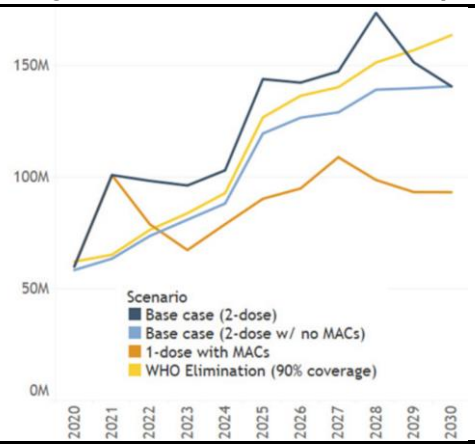
According to the WHO, there are 110 countries which have included HPV vaccines into their routine national immunization schedule by Nov 2020, with 10 more countries plan to add HPV vaccines into the list by end of 2021. The pace of introductions is substantially slower in low- and middle-income countries ("LICs and MICs"), despite these countries carrying the greatest share of disease burden. Based on Market Information for Access to Vaccine ('MI4A') estimates, in 2020, approximately 17% of the global HPV vaccine demand is for use in boys.

Based on the current WHO-recommended 2-dose schedule for girls under 15 years of age, WHO has estimated programmatic dose requirements for HPV vaccines. Forty-eight Gavi-supported countries are forecasted to conduct multi-age cohorts ("MACs") campaigns in the next 10 years. By including planned Gavi MAC campaigns in the base demand forecast, global demand will total around 60mn doses in 2020, according to the WHO estimates. Demand not constrained by supply is over 100mn doses for 2021, reaching 170mn doses in 2028E and stabilizing at 140mn doses by 2030E once MAC are completed.

As of China market, National Health Commission ("NHC") has formulated "Healthy China Initiative—Implementation Plan for Cancer Prevention and Treatment (2019-2022)", which emphasizes the broader promotion of HPV vaccination to accelerate the elimination of cervical cancer. In Dec 2020, NHC stated strong support to accelerate the elimination of cervical cancer, implying a potential near-term plan of HPV vaccines being included in Expanded Program on Immunization in China.

The introductions of China and India to national immunization programs (estimated for 2023 and after) are expected to drive the most significant increases in demand, representing ~1/3 of the market by 2030. Substantial increases in global vaccination coverage due to the global cervical cancer elimination strategy could result in an additional 20mn doses per year by 2030, according to WHO.

Figure 12: Potential evolution of global demand under different programmatic options

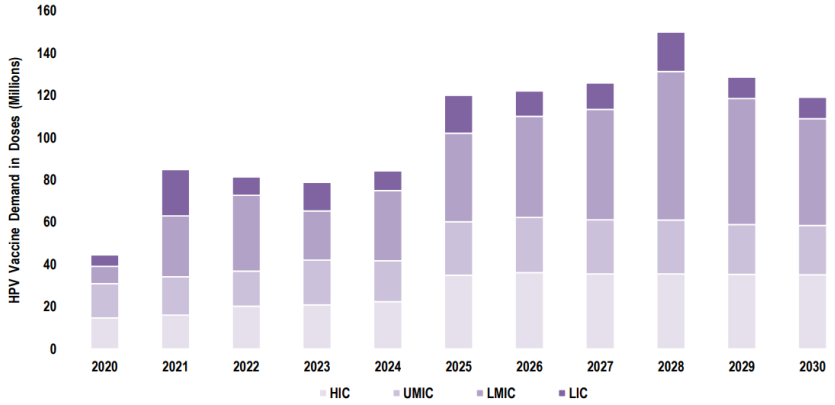


Source: WHO, Global Market Study HPV Vaccines 2020, CMBIGM
Notes:
1) The "base case" assumes continuation of a 2-dose routine schedule, planned Gavi MAC campaigns, and no new gender-neutral or older age cohorts' introductions. Continuation of current or near-term planned introductions in gender-neutral and older age cohorts are included in the base demand forecast, base demand with no MAC campaigns is also shown.
2) The "1-dose with MACs" scenario models a single-dose schedule with increased coverage for new introductions in LICs and MICs starting in 2022. Countries that have already introduced and HICs with future introductions are expected to use a 2-dose schedule.
3) The "elimination" scenario follows the same assumptions as the base case (2-dose schedule) but estimates that all countries reach at least 90% coverage by 2030. The elimination scenario assumes no MAC campaigns.

As per Linksbridge in 2020, the global market volume for HPV vaccines was approximately 44.5mn doses, having increased from an average of 30-35mn doses per year during 2010 and 2016, representing an increase of 21% over the past 4 years. As of 2020, HICs and upper middle-income countries ("UMICs") made up 69% of the global volume share, while lower middle-income countries

("LMICs") and low-income countries ("LICs") accounting for 18% and 12% of the total volume, respectively.

Figure 13: Global HPV demand by country income group, as of Sep 2020



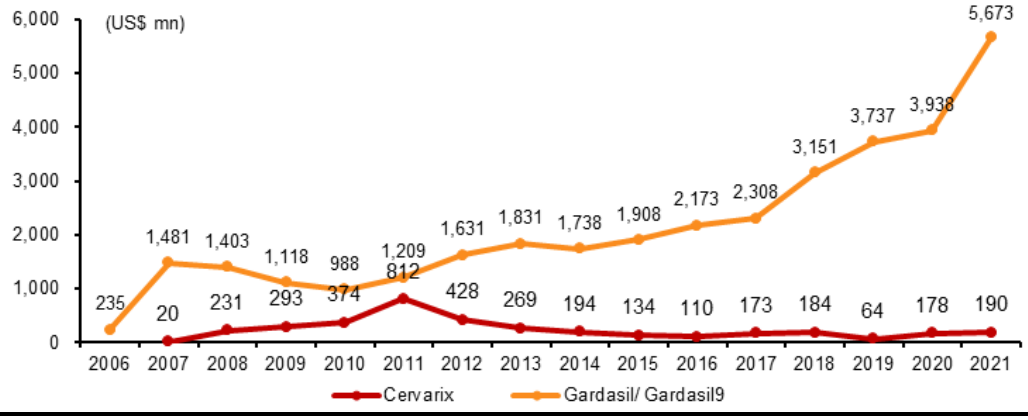
Source: Linksbridge, The Global Vaccine Market Model 2020, CMBIGM
Notes: "HIC" represents for high-income countries, "UMIC" represents for upper middle-income countries, "LMIC" represents for lower middle-income countries, "LIC" represents for low-income countries

Gardasil was first approved by the FDA for the U.S. market in Jun 2006 and recommended in the same month by the Advisory Committee on Immunization Practices ("ACIP") under the U.S. Center for Disease Control ("CDC") for initial and catch-up vaccinations. In Sep 2006, Gardasil was approved for use in European markets. Merck also launched a series of on-going studies in over 30 countries to evaluate the efficacy of Gardasil in women 27-45 years of age and males 16-26 years of age. Inclusion in the CDC's Vaccines for Children ("VFC") Program for free, subsidized vaccinations bolstered sales. By the end of 2007, Gardasil was licensed in 93 countries.

Cervarix was first licensed for use in Europe in Sep 2007, and in over 50 countries by the end of 2007. The UK Department of Health chose Cervarix in 2008 and launched a catch-up program. US approval in 2009 contributed to increased sales in Europe, while sales in developing countries increased sales in 2010 and 2011. Sales in 2012 decreased as Japan dropped its national campaign over safety concerns.

The figure below shows the sales trend and competition between Merck and GSK, sales data were extracted from Merck and GSK Annual and Quarterly Reports from 2006 to 2021. Units in GBP (British pounds) were converted into USD using the average exchange rate for each year. As Cervarix entered the market in 2008, sales of Gardasil decreased over the next two years. The FDA helped revive sales in 2010 by broadening the approval of Gardasil. Increased sales in the Latin America and Asian Pacific regions, as well as to males in the US bolstered sales of the Quadrivalent HPV vaccine. In 2015, with the launch of Gardasil9, preference has totally shifted to Gardasil, sales of Cervarix have continued to decline from the 2011 peak. The sales data of Gardasil include supply sales to Sanofi and Zhifei, which sold doses in Europe and in China.

Figure 14: Sales trend of Cervarix vs Gardasil/ Gardasil9 (2006-2021)



Source: Corporate filings, CMBIGM

From 2015 to 2020, the global sales revenue of HPV products of Merck has increased from US$1.9bn to US$3.9bn at a CAGR of 15.6%, indicating their efforts in scaling up the manufacturing capacities of HPV vaccines. Since the approval of Gardasil and Gardasil 9 in China in 2017 and 2018, the total lot release till 2020 in China amounted to 16.9mn and 9.6mn, respectively, according to F&S.

Nevertheless, according to F&S, HPV vaccines generally have a low vaccination rate of less than 1% in China in terms of total population and it is expected that there will be 233.9mn females in China aged 9-45 unvaccinated for HPV in 2025, representing a potentially total of additional 701.7mn doses needed assuming 3 doses per person. Even if the manufacturing capacity of Merck continues to scale up at a similar level, there will be a significant supply gap of HPV vaccines in China.

China lags behind developing countries in HPV vaccination

According to a systematic review of the epidemiology of high-risk HPV infections in mainland China published in Cancer in Apr 2019, among adult Chinese females, the rate of high-risk HPV infection is 19.4% by random sampling in hospitals, and 15.0% among general population, while the infection rate of women aged 15–19 years (who have had sexual experience) has reached 31%. Among high-risk HPV positive cases, 72% were infected with single HPV type, 20% were infected with two HPV types, and 8% with three or more HPV types. Age-specific HPV prevalence peaked at two age groups in Chinese women (17–24 years old and 40–44 years old).

According to “Chinese expert consensus on clinical application of HPV vaccine”, young females aged 9 - 26 are strongly recommended to receive HPV vaccination and females aged 27 – 45 are also recommended to receive vaccination.

Figure 15: Recommended levels of HPV vaccination

Population characteristics	Recommendation level
General population	
9~26-year female	Strongly recommend
27~45-year female	Recommend
Special population	
People with genetic susceptible population and high-risk population of cervical cancer	Strongly recommend
HPV infection/cytological abnormal	Recommend
Nursing woman	Cautiously recommend
Pregnancy woman	Not recommend

Source: Chinese expert consensus on clinical application of human papillomavirus vaccine 2019, CMBIGM

According to data from China's National Institute for Food and Drug Control ("NIFDC"), approved HPV vaccine shots increased from 1.45mn in 2017 to 15.43mn shots in 2020. As of year-end 2020, the total number of Chinese females fully vaccined with Gardasil/ Gardasil 9 were less than 8.8mn.

According to "HPV vaccination rate in Shanghai in 2017–2019 and suspect abnormal reactions surveillance" published on "China vaccine and immunization", full vaccination rate was 2.83% in women aged 9-45 years. As of girls aged 9-14 years, the full vaccination rate was only 0.55%. Among all vaccinated women, the primary group receiving vaccine were the 25–44 years group, girls aged 9–14 years only constituted 1%.

Some local governments in China are exploring to provide free HPV vaccination to young girls. In Aug 2020, the Municipality of Erdos in Inner Mongolia launched a public welfare project ''girls' health promotion in school,'' which provided free bivalent HPV vaccination for nearly 10,000 school girls aged 13–18 years. In Sep 2020, the city of Xiamen in Fujian Province announced to provide free domestic bivalent HPV vaccination to girls aged 13–14.5 years during 2020–2022, on voluntary basis.

Structural global supply shortage of HPV vaccines

To date, four HPV vaccines are approved worldwide, among which Innovax (万泰生物)'s bivalent HPV vaccine, brand name Cecolin, has recently received WHO prequalification. As per 2019 Joint Reporting Form on Immunization ("JRF") purchase data and MI4A estimates, globally, HPV vaccines make up only 2% of the vaccine market by volume, while accounting for 15% of global market value. According to an UNICEF survey, in 2020, the current estimated global HPV vaccine market share by volume is 23% for bivalent vaccines, 52% for quadrivalent vaccines, and 25% for 9-valent HPV vaccines.

Figure 16: Four commercial HPV vaccines

Brand name	Cecolin	Cervarix	Gardasil	Gardasil 9
Company	Innovax, China	GSK, UK	MSD, US	MSD, US
Valent	Bivalent recombinant	Bivalent recombinant	Quadrivalent recombinant	9-valent recombinant
Prevention of HPV serotypes	16/18	16/18	6/11/16/18	6/11/16/18/31/33/45/52/58
VLP types	HPV-16 (40 μg), HPV-18 (20 μg)	HPV-16 (20 μg), HPV-18 (20 μg)	HPV-6 (20 μg), HPV-11 (40 μg), HPV-16 (40 μg), HPV-18 (20 μg)	HPV-6 (30 μg), HPV-11 (40 μg), HPV-16 (60 μg), HPV-18 (40 μg), HPV-31 (20 μg), HPV-33 (20 μg), HPV-45 (20 μg), HPV-52 (20 μg), HPV-58 (20 μg)
Adjuvant	280 μg Al(OH)3	50 μg MPL absorbed on 500 μg Al(OH)3 (AS04)	225 μg AAHS	500 μg AAHS
Expression system	Escherichia coli expressing L1	Baculovirus - Insect Cell	Saccharomyces cerevisiae	Saccharomyces cerevisiae
Dosage	0.5 mL each	0.5 mL each	0.5 mL each	0.5 mL each
FDA approval	/	Oct-09	Jun-06	Dec-14
EMA approval	/	Sep-07	Sep-06	Jun-15
NMPA approval	Dec-19	Jul-16	May-17	Apr-18

Source: Cheng L et al, Vaccines 2020, F&S, CMBIGM

Figure 17: HPV vaccine market in China

Brand name	Cecolin	Cervarix	Gardasil	Gardasil 9
Prevention of disease types (approved in China)	Cervical cancer, CIN1, CIN2/3, AIS, HPV16/18 persistent infection	Cervical cancer, CIN1, CIN2/3, AIS	Cervical cancer, CIN1, CIN2/3, AIS	Cervical cancer, CIN1, CIN2/3, AIS,9 HPV-associated subtypes of infection
Approved age of vaccination in China	9–45 yrs	9–45 yrs	9–45 yrs	16–26 yrs
Vaccination schedule	0M,1M, 6M (9–14yrs: 0M,6M)	0M,1M, 6M	0M,2M, 6M	0M,2M, 6M
NMPA approval	Dec-19	Jul-16	May-17	Apr-18
Lot release in China ('000 doses, 2020)	2,456	690	7,220	5,066
Bidding price in China (RMB per dose)	329	580	798	1,298
Production Value in China (RMB mn, 2020)	808	400	5,761	6,576
Bidding market share in China (2020)	6.0%	3.0%	42.5%	48.5%

Source: F&S, NMPA, CMBIGM

Despite strong demand in HPV vaccines worldwide, supply is limited due to lengthy clinical trial process and high technical barriers in manufacturing HPV vaccines, especially higher-valent HPV vaccines.

It often takes many years for HPV infections to be clinically detectable and may take even longer to detect potential cervical lesion, thus the evaluation of the efficacy of HPV vaccines is more time-consuming. From the regulatory history of existing launched HPV vaccines, it usually takes nearly 10 years from phase I clinical trials to the final launch of the product. The long R&D cycle also leads to expensive R&D investments. A study has shown that the estimated R&D costs for clinical trials (phase I-III) for both GARDASIL and GARDASIL 9 vaccines combined generally fell in the range between US$1.05bn to US$1.21bn. Furthermore, the higher the valent of the vaccine candidates, the more complex the manufacturing process.

Development landscape of HPV vaccines in China

Competition in HPV vaccine development is fierce in China as there are approximately 17 clinical-stage HPV vaccine candidates, including four bivalent vaccines, four quadrivalent vaccines, six 9-valent vaccines and others.

Some companies are developing higher-valent HPV vaccines, such as 11-valent or 14 valent. However, higher-valent HPV vaccines face both technical and safety challenges. HPV vaccine composes of VLPs formed by recombinant HPV L1 protein. Only VLPs with the same or similar structure as natural viruses can induce immunogenicity to prevent diseases caused by HPV infection. Therefore, since 11-valent HPV vaccines and 14-valent HPV vaccines comprise additional two to five VLPs than 9-valent HPV vaccines, it makes the research and development of the higher-valent HPV vaccines more difficult. In order to produce VLP with the same or similar structure as the natural virus, it requires the correct gene sequence, suitable culture conditions and intracellular microenvironment, complete and consistent assembly of VLP particles, good stability and expression of VLP particles, and establishment of a reliable subsequent purification process. Thus, the research and development of 11-valent HPV and 14-valent HPV vaccines have a high technical barrier. In addition, interferences between different HPV serotypes and the increasing antigen content may lead to safety issues, which require more safety studies to ensure the safety profile of HPV vaccines with higher valent.

Figure 18: HPV vaccines under clinical development in China

Valent	Vaccine	Serotypes	Company	Adjuvant	Clinical phase	First posted time	Applicable age
2-valent	REC602	6, 11	Recbio	N/A	Ph I	Jan 2021	18-45
	REC601	16, 18	Recbio	N/A	Ph I	Jan 2019	9-45
	Recombinant HPV vaccine (Yeast)	16, 18	Shanghai Zerun (泽润生物)	AlPO4	BLA	Apr 2021	9-30
	Recombinant HPV vaccine (E.coli)	6, 11	Innovax (万泰生物)	Aluminum	Ph II	Mar 2016	18+
3-valent	Recombinant HPV vaccine (E.coli)	16, 18, 58	Beijing Health Guard (康乐卫士)	Aluminum	Ph III	Sep 2020	18-45
4-valent	Recombinant HPV vaccine (H.polymorpha)	6, 11, 16, 18	Shanghai Bowei (博唯生物)	N/A	Ph III	Aug 2020	9-19
					Ph III	May 2020	20-45
	Recombinant HPV vaccine (S.cerevisiae)	6, 11, 16, 18	MSD	AAHS	Ph III	Jun 2018	9-26
	Recombinant HPV vaccine (H.polymorpha)	6, 11, 16, 18	China National Pharmaceutical (国药集团)	N/A	Ph III	Jan 2018	18-45
					Ph II	Dec 2017	9-45
					Ph I	Jun 2017	31-45
					Ph I	Sep 2016	9-17
	Recombinant HPV VLPs vaccine (Pichia pastoris)	16,18,52,58	Shanghai Institute of Biological Products (上海生物制品研究所)	N/A	Ph II	Mar 2019	20-45
					Ph I	Mar 2019	9-45
9-valent	REC603 (H.polymorpha)	6, 11, 16, 18, 31, 33, 45, 52, 58	Recbio	Aluminum	Ph III	Jun 2021	9-45
	Rrecombinant HPV vaccine (H.polymorpha)	6, 11, 16, 18, 31, 33, 45, 52, 58	Shanghai Bowei (博唯生物)	AAHS	Ph III	May 2021	9-45
					Ph III	Jul 2020	16-26
					Ph III	Apr 2020	20-45
	Recombinant HPV vaccine (E.coli)	6, 11, 16, 18, 31, 33, 45, 52, 58	Beijing Health Guard (康乐卫士)	N/A	Ph III	Apr 2021	20-45
				Al(OH)3	Ph I	Jun 2021	9-45 (male)
	Recombinant HPV vaccine (E.coli)	6, 11, 16, 18, 31, 33, 45, 52, 58	Innovax (万泰生物)	N/A	Ph III	Mar 2021	18-26
					Ph III	Aug 2020	18-45
	Recombinant HPV vaccine (S. cerevisiae)	6, 11, 16, 18, 31, 33, 45, 52, 58	MSD	AAHS	Ph III	Oct 2021	20-45 (male)
					Ph III	May 2019	20-45
					Ph III	Mar 2019	9-45
	Recombinant HPV VLPs vaccine	6, 11, 16, 18, 31, 33, 45, 52, 58	Shanghai Zerun (泽润生物)	Amorphous phosphate	Ph I	Mar 2019	9-45
11-valent	Recombinant HPV vaccine (H.polymorpha)	6, 11, 16, 18, 31, 33, 45, 52, 58, 59, 68	China National Pharmaceutical (国药集团)	N/A	Ph II	Jul 2020	18-26
					Ph I	Sep 2019	9-45
14-valent	Recombinant HPV vaccine	6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59	Sinocelltech (神州细胞)	Aluminum	Ph I	May 2021	18-45

Source: CDE, ClinicalTrials.gov, F&S, CMBIGM

The prophylactic HPV vaccine candidates go through clinical trials assessing their protection against cervical persistent infections and CIN2+ linked to HPV serotypes. Given that cervical cancer usually develope infrequently and slowly, HPV vaccines need to go through large size and time-consuming Ph III trials.

Currently, the WHO and NMPA suggest the use of CIN2+ instead of cervical cancer as primary endpoint for HPV vaccines' registrational studies. Some organizations, such as the International Agency for Research on Cancer (IARC), recommend using HPV persistent infection as a primary endpoint, which can be reproducibly measured and occurs more frequently than CIN2+. In China, the NMPA currently admits 12-month persistent infection ("PI12") as a secondary endpoint which may support conditional approvals of HPV vaccines.

Figure 19: Active Phase III efficacy study of 9-valent HPV vaccines in China

Company	Valent	Target enrollment	Location	1st enrollment	Enrollment completion	Control	Endpoint
Recbio	9-valent	12,500	Henan, Yunnan, Shanxi, Beijing	26-Jun-21	Oct-21	Placebo	1) Protection against CIN2+; 2) Protection against PI12
Shanghai Bowei (博唯生物)	9-valent	8,000	Guangxi, Zhejiang, Sichuan, Hebei	28-Apr-20	09-Aug-20	Gardasil (4-valent)	Protection against CIN2+ generated by HPV 31、33、45、52、58;
Innovax (万泰生物)	9-valent	9,327	Jiangsu, Sichuan	5-Sep-20	31-Dec-20	Cecolin (2-valent)	1) Non-inferiority protection against Cecolin; 2) Protection against PI12 of HPV 31、33、45、52、58; 3) Protection against CIN2+/ VIN2+/ VaIN2+
Beijing Health Guard (康乐卫士)	9-valent	12,000	Jiangsu, Guangdong, Shanxi	5-Dec-20	14-Sep-21	Gardasil (4-valent)	1) Protection against CIN2+, AIS, VIN2+, VaIN2+, AIN2+; 2) Protection against PI12

Source: NMPA, Pharmacube, CMBIGM

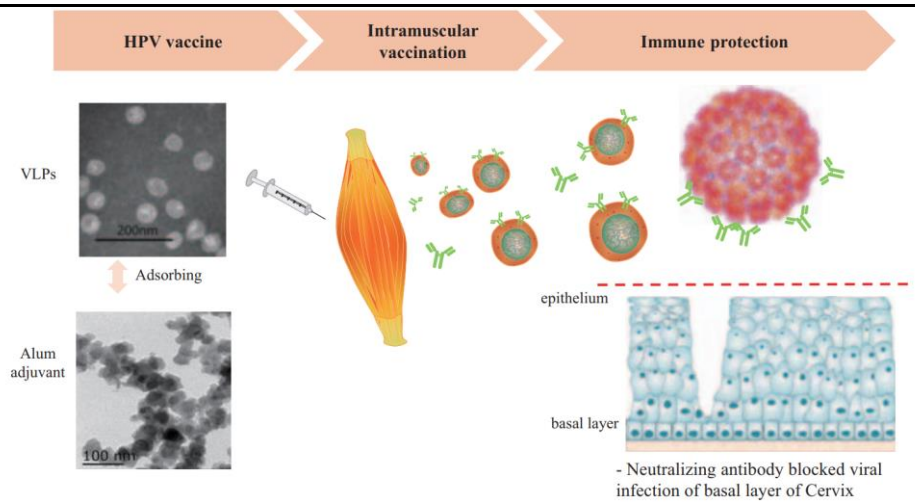
REC603, a potential first-to-market domestic 9-valent HPV vaccine

REC603, Recbio's core product, is 9-valent HPV vaccine against HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58. REC603 obtained IND approval in Jul 2018, the umbrella IND approval covers all three phases of clinical trials. After completed the Ph I clinical trial in China in Jul 2018, the CDE agreed Recbio to waive Ph II clinical trial and to directly proceed a Ph III clinical trial in China. The Company initiated the Ph III clinical trial of REC603 in China in Jun 2021 (CTR20210947), in Oct 2021, Recbio has completed all 12,500 subject enrollment in potency tests and plans to complete the three-shot dosing in 1H22. Recbio also plans to submit BLA to the NMPA by 2025E.

Mechanism of action

Persistent infection of high-risk HPV types leads to cervical cancer. Recbio's recombinant 9-valent HPV vaccine adopts the H. polymorpha (a type of yeast) expression system to produce oncogenic protein subunit L1 virus-like particles (L1 VLPs), which are molecules that resemble viruses but non-infectious due to lack of virus's DNA. The mechanism of protection is mediated by production of neutralizing antibodies against these L1 VLPs, and elicit strong immune response to prevent HPV infection.

Figure 20: Mechanism of action of REC603



Source: Company data, CMBIGM

Competitive advantages of REC603

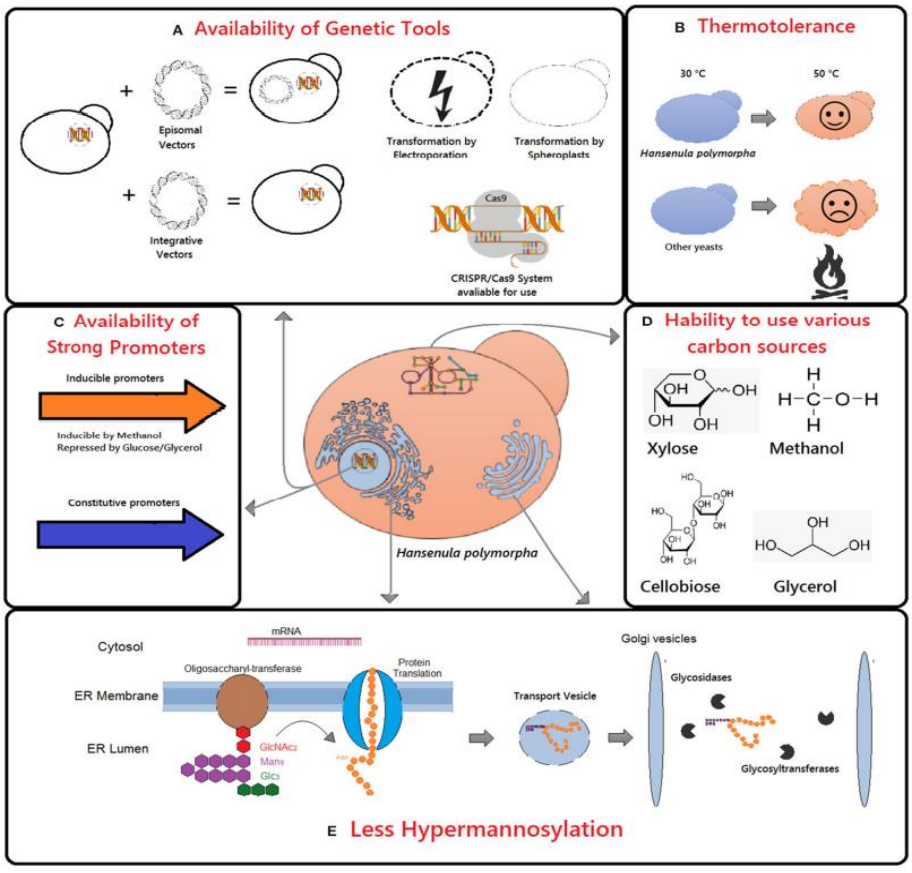
Promising immunogenicity profile: REC603 demonstrates a promising immunogenicity profile in Ph I trial, showing a significant increase in NAb geometric mean titers (GMT) level against all target HPV types.

Favorable safety profile: REC603 was safe and well-tolerated in Ph I trial, with no statistical difference of AE reported between the vaccine and placebo group. There were only 43 AE cases (53.75%) reported from the vaccine group, showing a good safety profile. The main adverse reactions were fever and injection site pain, but most were transient and mild.

High-yield and stable production of HPV VLPs: REC603 adopts H. polymorpha (yeast) expression system, which is able to grow to high cell density rapidly on simple media. In general, the VLPs expressed from different expression systems are all highly similar to natural HPV capsid in structure and epitope in order to trigger immune response after vaccination, including those being produced by H. polymorpha expression system. Owing to its high secretion capacity and lower hyperglycosylation activity compared to S. cerevisiae (another type of yeast), H. polymorpha is suitable for production of recombinant proteins for medical use. Moreover, the use of H. polymorpha is key to achieving high-yield and stable expression of HPV VLPs, making REC603 more suitable for commercial production.

Scalable manufacturing potential: Recbio can achieve high and stable yield in bulk production thanks to its patented HPV VLPs technology in combination with optimized fermentation strategy and purification process. With well-defined critical process parameters, manufacturing of REC603 can be easily scaled-up to meet commercial demand domestically and globally.

Figure 21: Main advantages of H. polymorpha for recombinant protein production



Source: Manfrão-Netto JHC et al, Frontiers in Bioengineering and Biotechnology 2019, CMBIGM
Notes: A,C) Main advantages of Hansenula polymorpha as chassi for recombinant protein production include the availability of genetic tools, B) thermotolerance, D) ability to use various carbon sources, and E) glycosylation pattern

Ongoing phase III clinical trial in China:

In Jun 2021, Recbio commenced a multi-center, randomized, blinded and placebo-controlled Ph III clinical trial for REC603 in China. The trial also includes a head-to-head comparison with Gardasil 9, the only approved HPV 9-valent vaccine in China. The leading PIs for this clinical trial are Mr. Xia Shengli from Henan CDC and Mr. Zhao Jian from Peking University No. 1 Hospital.

Recbio has completed 12,500 subjects enrollment of female aged from 9 to 45 years, for the potency tests for its Ph III trial. All subjects are divided into three cohorts, namely REC603-cohort, placebo-cohort and Gardasil 9-cohort. Each subject will receive three-shot of the vaccine/placebo. The primary endpoint is the cervical intraepithelial neoplasia (CIN) caused by HPV type 6/11/16/18/31/33/45/52/58 within one month after completing the three-shot. In order to evaluate the long-term immunogenicity of REC603, Recbio will conduct follow-up evaluations and studies at seven months, 12 months and once every month afterwards up to 60 months following the receiving of the third shot. The clinical protocol has been reviewed and agreed by the CDE of NMPA, which shall form the basis for the BLA application of REC603 in China.

Given the fact that the current HPV vaccine market in China is significantly under-served with only one commercialized HPV 9-valent vaccine and the growing awareness of cervical cancer prevention in China, Recbio has been able to enroll over 1,500 subjects within the first three weeks after the clinical trial was initiated. In Oct 2021, Recbio has completed subject enrollment and plan to complete the three-shot dosing in 1H22. The Company plans to submit the BLA application for REC603 to the NMPA in 2025 based on interim results obtained for up to 36 months after dosing.

Figure 22: Clinical results of major HPV vaccine candidates

Vaccine	Subject	Trial	Location	Endpoint	Efficacy	Vaccine Group		Control Group	
						Total No.	No. With Outcome	Total No.	No. With Outcome
Cecolin	Women aged 18–45	Efficacy trial in women, CTR20130951	China	CIN2+, VIN2+, VaIN2+	100.0%	3,306	0	3,296	10
Cervarix	Women aged 15–25	PATRICIA, NCT00122681	14 Countries in Asia Pacific, Europe, North America, Latin America	CIN2+	94.9%	7,338	5	7,305	97
	Women aged 18–25	CVT, NCT00128661	Costa Rica	Incident persistent infection	90.9%	2,635	8	2,677	89
				CIN2+	89.9%	2,635	1	2,677	10
	Women aged >=26	VIVIANE, NCT00294047	12 Countries in Asia Pacific, Europe, North America, Latin America	Incidence persistent infection or CIN1+	90.5%	1,852	7	1,818	71
				CIN2+	83.7%	1,852	1	1,818	6
Gardasil	Women aged 15–26	FUTURE I, NCT00092521 FUTURE II, NCT00092534	16 and 13 Countries in Asia Pacific, Europe, North America, Latin America	CIN2+	98.2%	7,864	2	7,865	110
				Anogenital warts	99.0%	7,665	2	7,669	190
	Women aged 24–45	FUTURE III, NCT00090220	Colombia, France, Germany, Philippines, Spain, Thailand, United States	Incidence persistent infection, CIN1+, or EGLs	88.7%	1,581	10	1,584	86
				CIN2+	83.3%	1,581	1	1,584	6
	Men aged 16–26	Efficacy trial in men, NCT00090285	18 Countries in Asia Pacific, Europe, North America, Latin America	Anogenital warts	89.4%	1,397	3	1,408	28
Gardasil 9	Women aged 16–26	NCT00543543	18 Countries in Asia Pacific, Europe, North America, Latin America	HPV types 31, 33, 45, 52, 58 CIN2+, VIN2+, VaIN2+	97.4%	6,016	1	6,017	38

Source: Markowitz LE et al, The Journal of infectious diseases 2021, CMBIGM
Notes: AIN, anal intraepithelial neoplasia, CI, confidence interval 95%, CIN, cervical intraepithelial neoplasia, CIN2+, CIN grade 2 or higher or adenocarcinoma in situ, EGLs, external genital lesions, GSK, GlaxoSmithKline, HPV, human papillomavirus, VaIN, vaginal intraepithelial neoplasia grade 2, VIN, vulvar intraepithelial neoplasia.

Phase I clinical trial in China:

The Company conducted a randomized, double-blind and placebo-controlled Ph I trial of REC603 to evaluate its safety and immunogenicity profile from Mar 2019 to Jul 2020, with 160 subjects enrolled including 80 females aged 18-45 and 80 females aged 9-17. Each subject received three shots within six months. The primary endpoint was the incidences of adverse events (AE) and severe adverse events (SAE) from the first shot till six months following the third shot. All subjects had completed the vaccine trial, except for one subject failed to receive the third shot due to pregnancy.

Safety profile: There were no statistical differences in AEs incidences between the vaccine and placebo group. There were only 43 subjects experienced AEs in the vaccine group (53.75%). There were no significant differences in terms of vaccination-related AEs in the trial group (51.25%) and in the placebo group (45.00%) either. Four Grade 3 AE cases were reported, including one incidence of redness, two incidences of swollen and one incidence of RBC abnormality.

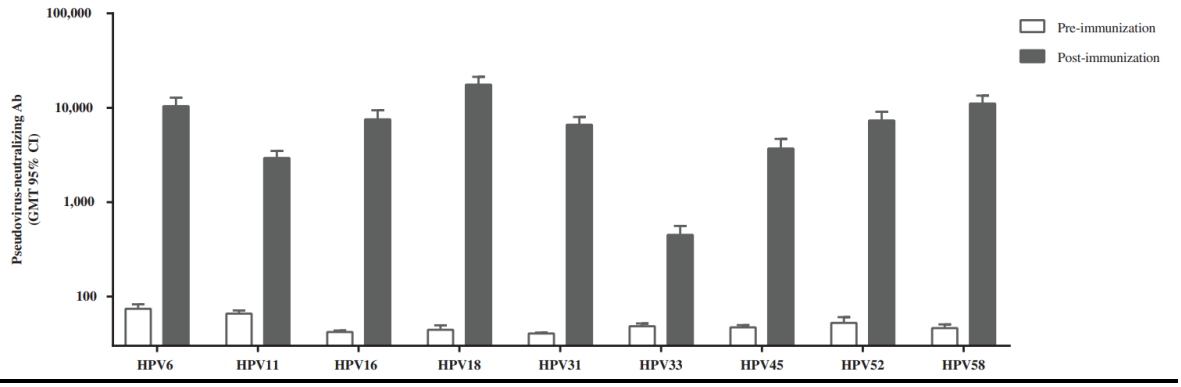
Figure 23: Adverse effects of four approved HPV vaccines

Vaccine	Very common >10%		Common 1%-10%		Accidental 0.1%- 1%	
	Local	Body	Local	Body	Local	Body
Cecolin	Pain	Fever	Induration redness, itching	Fatigue, headache, cough, myalgia, diarrhea, nausea, hypersensitivity, reactions	Rash	Vomiting
Cervarix	Pain, redness, swelling	Fatigue, myalgia, headache, fever (>37℃)	Induration and itching	Joint pain, gastrointestinal symptoms (including nausea, vomiting, diarrhea, and abdominal pain), hives and rashes	Rash	/
Gardasil	Pain, redness, swelling	/	Induration and itching	Diarrhea, hypersensitivity reactions, cough, nausea, vomiting	Rash	/
Gardasil 9	Pain, redness, swelling	/	Induration and itching	Diarrhea, hypersensitivity reactions, cough, nausea,vomiting	Rash	Allergic reaction

Source: Wei, L et al, Indian J Gynecol Oncology 2021, CMBIGM

Immunogenicity profile: Significant immune responses were induced in vaccine group with high neutralizing antibody titers against all targeted HPV types. Defined as 4-fold increase in neutralizing antibody titers, serologic conversion rates in vaccine group were 100% for HPV types 6, 11, 16, 18, 31, 45, 52 and 58.

Figure 24: NAb GMT profile of REC 603 in Phase I trial

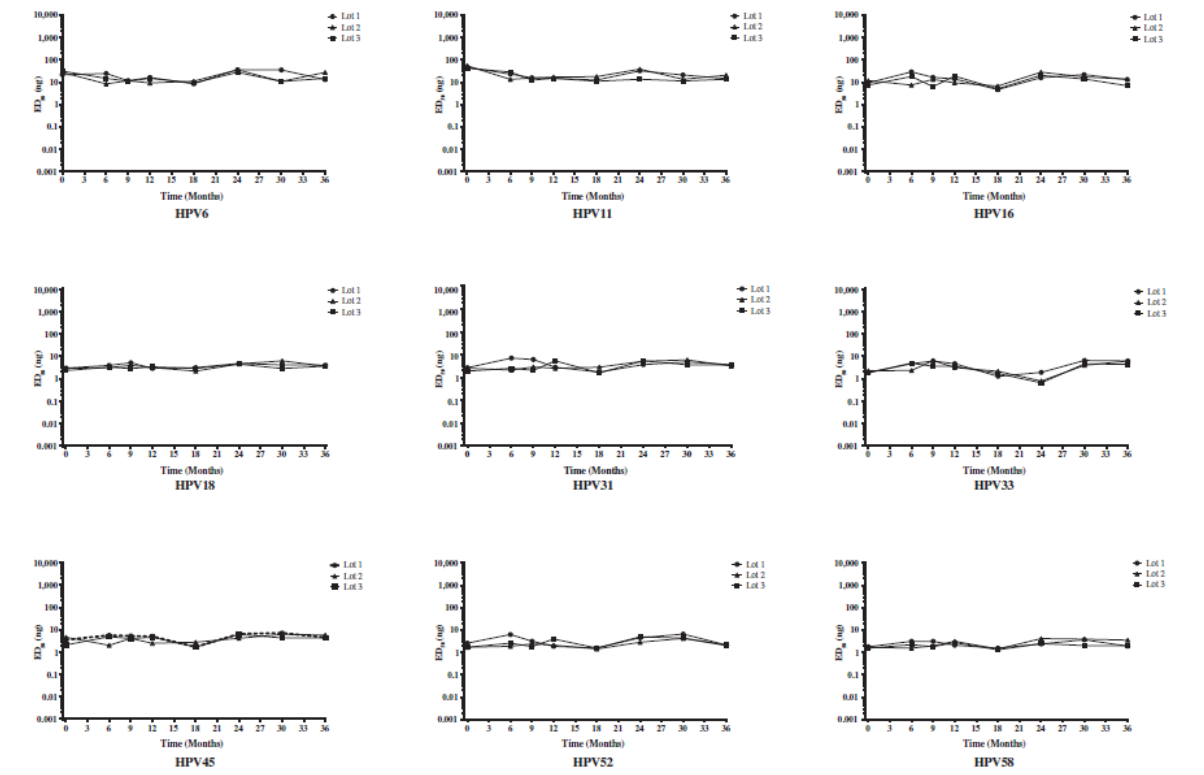


Source: Company data, CMBIGM

Preclinical studies REC603:

REC603 demonstrated favorable shelf life in preclinical studies. Its in-vivo potency measured by ED50 of each HPV type remained relatively stable when stored in temperature-controlled (2-8°C) environment.

Figure 25: REC603's ED50 of each target HPV type in three lots



Source: Company data, CMBIGM

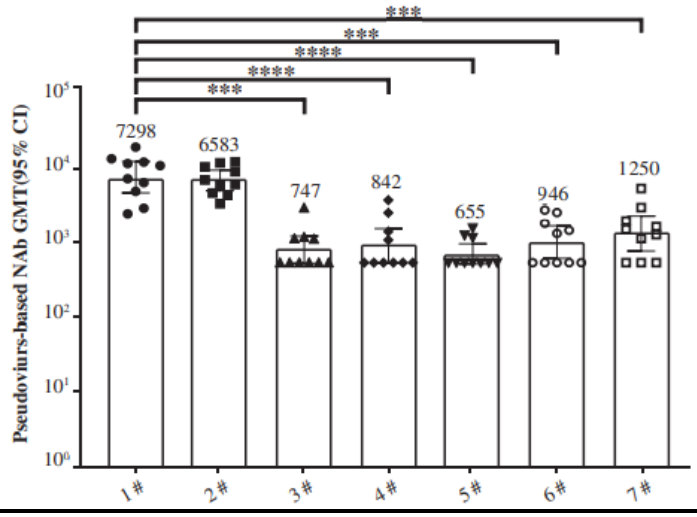
REC604a & REC604b, next-generation HPV vaccines

Recbio is developing two next-generation HPV vaccines, namely REC604a (a quadrivalent HPV vaccine) and REC604b (a 9-valent HPV vaccine), which are formulated with self-developed novel adjuvant, benchmarking AS04. REC604a and REC604b are designed to adopt a two-shot regimen, thanks to its enhanced efficacy and immunogenicity profile.

Recbio has conducted animal studies in BALB/c mice to evaluate the efficacy and immunogenicity profile of the vaccine with different types of self-developed novel adjuvants. Each mouse received two doses of REC604a and will be evaluated by GMT of nAbs based on pseudoviruses of HPV types. Through this approach, Recbio is able to identify the optimizing adjuvant that can be used in HPV vaccines.

Supported by this study, Recbio identified adjuvant 1# as the adjuvant to be used for REC604a, and REC604b. In an animal study conducted in mice, REC604a with a two-shot dosing has demonstrated its non-inferiority in terms of GMT level as compared to Gardasil with a three-shot dosing. Recbio is currently developing REC604a and REC604b. The Company plans to submit IND to the NMPA for REC604a 2022 and REC604b in 2023.

Figure 26: GMT of nAbs based on pseudoviruse study with different novel adjuvants



Source: Company data, CMBIGM

Adsorbed on aluminium salts, AS04 consists of 3-O-desacyl-4′ -monophosphoryl lipid A (MPL), a detoxified form of lipopolysaccharide (LPS) extracted from Salmonella minnesota. Studies in mice have revealed that MPL retains its complete immunostimulatory activity through TLR4 activation when adsorbed on alum. The adjuvant effect of AS04 is mediated by signalling through TLR4 on innate cells, in combination with the inherent immunomodulatory properties of alum. Demonstrating the added value of the TLR4 agonist MPL in humans, AS04 to the HPV vaccines is to induce higher levels of antibodies in comparison with the same antigens adjuvanted with just alum.

Compared to Merck's alum adjuvanted Gardasil, GSK's AS04-adjuvanted Cervarix demonstrated strong cross-protection effectiveness with higher titers NAb in clinical trials, suggesting enhanced immunogenicity of HPV vaccines with novel adjuvant. The higher immunogenicity also translated into a high and long-lasting efficacy of Cervarix, an HPV-16/18 vaccine.

A research article published at Lancet evaluated the sustainability of neutralising antibodies in vaccine trial participants 2–12 years after vaccination and the correlation with reported vaccine efficacy. 15% of the quadrivalent vaccine (Gardasil) recipients had no detectable HPV18 neutralising antibodies 2–12 years after vaccination, whereas all corresponding bivalent vaccine (Cervarix) recipients had HPV18 neutralising antibodies.

In seropositive Gardasil recipients, HPV16 geometric mean titres (GMT) halved by years 5–7 compared with years 2–4. Between 5 and 12 years after vaccination, GMT of neutralising antibodies to HPV16 and 18 were 5.7 times and 12.4 times higher, respectively, in seropositive Cervarix recipients than in Gardasil recipients. Cross-neutralising antibodies to HPV31, 33, 45, 52, and 58 were more prevalent in Cervarix recipients but, when measurable, sustainable up to 12 years after vaccination with similar GMTs in both vaccine cohorts.

Seroprevalence for HPV16, 31, 33, 52, and 58 significantly correlated with vaccine efficacy against persistent HPV infections in Cervarix recipients only. Correlation of protection with prevalence of neutralising or cross-neutralising HPV antibodies was not significant in Gardasil recipients.

Figure 27: Enhanced efficacy and immunogenicity profile of HPV vaccines formulated with novel adjuvant (AS04) compared to traditional adjuvant (alum)

HPV serotype	Product	Vaccine efficacy against HPV infections		GMT of neutralizing antibodies	
		Transient infection	Persistent infection	2–4 years	5–12 years
HPV6	Cervarix	9.8%	34.5%	284	171
	Gardasil	/	100.0%	4,568	3,646
HPV16	**Cervarix**	**93.1%**	**94.7%**	**22,970**	**18,568**
	Gardasil	**/**	**91.6%**	**6,141**	**3,276**
HPV18	**Cervarix**	**95.5%**	**92.3%**	**4,942**	**4,469**
	Gardasil	**/**	**91.6%**	**400**	**360**
HPV31	Cervarix	75.7%	77.1%	205	171
	Gardasil	/	46.2%	102	119
HPV33	Cervarix	34.8%	43.1%	108	120
	Gardasil	/	28.7%	63	158
HPV45	Cervarix	77.9%	79.0%	124	80
	Gardasil	/	7.8%	53	101
HPV52	Cervarix	16.5%	18.9%	117	126
	Gardasil	/	18.4%	157	112
HPV58	Cervarix	-8.9%	-6.2%	205	132
	Gardasil	/	5.5%	123	166

Source: Filipe CM et al, Lancet 2021, CMBIGM
Note: By definition, persistent infection results in subsequent detection of the same HPV type in the cervix, vulva, vagina, anus, or oropharynx for 6 months or longer. Conversely, transient infection consists of HPV detection over a period of as little as 3 months.

REC601 & REC602, bivalent HPV vaccines targeting mass market

REC601, a bivalent HPV (type 16/18) vaccine

REC601, is a bivalent HPV recombinant vaccine against HPV 16/18, which are the main cause of over 70% of cervical cancer cases, REC601 is currently in Ph I clinical trial. REC601 adopts a similar mechanism of actions ("MoA") with REC603, which is under Ph III clinical trial. As such, the Company plans to revisit the regulatory pathway of REC601 based on the interim clinical data from REC603. Recbio plans to initiate next Ph clinical trial in 2022E and submit the BLA application to the NMPA for REC601 in 2025E.

The Ph I trial of REC601 was initiated in Oct 2020 to evaluate its safety and immunogenicity. The trial plans to enroll 80 subjects, with 40 subjects aged between 20 and 45 and 40 subjects aged between 9 and 19. Recbio had already completed subject enrollment and the three-shot dosing for all subjects.

REC602, a bivalent HPV (type 6/11) vaccine

REC602 is a bivalent HPV vaccine candidate targeting HPV 6/11. The Company plans to complete the China Ph1 trial of REC 602 in the first half of 2022E and submit BLA to the NMPA by 2025E. REC602 adopts a similar MoA approach with the recombinant HPV 9-valent vaccine.

The Ph I trial of REC602 was initiated in May 2021 with the aim to evaluate its safety and immunogenicity profile. The clinical trial plans to enroll 60 subjects aged 18-45. The Company had completed subject enrollment. Recbio plans to complete the Ph I clinical trial for REC602 in the first half of 2022. Recbio expects to initiate next Ph clinical trial of REC602 in 2022E and submit BLA by the end of 2025E.

ReCOV, a new adjuvanted COVID-19 vaccine candidate

Current competitive landscape of COVID-19 vaccines

As of Mar 11, 2022, there are 32 COVID-19 vaccines on the market, including 11 recombinant protein vaccines and 67 candidates in phase III or later stage globally. There are in total 179 COVID-19 vaccine candidates under clinical development, including 61 recombinant protein vaccines. Among all of the recombinant protein COVID-19 vaccine under commercialization or clinical trial, ReCOV is the only one that targets a precision combination of NTD and RBD as an immunogen based on publicly available information.

Figure 28: Recombinant protein COVID-19 vaccines under clinical development globally

Company	Vaccine candidate	Immunogen	Clinical status
RecBio	**ReCOV**	**NTD-RBD (Trimer)**	**Ph III**
Nanogen	Nanocovax	S-protein	Ph III
Livzon Mabpharm	V-01	RBD	Ph III
Sanofi/GSK	Recombinant Protein	S-protein (Trimer)	Ph III
Sanofi/GSK	SP/ GSK subunit B.1.351 vaccine	S-protein	Ph III
Sanofi/GSK	SP/GSK subunit D614 vaccine	S-protein	Ph III
Shionogi	S-268019	Undisclosed	Ph III
COVAXX	UB-612	RBD + Epitope from other structure protein	Ph III
Clover	SCB 2019	S-protein (Trimer)	Ph III
SK Bioscience	GBP510	RBD	Ph III
West China Hospital	Recombinant COVID-19 vaccine (Sf9 cell)	RBD	Ph III
University Medical Center Groningen	AKS-452	RBD	Ph III
PLA ZHONGYIANKE Biotech	Recombinant COVID-19 vaccine (CHO Cells)	N/A	Ph III
Bagheiat-allah University of Medical Sciences	Noora vaccine	RBD	Ph III
Adimmune	AdimrSC-2f	RBD	Ph II
PT Bio Farma	SARS-CoV-2 Protein Subunit Recombinant Vaccine	Undisclosed	Ph II
Kentucky Bioprocessing	KBP-201	RBD	Ph II
Laboratorios Hipra SA	COVID-19 vaccine HIPRA	RBD	Ph II
Medigen	MVC-COV1901(Beta)	S-protein	Ph II
Novavax	SII Bivalent	Undisclosed	Ph II
Novavax	SII B.1.351	Undisclosed	Ph II
Novavax	SII B.1.617.2	Undisclosed	Ph II
Research Institute for biological safety problems	QazCoVac-P	N/A	Ph II
Icosavax	IVX-411	RBD	Ph II
Shanghai Zerun Biotechnology, Walvax Biotechnology	202-CoV	S-protein	Ph II
Sinocelltech	SCTV01C	S-protein	Ph II
Sinocelltech	SCTV01E	S-Trimer	Ph II
St. Petersburg Research Institute of Vaccines and Sera	Recombinant subunit vaccine	S-protein and other epitopes	Ph II
Tuebingen	CoVac-1	Multi-epitope	Ph II
University Medical Center Groningen	AKS-452X	SP/RBD	Ph II
University of Saskatchewan	COVAC-2	S-protein	Ph II
Instituto Finlay de Vacunas Cuba	FINLAY-FR-1	RBD	Ph II

Novavax	ICC Vaccine	RBD	Ph II
EuBiologics	EuCorVac-19	RBD	Ph II
CIGB	CIGB-669	RBD	Ph II
Clover	SCB-2020S	S-protein	Ph II
Biological E	BECOV2D	RBD	Ph II
Biological E	BECOV2C	RBD	Ph II
Biological E	BECOV2B	RBD	Ph II
Yisheng Biopharma	PIKA COVID-19 Vaccine	S-protein	Ph I
Emergex Vaccines Holdings	PepGNP-SARSCoV2	Undisclosed	Ph I
PT Bio Farma	SARS-CoV-2 Protein Subunit Recombinant Vaccine Adjuvanted With Alum+CpG 101	RBD	Ph I
HK inno.N Corporation	IN-B009	RBD	Ph I
SK Bioscience	NBP2001	RBD	Ph I
OSE Immunotherapeutics	CoVepiT	Multi-epitope	Ph I
University of Saskatchewan	COVAC-1	S-protein	Ph I
US Army Medical Research and Development Command	SpFN COVID-19 Vaccine	S-protein (Trimer)	Ph I
VaxForm	CoV2-OGEN1	Undisclosed	Ph I
Baiya Phytopharm	Baiya SARS-CoV-2 Vax 2 vaccine	N/A	Ph I
Baiya Phytopharm	Baiya SARS-CoV-2 Vax 1 vaccine	N/A	Ph I

Source: ClinicalTrials.gov, Literature research, Company website, F&S, CMBIGM

ReCOV, an ingenious recombinant COVID-19 vaccine

ReCOV is a recombinant two-component COVID-19 vaccine currently undergoing Ph II/ III trial in Philippines. ReCOV adopts an NTD-RBD-Foldon trimeric protein structure and is formulated with Recbio's novel adjuvant, BFA03 (benchmarking AS03). Recbio has yet finished with subject enrollment and two-shot dosing of ReCOV for the Ph II trial. Recently, Recbio has also received approval for Ph II/III trial in the UAE to evaluate ReCOV as a heterologous booster in adult subjects, as well as received clinical trial approval from the NMPA. Recbio expects to submit the EUA/BLA for ReCOV in 2022E.

Mechanism of Action

The foldon/trimerization structure of ReCOV was designed to mimic the natural structure of S protein to enhance immune response.

Mutations and transient conformational movements of the RBD that make neutralizing epitopes momentarily unavailable present immune escape routes for SARS-CoV-2. To mitigate viral escape, Jiangsu CDC has conducted neutralization-based immunogen design targeting SARS-CoV-2 NTD and RBD. NTD and RBD are the main immunodominant regions on the spike protein (S protein) of COVID-19 virus, which mediate the virus entry through its binding to angiotensin-converting enzyme 2 (ACE2) receptor on host cells. As NTD of the S protein will also bind and neutralize human antibodies, the combination of both RBD and NTD domains was designed to maximize the production of Nabs.

According to laboratory study, a combination of RBD-targeting NAbs and NTD-binding Nabs has enhanced the neutralization potency in cell-based assays and an animal model. Results of competitive surface plasmon resonance assays and cryo-electron microscopy structures of antigen-binding fragments bound to S unveil determinants of immunogenicity. Combinations of immunogens, identified in the NTD and RBD of S, when immunized in rabbits and macaques, elicited potent protective immune responses against SARS-CoV-2. More importantly, two immunizations of this combination of NTD and RBD immunogens provided complete protection in macaques against a SARS-CoV-2 challenge,

without observable antibody-dependent enhancement of infection. These results provide a proof of concept for neutralization-based immunogen design targeting SARS-CoV-2 NTD and RBD.

Figure 29: Proteins used as target antigens

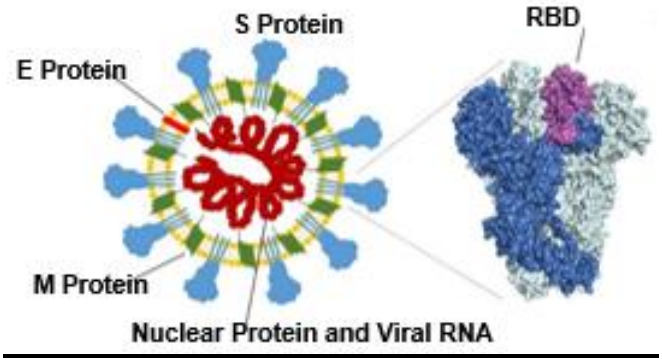
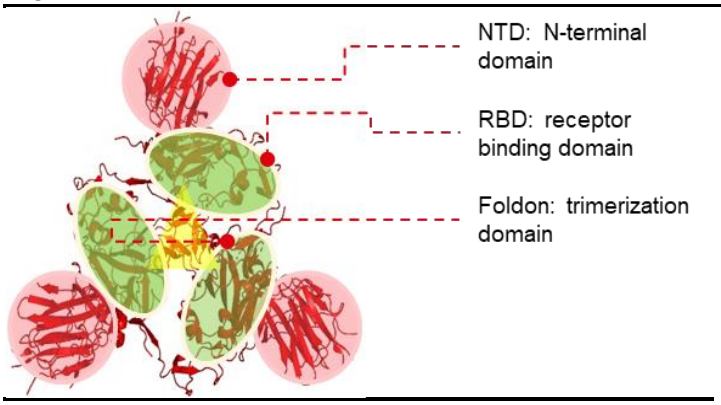


Figure 30: ReCOV's NTD-RBD-foldon trimmeric structure

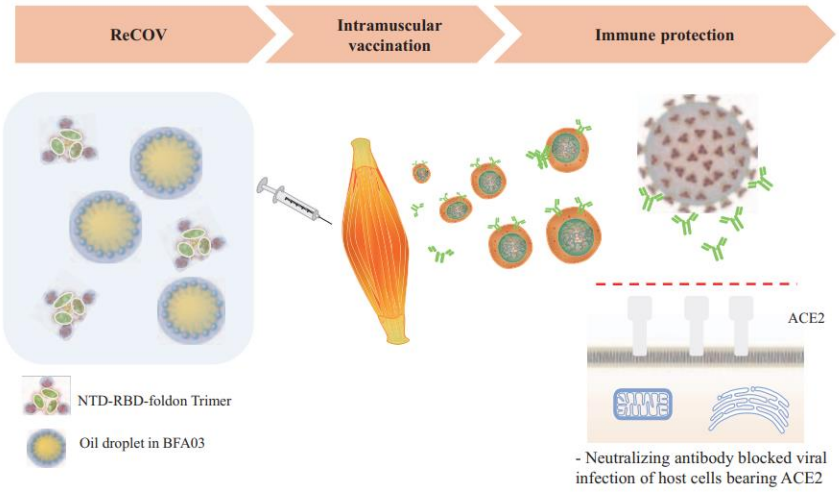


Source: Company data, CMBIGM

ReCOV adopts squalene-based novel adjuvant BFA03, benchmarking AS03. AS03 delivers a unique signal to the responsible APCs, B cells, and CD4+ T cells, in which α-tocopherol plays the key role. Similarly, BFA03 triggers a transient production of cytokines at the injection site and the draining lymph nodes, which subsequently triggers the promotion and enhancement of antigen-specific adaptive immune response.

Under the current regulation regime, BFA03 does not need to be separately registered with the FDA or the NMPA. As a self-developed novel adjuvant by Recbio, BFA03 also has the potential to be applied in the Company's other vaccine candidates. Concurrently, Recbio will not sell BFA03 to other independent third parties.

Figure 31: Mechanism of action of ReCOV

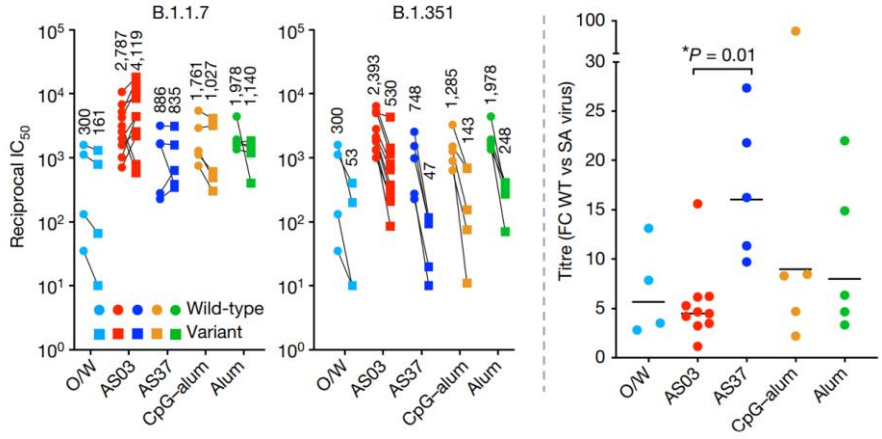


Source: Company data, CMBIGM

For reference, AS03 provided a longer-lasting cross-protection comparing with Alum in a COVID-19 vaccine candidate GBP510 (RBD-NP, a self-assembled nanoparticle vaccine candidate targeting RBD), which is developed by SK Biosciences. The neutralizing-antibody (nAb) response to live virus was maintained up to 180 days after vaccination with GBP-510 (RBD– NP-AS03).

As of cross-protection efficiency, even though RBD– NP-AS03 showed a reduced response against the B.1.351 variant (South Africa variant), the group only had a 4.5-fold reduction in neutralization, suggesting better protection than other adjuvants.

Figure 32: Cross protection efficiency of RBD–NP antigen combined with different adjuvants



Source: Prabhu SA et al, Nature 2021, CMBIGM
Notes: 1) Neutralizing-antibody titres against live wild-type (circles) or B.1.1.7 or B.1.351 variant (squares) measured in serum on day 42 (numbers indicate GMT), 2) The fold change in neutralizing-antibody titres for the B.1.351 variant versus wild-type

Summary of clinical trials of ReCOV

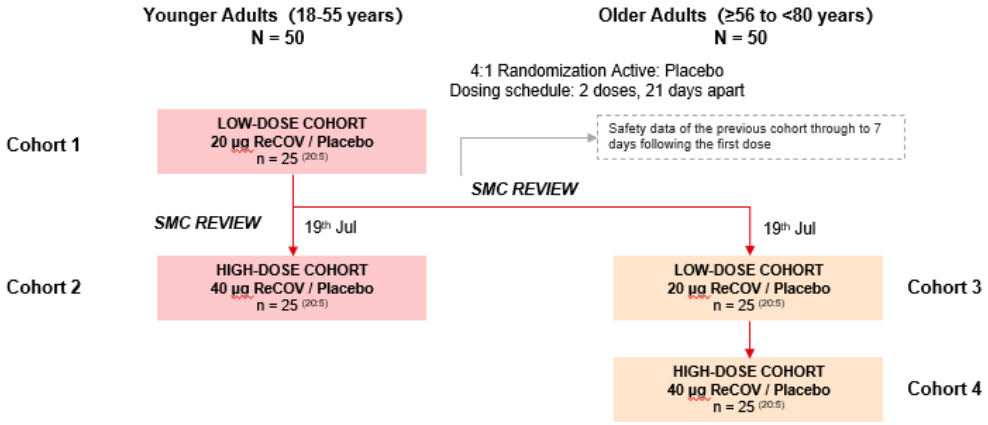
Phase I Clinical Trial in New Zealandl:

With IND approval obtained in New Zealand in Apr 2021, ReCOV commenced a multi-center randomized, double-blind Ph I trial since Jun 2021. Due to the recruitment challenges for older adults 56 to 80, this trial adjusted 99 subjects as suggested and agreed with the PI and CRO. To date, Recbio has obtained safety data for 99 subjects as well as the unblinded clinical data for all the four cohorts.

The Ph I trial has two trial arms, with 99 subjects further divided into four cohorts based on two dose levels (low-dose/ high-dose received 20 µg/ 40 µg, respectively) and two different age cohorts (younger adults/ elder adults aged 18 to 55/ 56 to 80, respectively). Cohort 1 refers to subjects of low-dose and younger adults, Cohort 2 refers to subjects of high-dose and younger adults, Cohort 3 refers to subjects of low-dose and elder adults, and Cohort 4 refers to subjects of high-dose and elder adults. For each cohort, five subjects enrolled will be randomized to receive placebo of normal saline. Each subject shall receive two doses of ReCOV with 21 days apart.

Subject in Cohort 1 is enrolled and dosed first. Following seven days after the first dose is completed in Cohort 1, the safety monitoring committee ("SMC") will conduct a preliminary safety review and Recbio will subsequently start the enrollment and dosing for Cohort 2 and Cohort 3. Following seven days after the first dose is completed in Cohort 3, the SMC will conduct another round of safety review based on the clinical data collected at that point, and Recbio will subsequently enroll and dose the Cohort 4.

Figure 33: Main design on ReCOV FIH Study

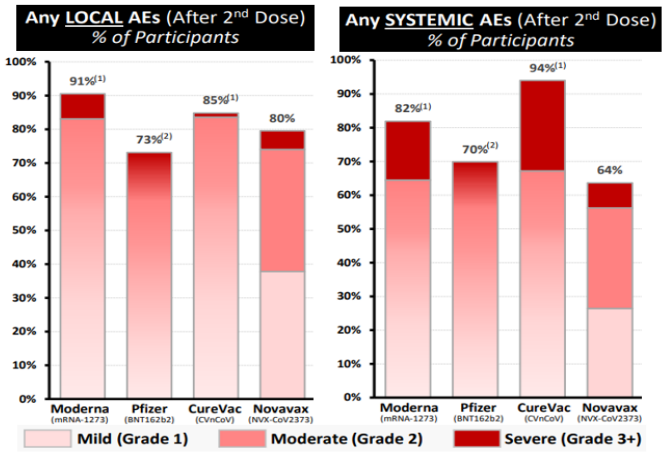


Source: Company data, CMBIGM

Safety Data:

ReCOV demonstrated a good safety profile for both low and high doses in participants aged 18 to 80 years old. No serious adverse event TEAE leading to an early discontinuation was reported and no clinically significant vital signs or clinical laboratory abnormalities were identified. Majority TEAE reported were mild in severity. Only four younger adults and two older adults experienced seven moderate TEAE and no severe or life-threatening TEAE was reported. The common TEAEs were similar to those reported by many approved vaccines.

Figure 34: Safety data of vaccine groups for COVID-19 vaccines in Phase II/III Trials

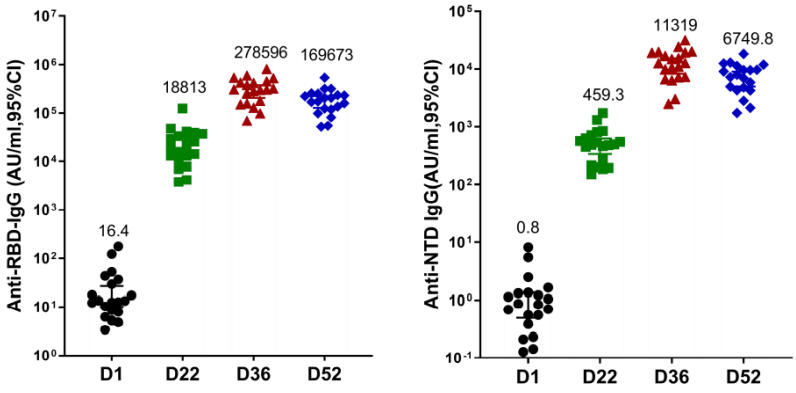


Source: Clover SPECTRA Phase II/ III clinical trial result press release

Partial Unblinded Immunogenicity Data:

In Oct 2021, as confirmed with the PI of this trial, Recbio obtained the unblinded safety and immunogenicity data for Cohort I. In the clinical data from Cohort I, ReCOV was observed to elicit strong neutralizing antibodies and antigen specific antibodies. Following the first dose of ReCOV, the seroconversion rate for Cohort 1 was nearly 100% and the geometric mean titer ("GMT") level reached peak at 14 days after the second dose. The following chart illustrates GMT of anti-RBD-IgG and Anti-NTD IgG.

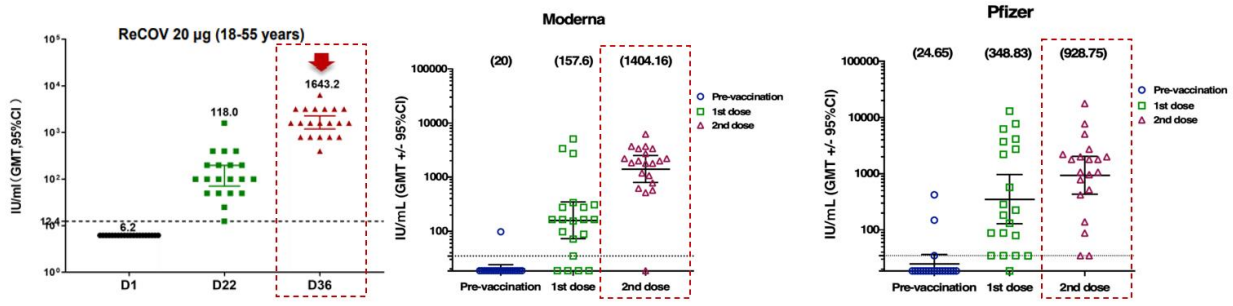
Figure 35: GMT of anti-RBD-IgG and Anti-NTD IgG elited by ReCOV



Source: Company data, CMBIGM
Notes: GMT of SARS-CoV-2 S RBD specific IgG in Cohort 1 were shown in left, and S NTD specific IgG in Cohort 1 were shown in right.

Clinical data from Cohort 1 shows that 20 μg ReCOV may potentially induce similar or higher level of nAb than other marketed mRNA COVID-19 vaccines and vaccine candidates, predicting a potential promising efficacy of ReCOV in preventing SARS-CoV-2 induced diseases. According to a recent pre-print study, the GMT of SARS-CoV-2 nAbs were 1404.16 IU/mL and 928.75 IU/mL 14 days after two doses for Moderna and BioNTech/Pfizer mRNA vaccines, respectively, under the WHO International Standard for anti-SARS-CoV Immunoglobulin (human) (NIBSC 20/136). Based on the partial unblinded data of Cohort I of the phase I trial of ReCOV, the GMT of SARS-CoV-2 nAbs amounts to 1,643.2 IU/mL after two doses of ReCOV.

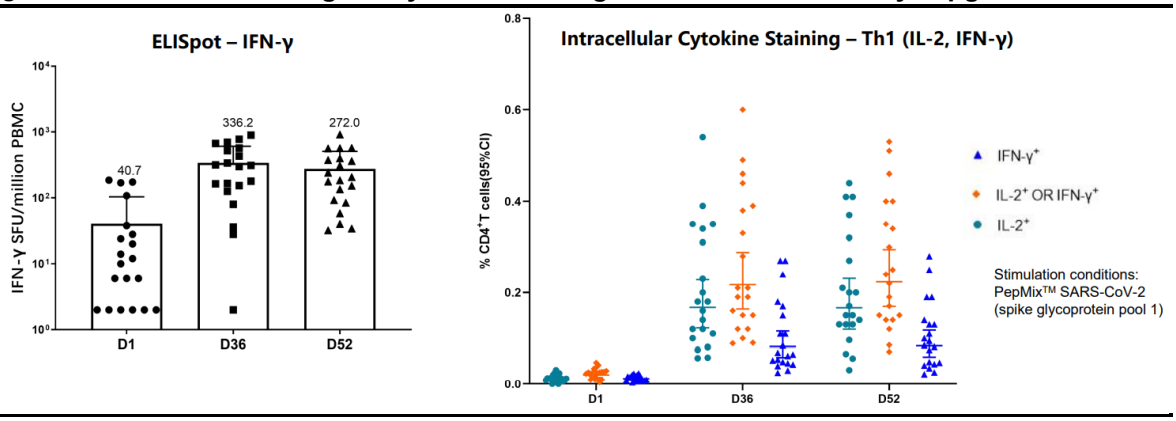
Figure 36: Comparison of GMT of SARS-CoV-2 nAbs elited by several vaccines



Source: Yu-An Kung, et al, infectious Diseases, 2021; Company data; CMBIGM
Notes: 1) the conversion of MN50 values to the international standard units (IU/mL); 2) the right 3 figures are serum samples for Moderna mRNA-1273 group, Pfizer BNT162b2 group and SCB-2019; 3) the above information was derived from multiple clinical trials conducted for different vaccines, without the support of controlled, head-to-head clinical studies.

In Cohort 1, it shows 20 μg ReCOV could induce antigen-specific CD4+ T cell responses, reflecting in IFN-γ and IL-2 production. IFN-γ is a pleiotropic molecule with associated antiproliferative, pro-apoptotic and antitumor mechanisms. IL-2 is an interleukin, a type of cytokine signaling molecule in the immune system. It shows an obvious trend toward Th1 phenotype immune response was observed with a peak level of Th1 cytokines detected 14 days after the second dose.

Figure 37: Cellular Immunogenicity Data in Younger Adults Vaccinated by 20μg ReCOV



Source: Company data, CMBIGM

Further developing plan:

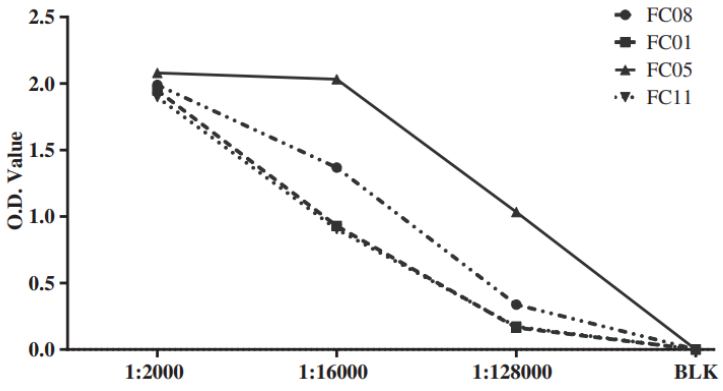
Recbio has obtained the major safety and immunogenicity data and the partially unblinded efficacy data from the Ph I New Zealand trial for ReCOV as of Feb 9, 2022, and is currently conducting data analysis for such trial.

The Company is currently initiating a global Ph II/III trial, which is designed to be a multi-center trial to study ReCOV in diverse populations and rapidly advance enrollment by accessing areas with larger patient populations. As part of this trial, Recbio has obtained approval from the Philippines FDA for ReCOV in Jan 2022. To date, Recbio has initiated subject enrollment for the Ph II/III trial in the Philippines. The Company plans to file the EUA/BLA in 2022.

Preclinical pharmacology study:

Recbio conducted characterization & pharmacology studies both in vitro and in vivo. During the in vitro studies, the binding effect of four monoclonal SARS-CoV-2 (FC01, FC05, FC08 and FC11) neutralizing antibodies and two antigens of the vaccine were tested, confirming that the folding of NTD-RBD-foldon protein is closer to the natural conformation of the virus.

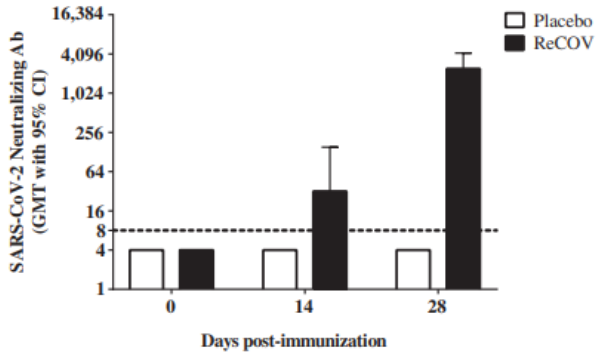
Figure 38: The binding effect of the NTD-RBD-foldon protein on 4 nAbs (indirect ELISA)



Source: Company data, CMBIGM

In its in vivo pharmacology animal studies on BALB/c mice, New Zealand white rabbit and rhesus monkeys, ReCOV was generally shown to induce high titers of NAb against COVID-19 virus. ReCOV has elicited good protective effect against in the challenge model of rhesus monkey after two doses of immunization.

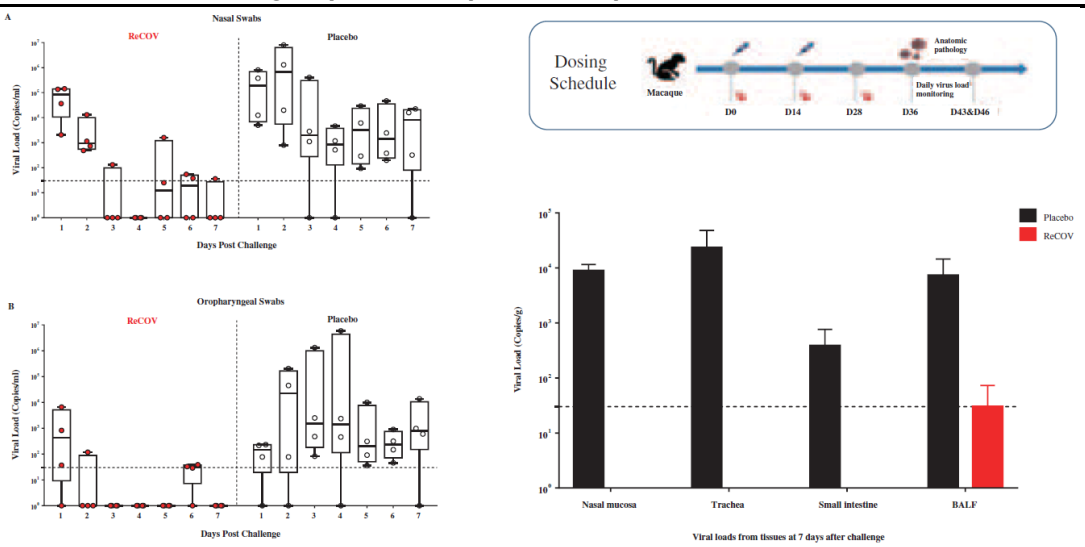
Figure 39: Level of immune response of ReCOV in rhesus monkeys



Source: Company data, CMBIGM

Moreover, in challenge study conducted in rhesus monkeys, the vaccine group was well protected upon intranasal inoculation by efficient clearance of viral infection and shedding.

Figure 40: ReCOV vaccine group was well protected upon intranasal inoculation



Source: Company data, CMBIGM

Preclinical toxicology studies:

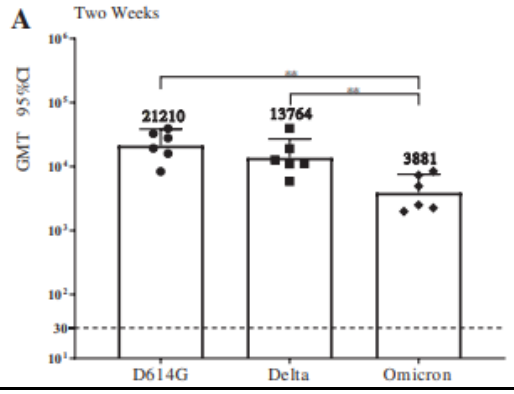
ReCOV demonstrated good safety and tolerance in preclinical toxicology studies. The study includes a single-dose toxicology study on rats, repeat-dose toxicology studies on rhesus monkeys and rats as well as a stimulation test on rabbits, as conducted by a certificated third-party. According to the study, of receiving the single-dose, local muscle swelling and palpated scleroma (hardened skin) were observed but can be recovered completely. There were no significant pathological changes, obvious abnormalities in body weight changes or abnormality in local muscle observed.

Animal studies in relation to the new variants of SARS CoV-2

Recbio has conducted several animals' studies in New Zealand rabbits, each rabbit completed two 40μg-dose at 0/21 day. To evaluates the nAb tiers at two weeks and 20 weeks following the second dose against the pseudoviruses of the ancestral strain, Delta variant and Omicron variant, at two weeks following the second dose, the GMT of nAbs maintained at a relatively high level, being 21,210 against the ancestral strain, 13,764 against Delta variant and 3,881 against Omicron variant. At 20 weeks following the second dose, the GMT of nAbs maintained at a relatively high level, being 826/ 609/ 587,

respectively. The serologic conversion rates for Omicron variant were 100% at 20 weeks following the second dose. In addition, ReCOV also showed promising immune persistence in BALB/c mice during 48 weeks following the second dose against the pseudoviruses of the ancestral strain, Delta variant and Omicron variant.

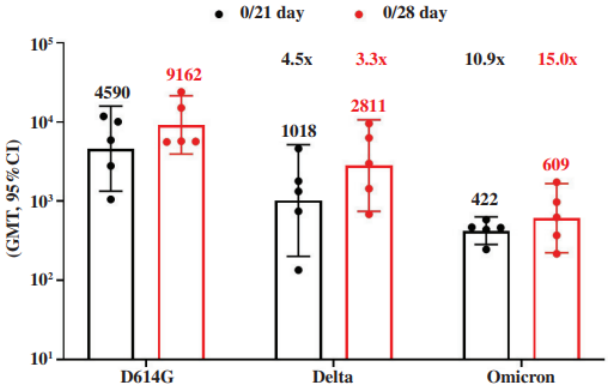
Figure 41: The nAb titers at 2 weeks following the 2nd dose of ReCOV (New Zealand rabbits)



Source: Company data, CMBIGM

Recbio also conducted an immune persistence study in BALB/c mice. The mice were categorized into two groups with different dosing regimen (two 4μg-dose at 0/21 day or 0/28 day) and the Company evaluates the nAb tiers during 48 weeks following the second dose against the pseudoviruses of the ancestral strain (D614G mutation of SARS CoV-2), Delta variant and Omicron variant. In the 0/21 day group, the GMT of nAbs was 4,590 against the ancestral strain, 1,018 against Delta variant and 422 against Omicron variant. In the 0/28 day group, the GMT of nAbs was 9,162/ 2,811/ 609, respectively.

Figure 42: Immune persistence of ReCOV against variants (BALB/c mice)



Source: Company data, CMBIGM

Recbio's outside collaborations in ReCOV's antigen

In May 2020, Recbio entered into a collaboration agreement with Jiangsu Provincial Center for Disease Control and Prevention ("Jiangsu CDC") and Taizhou Medical New & High-tech Industrial Development Zone ("Taizhou High-tech Committee") regarding the joint development of ReCOV. In Jul 2021, the agreement was supplemented to further clarify Recbio's exclusive rights in ReCOV.

Under the Collaboration Agreement, Recbio will lead the pre-clinical, clinical studies, manufacturing and commercialization of ReCOV. Jiangsu CDC is obliged to provide the laboratory data and results obtained from the preliminary research stage for ReCOV and is responsible for completing the immunological evaluation and preparing related application materials as required in the IND application. Taizhou High-tech will provide manufacturing sites and equipment, and is also responsible for applying

for government grants for the research and development of the recombinant COVID-19 (mutant strain) vaccine.

Recbio has paid Jiangsu CDC an upfront payment of RMB1.0mn on Nov 2020. As of milestone instalments, the whole payment will be up to RMB44.0mn, including 1) RMB2.0mn after the conclusion of pre-clinical in vivo tests, which demonstrated satisfactory nAb results (paid), 2) RMB10.0mn after obtaining the IND approval from the NMPA, and 3) RMB32.0mn after obtained the NDA or BLA and the manufacturing approval from the NMPA. After the successful commercialization of ReCOV, Recbio shall pay Jiangsu CDC a 1% sales commission, in terms of sales revenue.

Competing strengthen of ReCOV

As recombinant two-component COVID-19 vaccine adopting innovative adjuvant benchmarking AS03, ReCOV have several advantages: 1) novel mechanism of action: the NTD-RBD-foldon trimer potentially leads to higher protein yield and stronger immunogenicity, as well as more conserved epitopes, which potentially translating to better cross-protection against emerging variants; 2) promising safety profile: as the vaccine uses a high purity antigen protein and a clinically proven adjuvant; 3) strong scalability and cost-effective manufacturing: the Company has in-house novel adjuvant development capabilities; 4) highly stable for storage: ReCOV is stable for at least three months at room temperature or 24 months in standard cold chain, which is suitable for large population inoculation in developing countries and regions with limited cold-chain logistics and infrastructure; 5) cost advantages: the high yield of unit fermentation volume and the scalability enable ReCOV with cost advantages and worldwide accessibility.

REC610, an IND-enabling recombinant shingles vaccine candidate

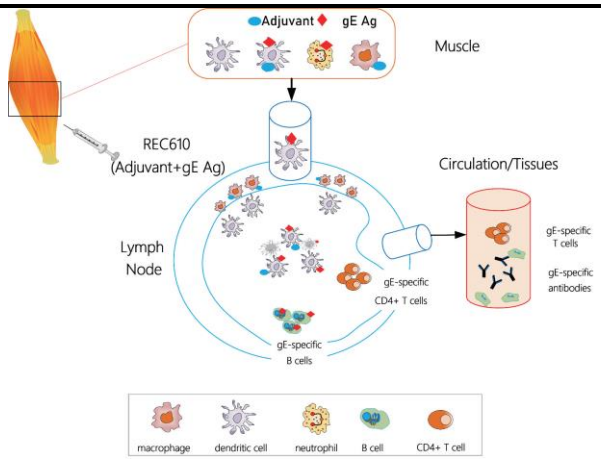
REC610 is a recombinant shingles vaccine formulated with self-developed novel adjuvant, currently undergoing pre-clinical development. REC610 adopts a similar recombinant protein technology as Shingrix which is the only recombinant adjuvanted shingles vaccine approved by the FDA/ NMPA in Oct 2017/ May 2019, respectively. REC610 has showed non-inferior immunogenicity compared to Shingrix in animal studies. Recbio plans to submit IND of REC610 to the China NMPA in 2022.

Shingles is caused by reactivation of latent infection of varicella-zoster virus (VZV). Active shingles are infectious through direct contact with fluid. Vaccination has been considered to be the most effective way to prevent spreading of infection. According to F&S, there are over 2.5mn people affected by shingles every year in China. The most common complication is persistence of neuropathic pain.

Mechanism of action of REC610

REC610 is comprised of VZV glycoprotein E (lgE), which is highly expressed on the surface of the virus responsible for virus-host receptor interaction and cell-to-cell transmission, and liposome-based adjuvant system. The novel adjuvant plays a role in stimulating and inducing a higher gE-specific cell mediated immune response. The adjuvant induces a local and transient activation of the innate immune system by two immune potentiators: MPL, and QS-21. Co-localization of both MPL and QS-21 is required to induce the maximal frequencies of gE-specific cytokine-producing CD4+ T cells and thus the highest titers of gE-specific antibodies.

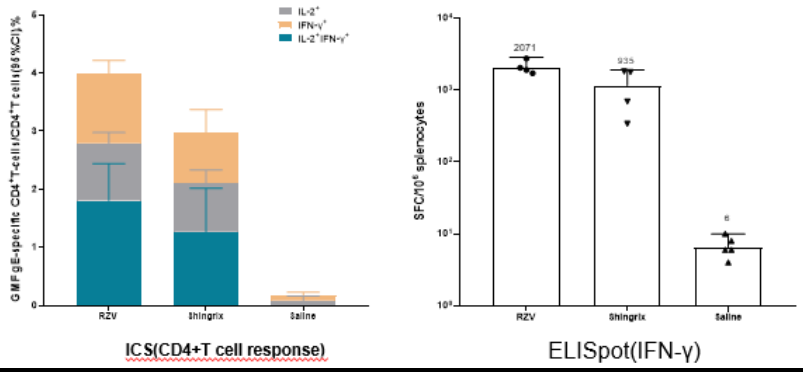
Figure 43: Mechanism of REC610



Source: Company data, CMBIGM

Recbio conducted pre-clinical animals' studies in C57BLL/6N mice to evaluate the immunogenicity profile of REC610. REC610 has shown a higher level of IFN-γ cytokine under ELISPOT test and higher levels of IFN-γ and IL-2IFN-γ as compared to Shingrix indicating its non-inferiority as compared to Shingrix in terms of immunogenicity.

Figure 44: Immunogenicity profile of REC610



Source: Company data, CMBIGM

Mild competition in shingles vaccine market

Globally, there are two commercial shingles vaccines, namely Merck's Zostavax and GSK's Shingrix. According to a head-to-head clinical trial in the US on 160 participants, Shingrix demonstrated higher CD4+ T cell responses, resulting in much better protective efficacy compare to Zostavax.

Figure 45: Clinical results comparison of Shingrix and Zostavax

Clinical Index		Shingrix	Zostavax
30 days after the last dose of vaccine	VZV-Specific IL-2+	Better	
	VZV-Specific IFN-g+	No sig. diff.	No sig. diff.
	VZV-Specific IL-2+IFN-g+	No sig. diff.	No sig. diff.
	gE-Specific IL-2+	Better	
	gE-Specific IFN-g+	Better	
	gE-Specific IL-2+IFN-g+	Better	
One year after the last dose of vaccine	VZV-Specific IL-2+	Better	
	VZV-Specific IFN-g+	No sig. diff.	No sig. diff.
	VZV-Specific IL-2+IFN-g+	No sig. diff.	No sig. diff.

	gE-Specific IL-2+	Better
	gE-Specific IFN-g+	Better
	gE-Specific IL-2+IFN-g+	Better
T cell generation	T Effector CD4+	Better
	T Effector memory CD4+	Better
	T Central memory CD4+	Better

Source: Company data, CMBIGM

Approved by the US FDA in 2006, Merck's Zostavax is a single-dose attenuated live vaccine, indicated for the prevention of shingles in adults aged 50 years or older. Approved by FDA in Oct 2017, Shingrix is a recombinant vaccine, indicated for the prevention of shingles in adults aged 50 years and olders and in adults aged over 18 years who are or will be at increased risk of shingles due to immunodeficiency or immunosuppression caused by known disease or therapy.

Due to greater effectiveness, the US CDC's Advisory Committee on Immunization Practices (ACIP) recommends Shingrix vaccine over Zostavax for herpes zoster (shingles) prevention. They also suggest those who received Zostavax in the past should be revaccinated with Shingrix for greater protection.

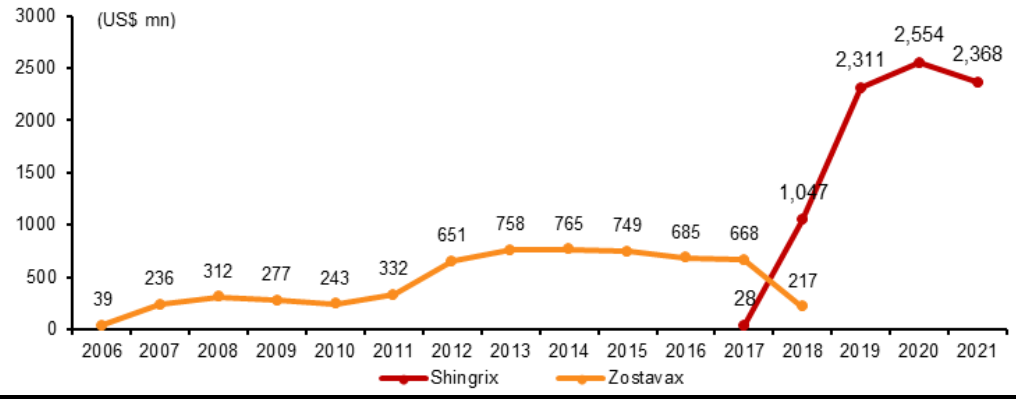
Figure 46: Two commercial shingles vaccines

Characteristic	Zostavax, Merck (Zoster Vaccine Live)	Shingrix, GSK (Recombinant Zoster Vaccine)
Vaccine type	Live-attenuated VZV (Oka/Merck); ⩾19 400 PFU	Recombinant VZV gE, adjuvanted
Vaccine composition Storage	1) lyophilized vaccine, 2) sterile diluent -50°C to -15°C	1) lyophilized gE antigen, 2) AS01B adjuvant +2°C to +8°C
Shelf life	18 months from the date of manufacture of the final filled container when stored at =< -15°C	36 months from the date of manufacture when stored at +2°C to +8°C
Dosage and administration	1 dose SQ in deltoid region of upper arm; 0.65 mL/dose	2 doses IM in deltoid region of the upper arm, 2 to 6 months apart; 0.5 mL/dose
Reactogenicity	Low	High
Overall efficacy against incidence of HZ	51.30%	97.20%
Overall efficacy against incidence of PHN	66.50%	91.20%
Persistence of protection against HZ	Up to 8 years	>=10 years (studied up to 10 years)
FDA approval	May 25, 2006 for adults aged >=60 yr; Mar 24, 2011 for adults aged 50–59 yr	Oct 2017 for adults aged >=50 yr, Jul 2021 for adults >=18 yr who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy
ACIP recommendations	For use in immunocompetent adults aged ⩾ 60 years	1) For use in immunocompetent adults aged >=50 yr, 2) For use in immunocompetent adults aged >=50 yr who previously received Zostavax, 3) Preferred over Zostavax, should wait at least 8 weeks if previously administered Zostavax

Source: Ruth H et al, The Journal of Infectious Diseases 2021, CMBIGM

In 2017, the launch of Shingrix ended the market monopoly of Zostavax. Later, Shingrix was approved by the EU EMA and Japan in Mar 2018, in China in May 2019, in New Zealand in Jan 2020, in Hong Kong in Oct 2020, and in Singapore in Jan 2021, respectively. With better efficacy data, Shingrix increased its influence rapidly. In 2019/ 2020/ 2021, the global sales of Shingrix reached US$2,311/ 2,554/ 2,368mn, respectively. As for Zostavax, since its approval in 2006, the peak sales were only US$765mn, of which has dropped drastically since the launch of Shingrix. It is also worth mention that as of Nov 2020, Zostavax is no longer available in the US.

Figure 47: Sales trend of Shingrix vs Zostavax (2006-2021)



Source: Corporate filings, CMBIGM
Notes: Units in GBP (British pounds) were converted into USD using the average exchange rate for each year

Both currently licensed vaccines have disadvantages, Zoatavax efficacy for HZ incidence is low, compared with Shingrix, and the efficacy wanes over several years. In addition, as a live-attenuated vaccine, it cannot be used in severely immunocompromised patients. On the other hand, Shingrix requires 2 doses, separated by 2–6 months, and the potent AS01B adjuvant makes Shingrix more reactogenic. Thus, the development of further zoster vaccines in being pursued.

Other than the upper two globally approved shingles vaccines, Live-attenuated zoster vaccine NBP608 (SKY Zoster), manufactured with vOka by SK Bioscience, was approved by the Korean Ministry of Food and Drug Safety in Oct 2017. A phase III trial demonstrated that NBP608 was safe and immunogenic and noninferior to Zostavax in healthy adults elder than 50 years.

Figure 48: Other global main shingles vaccine candidates

Company Name	Country	Vaccine	Characteristics	Status
SK Bioscience	South Korea	SKY Zoster (NBP608)	Live-attenuated Oka/SK strain	NCT03120364 Ph III (completed); approved in 2017 in Korea for adults >=50 yr
Curevo/ GC Pharma/IDRI	USA/South Korea	CRV-101	gE subunit vaccine with proprietary adjuvant	NCT03820414 Ph I (completed)
EyeGene/ Novotech	South Korea/Australia	EG-HZ	Adjuvanted recombinant VZV gE protein	NCT04210752 Ph I (completed)
BCHT Biotechnology	China	Zoster Vaccine, Live	Live-attenuated Oka VZV vaccine	NCT04334577 Ph III (not yet recruiting)
Vaccitech/ CanSino Biologics	UK/HK	VTP-400 (CSB016)	Adenoviral vaccine (ChAdOx1) encoding VZV gE	Preclinical
GeneOne Life Science	South Korea	GLS-5100	plasmid containing VZV-derived gene encoding a VZV protein; administered to the body using electroporation	Preclinical
Akshaya Bio	Canada	Chimigen ShingVax	recombinant proteins, antigens fused to the Fc fragment of a murine monoclonal antibody through proprietary peptide linkers.	Preclinical
Merck/ Moderna	USA	VZV gE mRNA/LNP	mRNA expressing truncated VZV gE protein in lipid nanoparticles	Nonhuman primate studies
CPL Biologicals	India	VZV Vaccine	Based on nanoparticle technology from Novavax (will target varicella and HZ)	In development

Source: ClinicalTrials.gov, Ruth H et al, The Journal of Infectious Diseases 2021, CMBIGM

In China, Shingrix is the only NMPA approved shingles vaccine. As of Nov 2021, there are three shingles vaccine candidates under clinical development in China, including two attenuated vaccines and one recombinant vaccine. REC610 has potential to become one of the early movers in China.

Figure 49: Shingles vaccine candidates under clinical development in China

Vaccine type	Vaccine type	Company	Phase	First posted time	Vaccination schedule
Attenuated Zoster Vaccine, Live	Attenuated	Changchun BCHT Biotechnology (长春百克生物)	Ph III	Feb 2020	1 dose
Recombinant vaccine (CHO cell)	Recombinant	Ab&b Biotech (江苏中慧元通生物科技有限公司)	Ph II	Oct 2021	2 doses
Attenuated Zoster Vaccine, Live	Attenuated	Shanghai Institute of Biological Products (上海生物制品研究所)	Ph II	Dec 2018	1 dose

Source: F&S, Pharmcube, CMBIGM

Other vaccine franchises

R520A, a pre-clinical stage mRNA COVID-19 vaccine targeting Omicron

In Aug 2021, Recbio established a JV, named Wuhan Ruikeji together with Shenzhen Ruiji. As the first step of this collaboration, the Company are developing R520A, a pre-clinical stage mRNA COVID-19 vaccine candidate, which specifically targets Omicron variant. R520A is designed to adopt a proprietary freeze-drying technology, enabling it to be stored and transported in a 2-8°C environment, thereby making them more stable and extending their shelf lives. Recbio is currently conducting pre-clinical R&D activities for R520A and plans to submit the IND application in 1H22.

R520A has adopted a self-developed Lyophilized mRNA-lipid nanoparticles technology, which enables easy storage and transportation. Through this approach, R520A can effectively sustain the physiochemical properties and bioactivity of mRNA-LNP and achieve long-term storage at 2℃to 8℃. During pre-clinical studies, R520A did not exhibit any change and sustained the size and encapsulation efficiency at 25℃ after 18 days, indicating high stability. In Feb 2022, the Company published a pre-print paper headed Lyophilized mRNA-lipid nanoparticles vaccine with long-term stability and high antigenicity against SARS-CoV-2 on bioRxiv.org to introduce its lyophilized mRNA LNP technology.

In order to assess the transfection efficiency of lyophilized LNPs, the Company conducted animal studies in BALB/c mice. Generally, the level of IgG antibody titers was non-inferior between mice receiving pre-lyophilization R520A and post-lyophilization R520A, indicating that the lyophilization process did not affect the product's bioactivity profile. Further, in other animals' studies in BALB/c mice, the level of nAb titers against Omicron variant increased to a high level of 4,758 and it can also induce neutralization response against Delta variant, indicating its promising immunogenicity profile.

REC606 and REC607, early-stage TB vaccine candidates

REC606, a novel recombinant adult TB vaccine

REC606 is an in-house developed novel recombinant adult TB vaccine formulated with a novel adjuvant, BFA 01, benchmarking AS01. It is currently being investigated under pre-clinical trial in China. The Company plans to submit IND to NMPA in 2023, followed by BLA submission in 2026.

REC607, a virus vector adult TB vaccine

REC607 is a virus vector adult TB vaccine candidate. In Feb 2021, Recbio entered into a collaboration agreement with Shanghai Public Health Clinical Center (上海公共卫生临床中心), ID Pharma and Shanghai Saimo Biotechnology (上海赛墨生物技术), under which Recbio obtained exclusive global development rights of REC607. Recbio paid an upfront payment of RMB3.0mn in Mar 2021, and is entitled to pay milestone instalments of RMB47.0mn, and a low single-digit percentage of global net sales of REC607 as royalties.

REC607 is based on non-replicating Sendai virus vector inserted with encoded M. tuberculosis immunodominant antigen. Sendai virus (SeV), also known as murine parainfluenza virus type 1, is a negative sense, single-strand, and non-integrating RNA virus, which has low pathogenicity and powerful capacity for wide host range. It has been applied in HIV vaccine development, with clinical data showing satisfactory safety profile and effectiveness in eliciting antigen specific T cell immune responses.REC607 is currently undergoing pre-clinical development. The Company plans to submit IND to NMPA in 2023E, followed by the BLA submission in 2026E.

Tuberculosis disease profile

Tuberculosis (TB) is a communicable disease, among one of the top 10 cause of deaths globally, as per WHO report. TB is caused by bacterium called Mycobacterium tuberculosis, which can spread in the air, such as by coughing.

There were approximately 9.2mn new TB cases globally in 2020, according to F&S. China had the third largest number of TB incidence with 775,800 new cases in 2019, according to F&S. WHO and its member countries have pledged to reduce TB incidence and deaths by 90% and 95%, respectively, by 2035, indicating significant market demand for tuberculosis vaccines.

Market competitive landscape of TB vaccines

So far, there is only one commercial adult TB vaccine in China, namely Anhui Zhifei's Vaccae which was approved in Jun 2021 for latent infection. In addition, only one adult TB vaccine candidate is being assessed in clinical trial in China which is a recombinant tuberculosis vaccine developed by Anhui Zhifei.

Figure 50: TB vaccine candidate under clinical trial in China

General name	Vaccine type	Adjuvant	Company	Phase	Age Criteria of Enrollment
Recombinant tuberculosis vaccine (AEC/BC02)	Recombinant	BC02	Anhui Zhifei	Ph I	18-45

Source: Company data, CMBIGM

REC617, an early-stage recombinant quadrivalent flu vaccine candidate

REC617, is a recombinant quadrivalent influenza vaccine (QIV) candidate formulated with self-developed novel adjuvant. The Company plans to submit IND to China's NMPA in 1H23E, followed by BLA submission in 2025E.

Influenza disease profile

Influenza is a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and sometimes the lungs. The best way to prevent flu is by flu vaccination every year. According to the National Bureau of Disease Control and Prevention, there were approximately 1.1mn new influenza cases and 70 deaths in China in 2020.

Market competitive landscape of influenza vaccines

In China, all the approved influenza vaccines are split vaccines (裂解疫苗). Approved by the US FDA in 2016, Sanofi's Flublok is the first recombinant influenza quadrivalent vaccine which is deemed as the optimal vaccine for influenza. In a head-to-head study comparing Flublok (recombinant adjuvanted QIV) with GSKs Fluarix (split QIV), patients inoculated with Flublok resulted in 30% less likelihood of experiencing influenza-like illnesses compared to Fluarix. Sanofi has completed a Ph III clinical trial of Flublok in China in Oct 2020. As Flublok is currently the only clinical stage recombinant influenza

quadrivalent vaccine in China, we believe REC617 has potential to become a second-to-market recombinant influenza quadrivalent vaccine in China.

Figure 51: Recombinant influenza vaccine candidate under clinical trial in China

General name	Vaccine type	Adjuvant	Company	Phase	Age Criteria of Enrollment
Flublok Quadrivalent	Recombinant	N/A	Sanofi	I	18+

Source: NMPA, CMBIGM

REC605, an early-stage recombinant quadrivalent HFMD vaccine candidate

REC605 is a recombinant hand, foot and mouth disease (HFMD) quadrivalent vaccine candidate, currently undergoing pre-clinical trial in China. The Company plans to submit IND to the China NMPA in 2023E, followed by BLA filing in 2026E.

HFMD is a mild contagious viral infection, normally occur in children under five years old. Common viruses including Enterovirus 71 (EV71), Coxsackievirus A16 (CA16), Coxsackievirus A10 (CA10) and Coxsackievirus A6 (CA6) lead to over 90% of HFMD cases in China. In 2020, There were 760,000 HFMD cases reported in 2020, ranked the fourth among infectious diseases in China.

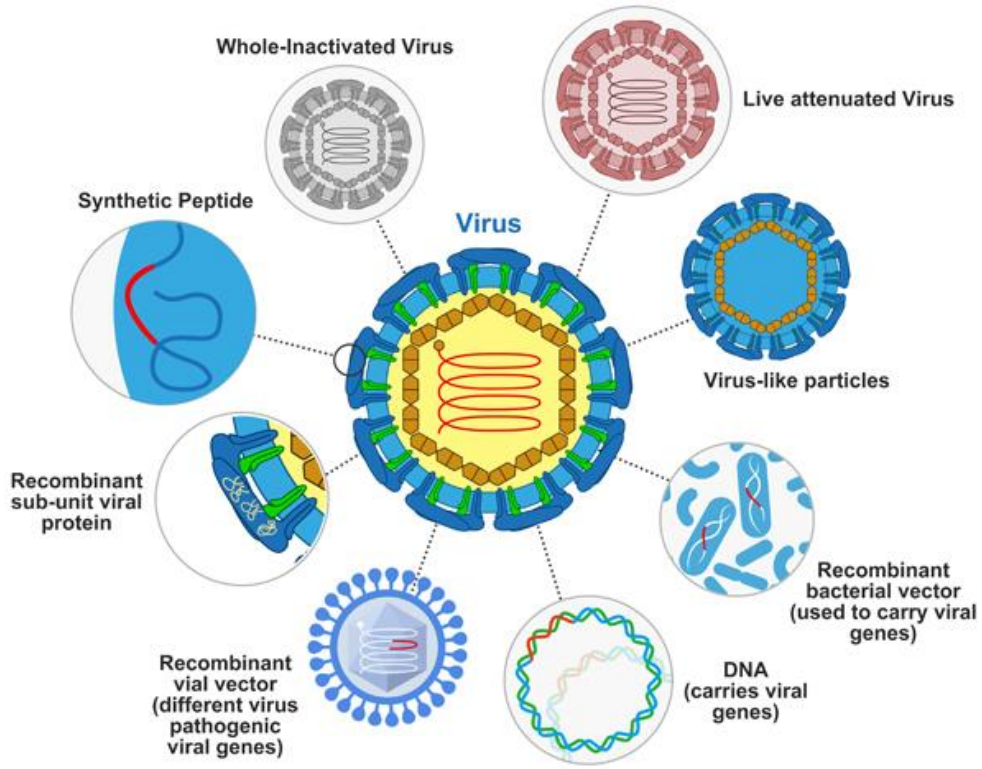
Sinovac (北京科兴生物)'s EV71 inactivated vaccine is the only HFMD vaccine approved globally and in China. Leveraging Recbio's protein engineering technology, REC605 is designed with increased serotype coverage of EV71, CA16, CA10 and CA6 and thus with enhanced protection. We believe REC605 has potential to become second-to-market HFMD vaccine worldwide.

Vaccine market overview

Complexity of vaccine development and supply

Vaccines are biological preparations that contain one or several antigens from, or similar to, a disease-causing microorganism, aiming to provide active acquired immunity against a particular disease upon administration. Vaccines can be categorized into whole pathogen vaccines and subunit vaccines, according to NIH. Whole pathogen vaccines are traditional vaccines consisting of virus particles or bacteria in an attenuated or inactivated form, whereas subunit vaccines are deemed as innovative vaccines including recombinant protein vaccines, viral vector vaccines, and nucleic acid vaccines.

Figure 52: Various vaccine development approaches



Source: GenScript, CMBIGM

Antigen design in vaccines development

Recombinant protein vaccines are one of the most efficacious and safest options among innovative vaccines. Using genetic engineering techniques to produce certain part of the pathogen, it is also relatively inexpensive.

Recombinant protein vaccines have been used in a number of disease areas, including hepatitis B, cervical cancers, shingles, etc. However, compared with inactivated vaccines, live attenuated vaccines or toxoid vaccines, the level of immune response generated by recombinant protein vaccines may be lower. Therefore, recombinant protein vaccines often require the incorporation of adjuvants to elicit a strong protective immune response.

Figure 53: Comparison of technology used in antigen design

Form	Applications	Advantages	Disadvantages	Limitations
Whole pathogen: live attenuate	· Oral poliovirus, · MMR (Measles-mumps-rubella), varicella, · Influenza, · BCG (Bacillus Calmette Guerin)	Mimics natural infection, and effective priming with durable immune	1) Rarely may revert to virulence, 2) not suitable for some populations, 3) may induce mild disease symptoms, 4) can be difficult to produce consistent	Not suitable for micro-organisms that do not grow well in culture, or whose characteristics change throughout their life-cycle (parasites) or pathogens with effective immune evasion or latent stages
Whole pathogen: killed	· Inactivated poliovirus, · Hepatitis A, · Whole-cell pertussis	Induces broad immune response to multiple antigen	1) Multiple doses needed, 2) reactogenic, key epitopes maybe destroyed by the inactivation process	/
Related nonpathogen	· Cowpox (small pox)	Induces broad immune response to multiple antigens	Not suitable for some populations, and may induce mild disease symptoms	Not many micro-organisms are suitable
Purified protein (split or subunit)	· Acellular pertussis vaccines, · influenza	Induces a highly specific response, non-infectious, low reactogenicity, synthetic production may ease produce	1) Correct 3-dimensional structure may be difficult to achieve, 2) multiple subunits are often necessary, 3) little cross-reactivity, 4) potential for escape mutants,5) lower immunogenicity requiring adjuvants	Not suitable for pathogens with characteristics that change throughout their life-cycle (parasites, some chronic or latent infections)
Polysaccharide–protein conjugates	· Neisseria meningitidis, · Streptococcus pneumoniae, · Haemophilus influenzae type b	Conjugation triggers T-cell dependent mechanisms and immune memory	1) Technically difficult and costly to produce, 2) finite number of strains possible in one vaccine	/
Pathogen-like particles	· Malaria, · Hepatitis B, · HPV (Human papilloma virus)	Can induce enhanced responses compared to natural immunity	The assembly of the particles is sometimes challenging	/
RNA replicon	· Influenza	Unable to produce infection, suitable for pathogens that do not grow in culture	1) Antigen dissemination may be limited, 2) potential for recombination to infectious form	/
Recombinant DNA technology	· Hepatitis B, · HPV (Human papilloma virus), · Herpes zoster	Suitable for pathogens that do not grow well in culture, efficient to manufacture	Lower immunogenicity requiring adjuvants or multiple peptides	/
Viral/bacterial vectors	· RSV (Respiratory syncytial virus), · Ebola	Suitable for pathogens that do not grow well in culture	1) Pre-existing antibody may limit response, 2) different vaccines may be needed for priming and boosting	Potentially unsuitable for immunocompromised or pregnant women
mRNA technology	· Infectious Diseases (COVID-19)	1) Expression within hours Repeated dosing, 2) Easy to scale up production, 3) Well-tolerated clinical safety profile, 4) Potentially different biodistribution, 5) Cell-free production	1) Short-lived expression, 2) IV administration, 3) No chemical modifications or antibody conjugates	/
Recombinant protein	· Malaria, · Hepatitis B, · HPV (Human papilloma virus)	1) Immediate peak circulating antibody, 2) Repeated dosing, 3) SC and IM delivery possible, 4) High mass titers rapidly achievable	1) Duration of circulating level dependent upon serum half-life of antibody, 2) Length of production time and manufacturing	/

Source: Cunningham AL et al, Vaccine 2016, CMBIGM

Adjuvants play a key role

Adjuvants are substances that can assist in antigen response and stimulate or suppress immune response. The functions of adjuvants mainly include: 1) improving the immunogenicity of the vaccine; 2) changing the nature of immune response; and 3) reducing the amount of antigen and the required number of shots of immunization.

Traditionally, alum adjuvants have been used in vaccine development. In recent decades, emerging subunit vaccines, especially recombinant protein vaccines, have significantly driven the development of innovative and more effective adjuvants.

Generally, vaccine adjuvants are not approved independently as a drug but a component of a vaccine. However, these novel adjuvants are generally difficult to manufacture, for example, AS01, a liposome-based adjuvant system, is manufactured through complex processes and quality control standards which only a few companies can achieve. Since the adjuvants formulated in vaccine are designed to be used in healthy population, it requires higher manufacturing techniques and more stringent regulatory standards. There are only five novel adjuvants applied in FDA-approved human vaccines, namely AS01, AS03, AS04, CpG1018, and MF59.

Figure 54: FDA-approved vaccine adjuvants

Licensed adjuvanted pediatric and adult vaccines				
Adjuvant	**Vaccines**	**Vaccine type**	**Company**	**First use**
Alum	Daptacel (DTaP), Gardasil 9 (HPV), Prevnar 13 (pneumococcal), etc.	Various	Various	1926
Licensed adjuvanted adult vaccines				
Adjuvant	**Composition**	**Vaccines**	**Difficulty in manufacturing**	**FDA Approval**
AS04 by GSK	Monophosphoryl lipid A (MPL)	Cervarix (HPV 16/18 vaccine)	Separation and purification of lipopolysaccharide (MPL's raw material) is difficult	2009
AS03 by GSK	Oil in water emulsion composed of α tocopherol, squalene and surfactant Tween 80	Q-Pan H5N1 (Influenza A H5N1 vaccine)	Natural sources of tocopherol and squalene are limited, while artificial synthesis is either cumbersome or with low yield	2013
MF59 by Seqirus	Squalene and Tween 80 and Span 85 (two surfactants) in an oil in water emulsion	FLUAD (Influenza vaccine)	Natural sources of squalene are limited, while artificial synthesis is either cumbersome or with low yield	2015
AS01 by GSK	Monophosphoryl lipid A (MPL), and QS 21, a natural compound extracted from the Chilean soapbark tree, combined in a liposomal formulation	Shingrix (Herpes Zoste vaccine)	Natural sources of QS 21 is limited; Separation and purification of lipopolysaccharide (MPL's raw material) is difficult	2017
CpG1018 by Dynavax	CpG ODN (cytosine phosphoguanosine oligodeoxynucleotide, microbial derivations)	Heplisav B (HBV vaccine)	Synthesis and purification of nucleic acid are required in production	2017

Source: Bali P, Nature Review 2021, CMBIGM

Due to the complexity in developing and manufacturing of adjuvants, most vaccine companies do not have commercial manufacturing capability for adjuvants thus rely on qualified suppliers. Vaccine companies with adjuvant manufacturing capability are thus enjoy advantages in terms of scalability.

Lengthy process of vaccine development

Vaccine development process is lengthy and costly, which follows the same procedures as drug development (target identification, preclinical assessment, clinical development, etc.). However, vaccine Ph III trials typically require large size and long duration for confirmation of safety and efficacy.

Figure 55: Process of vaccine development activity

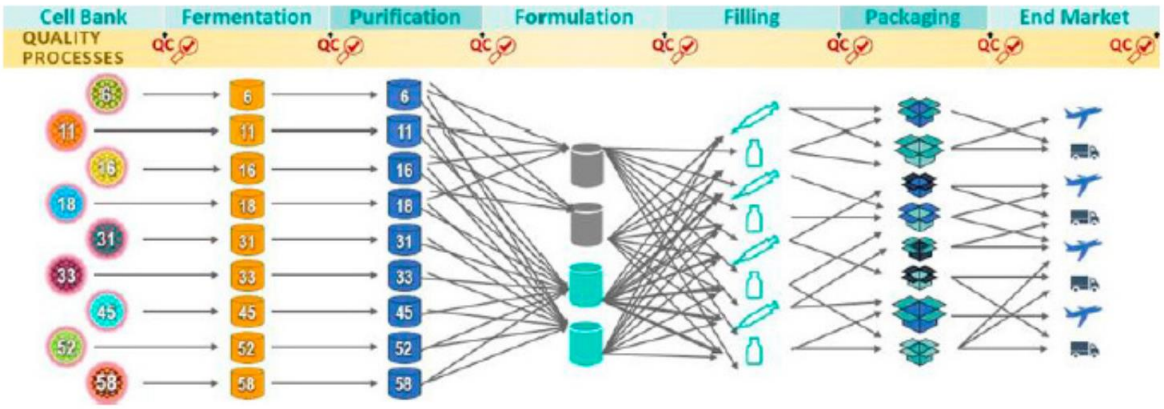
Clinical trials	Post-licensure safety	Manufacturing	Regulatory	Vaccination implementation
• Long-term follow-up of cohorts for effectiveness up to at least 10 years • Trials for new indications: adults>26 years of age, oropharyngeal cancer, alternative dosing regimens in young adolescents • Local registration trials (China, Japan, Vietnam)	• Routine pharmacovigilance • Post-authorization safety study in >200,000 individuals • Pregnancy registry • Periodic safety update reports to regulatory agencies	• Manufacturing improvements and efficiencies to keep process optimized and incorporate advances in science and manufacturing methods to ensure consistent supply • Build new facilities, initiate manufacturing, file regulatory applications and gain approval to expand manufacturing capacity.	• Supplemental applications and obtain approval • Post-marketing commitments • In additional countries and obtain approval • License renewal where required • Products label updates	• Generate and share scientific information to support vaccine recommendations by National Immunization Technical Advisory Groups (NITAG) and assist Health Technology Assessment (HTA) agencies for improved vaccine uptake • Partner with health authorities to address vaccine hesitancy

Source: Merck, CMBIGM

Challenges in vaccine manufacturing

Vaccine manufacturing is a multistep process (large-scale cell culture, harvest, purification, formulation and filling). Taking HPV vaccines as an example, hundreds of analytical tests are completed before the vaccine is released to the market. HPV vaccine antigens are large complex molecules, which requires 360 HPV L1 proteins self-assembled into VLPs, produced by inherently variable biotechnological processes. VLP corresponding to each HPV type are produced separately in early manufacturing stages (cell bank, fermentation, purification), then combined into a single vaccine process in the formulation stage. Thus, producing vaccines at commercial scale requires sophisticated manufacturing facilities, highly skilled manufacturing workforce and rich knowhows.

Figure 56: Process of HPV 9-valent vaccine manufacturing



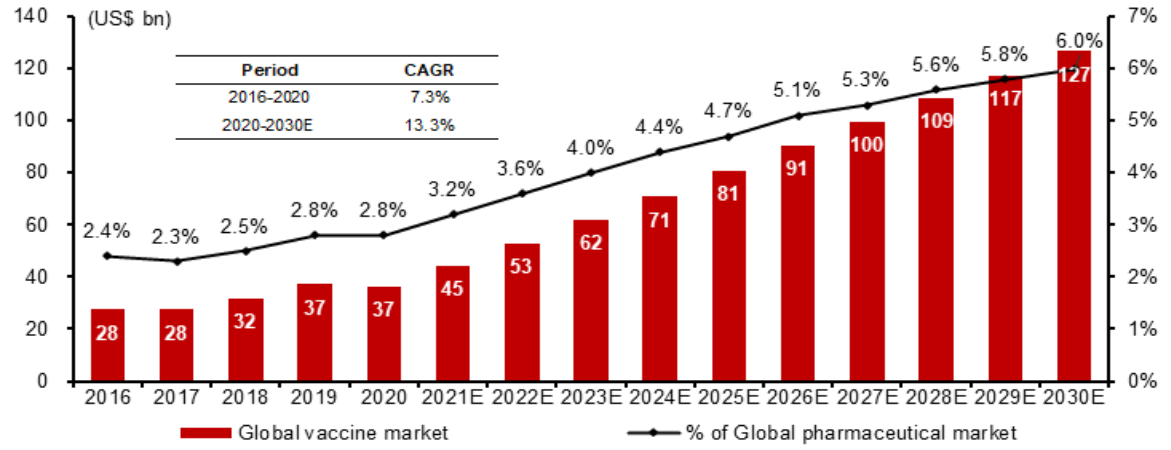
Source: Merck, CMBIGM

Regulatory authorities license not only the vaccine entity, but also the manufacturing facilities and processes used for the production, testing and release of the vaccine. Changes to manufacturing processes or facilities often require validation, regulatory review and approval which can take from several months to several years. Meanwhile, there may also be country-specific regulations, making manufacturing and distribution extraordinarily complex and limits flexibility of inventory.

Overview of global vaccine market

Global vaccine market has grown from US$27.5bn in 2016 to US$36.5bn in 2020 at a CAGR of 7.3%, accounting for 2.8% of the total global pharmaceutical market, according to F&S. Constantly driven by the development of innovative vaccines, as well as market growth in developing countries, global vaccine market is expected to reach US$126.8bn 2030E at a CAGR of 13.3% from 2020 to 2030E.

Figure 57: Global vaccine market by sales (2016-2030E)



Source: F&S, CMBIGM

Among the global top 10 best-selling vaccines, 8 are innovative vaccines. Recombinant protein vaccines are one of the most efficacious, safe and relatively inexpensive options, and have been used in various disease areas, such as hepatitis B, cervical cancers and shingles. MSD's HPV vaccine franchise, Gardasil and Gardasil 9, generated a total global sale of US$3.9bn in 2020, according to F&S.

Figure 58: Worldwide sales of global top 10 bestselling vaccines

Ranking	Vaccine	Virus/infection	Company	2018 (US$ mn)	2019 (US$ mn)	2020 (US$ mn)	Innovative vaccine
1	Prevnar13 / Prevenar 13	Pneumococcal	Pfizer	5,802	5,847	5,850	✓
2	Gardasil / Gardasil 9	HPV	MSD	3,151	3,737	3,938	✓
3	Influenza Vaccines	Influenza	Sanofi	2,015	2,118	2,819	✓
4	Shingrix	Shingles	GSK	1,045	2,311	2,552	✓
5	Polio/Pertussis/Hib Vaccines	Polio	Sanofi	2,064	2,179	2,402	✓
6	ProQuad/M-M-R II/Varivax	Measles, mumps, rubella, and varicella	MSD	1,798	2,275	1,878	-
7	Pneumovax 23	Pneumococcal	MSD	907	926	1,087	✓
8	Fluarix, FluLaval	Influenza	GSK	–	691	940	-
9	Bexsero	Meningitis B	GSK	–	867	834	✓
10	Infanrix, Pediarix	Diphtheria, tetanus, pertussis, infections caused by hepatitis B virus, and poliomyelitis	GSK	907	936	807	✓

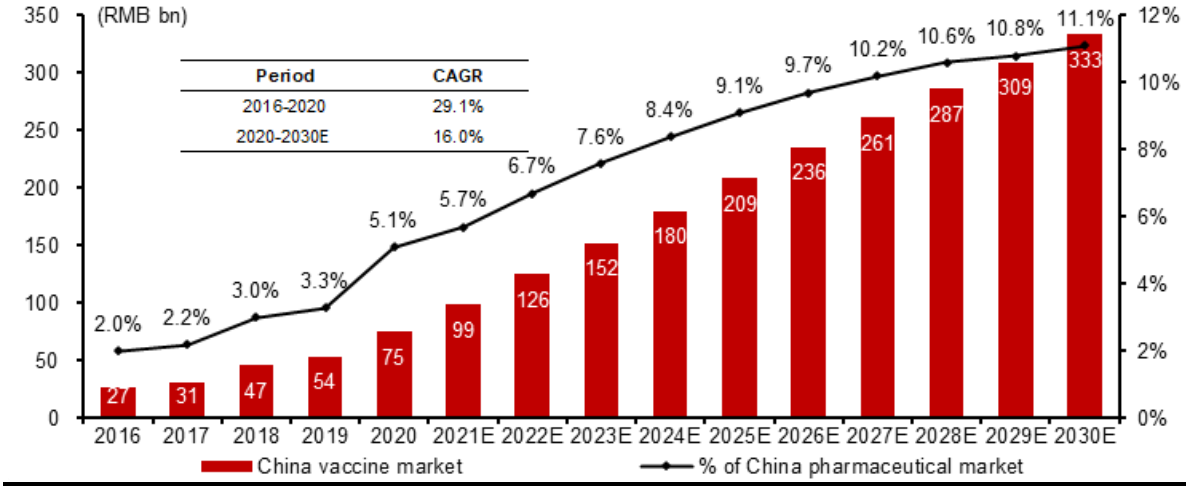
Source: F&S, CMBIGM

Demand for vaccines, especially innovative vaccines significantly exceed the supply in developing countries. Only less than 30% of low-middle income countries have included HPV vaccines into their national immunization schedules, while more than 85% of high-income countries have done so. Moreover, HPV vaccination rate varies significantly across countries, with 60% in Americas, compared to 5% in South East Asia, and less than 1% in China.

Overview of China vaccine market

Driven by favorable government policies, innovations in vaccine technologies, increasing availability of innovative vaccines, and rising awareness of vaccination, China's vaccine market by production value is expected to grow from RMB75.3bn in 2020 to reach RMB333.3bn in 2030E at a CAGR of 16.0% from 2020 to 2030E, according to F&S.

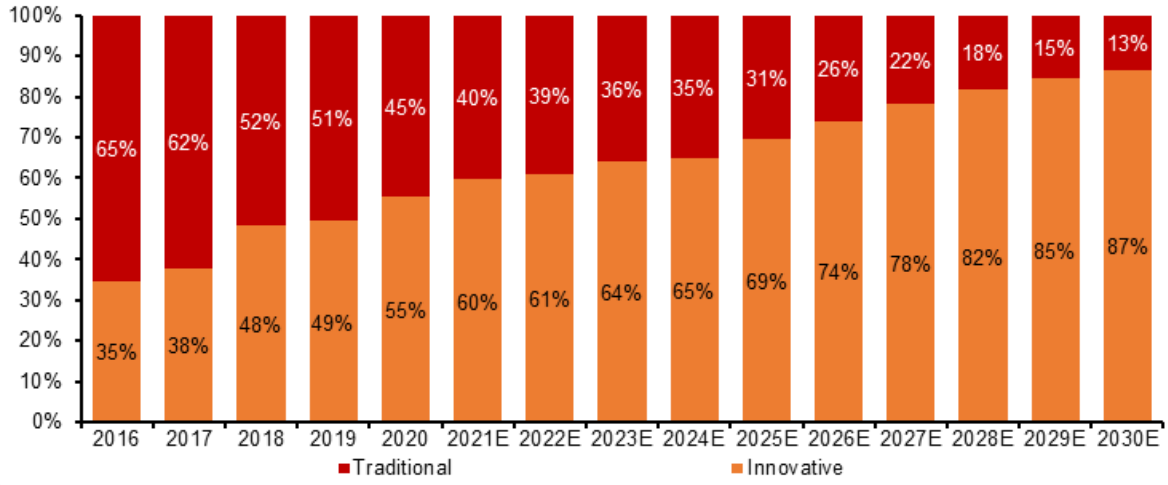
Figure 59: China vaccine market by production value (2016-2030E)



Source: F&S, CMBIGM

According to F&S, market share of innovative vaccines in China, in terms of production value, has increased significantly, from 34.7% in 2016 to 55.4% in 2020, which is expected to further increase to 86.6% in 2030E.

Figure 60: Breakdown of China vaccine market by production value (2016-2030E)



Source: F&S, CMBIGM

We think China's vaccine market are fueled by:

1) Innovation and availability of vaccines. Driven by the novel vaccine technologies, innovative vaccines have become crucial in propelling the overall vaccine market, which leads to development of vaccines of greater clinical value.

2) Favorable government policies. The Chinese health authority has increasingly expanded national immunization program, exemplified by reimbursement of Class II vaccines (i.e. self-paid vaccines) by certain local governments in recent years.

3) Increasing affordability and awareness of vaccines. We think the greater vaccination rate is driven by increasing disposable income, and improved health literacy, and general vaccination awareness fueled by the COVID pandemic.

4) Increasing supply of domestic vaccines. With increasing government incentives to spur production of domestic innovative vaccines, according to "Opinions on Further Strengthening Vaccine Circulation and Vaccination Management" (《关于进一步加强疫苗流通和预防接种管理工作的意见》), we expect continued market consolidation with growing vaccine supply by domestic players.

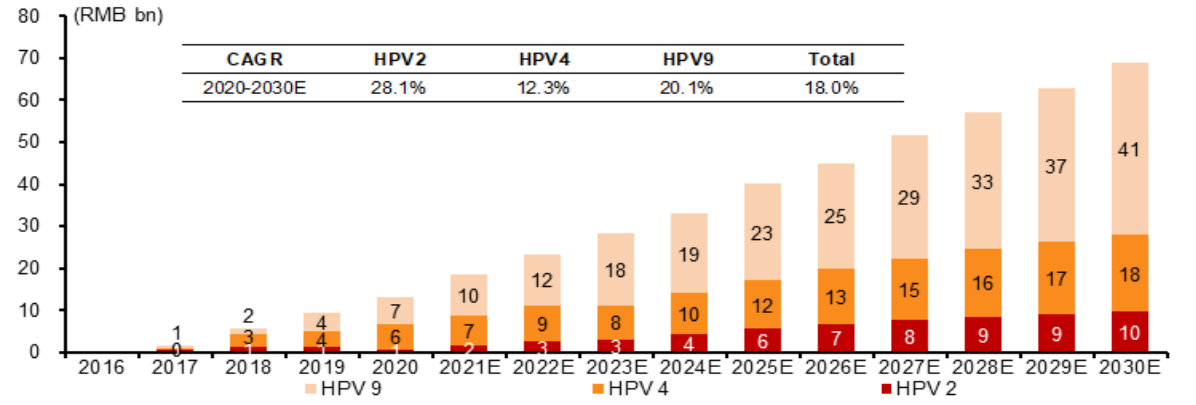
Overview of HPV vaccine market

Human papillomavirus (HPV) is the most common pathogen of reproductive tract. Although most HPV infections may clear up within a few months without any intervention, certain infections can persist and progress to cervical cancer. There are more than 100 types of HPV, of which at least 14 types (16, 18, 31, 45, 33, 35, 39, 51, 52, 56, 58, 66, 68, 70) are cancer-causing as high-risk types. Two HPV types (16 and 18) cause 70% of cervical cancers or pre-cancerous cervical lesions, according to WHO.

In 2020, WHO issued "Global Strategy to Accelerate the Elimination of Cervical Cancer", which recommended 90% of girls to be fully vaccinated by HPV vaccine by age 15 by 2030. In China, National Health Commission (NHC) has formulated "Healthy China Initiative—Implementation Plan for Cancer Prevention and Treatment (2019-2022)", which emphasizes the broader promotion of HPV vaccination to accelerate the elimination of cervical cancer. In Dec 2020, NHC stated strong support to accelerate the elimination of cervical cancer, implying a potential near-term plan of HPV vaccines being included in Expanded Program on Immunization in China.

Ever since the first HPV vaccine was approved in China in 2017, China's HPV vaccine market has grown significantly to RMB13.1bn in 2020, which is expected to reach RMB69.0bn in 2030E, representing a 2020-2030E CAGR of 18.0%, according to F&S. Among the HPV vaccine market, the 9-valent HPV vaccine is expected to take the largest market share in 2030E. On the other hand, the HPV bivalent vaccine market is expected to experience the most rapid growth thanks to its better affordability and thus greater accessibility in larger population.

Figure 61: Breakdown of China HPV vaccine market by vaccine type (2016-2030E)



Source: F&S, CMBIGM

We believe China's HPV vaccine market will be driven by following factors:

1) High burden of cervical cancer. Meanwhile, the five-year survival rate of cervical cancer in China is only 12.9% when the cancer is at the stage of distant metastasis. The mortality number of cervical cancer in China was 59.1 thousand in 2020. Globally, there were 604.1 thousand confirmed cervical cancer cases and 341.8 thousand deaths in 2020, respectively. Such high disease burden of cervical cancer will drive the growth of China's HPV market.

2) Favorable global strategies and domestic policies. WHO announced the Global Strategy to Accelerate the Elimination of Cervical Cancer in November 2020, with the objective of complete 90% HPV vaccination for the girls before age of 15 by 2030. Similarly, the Department of Maternal and Child Health of the National Health Commission stated that China will fully support the Strategy in China. In response to the Strategy, the PRC government encouraged qualified provinces to include the HPV vaccine in the scope of public vaccination and a pilot program was officially launched in Ordos in April 2021.

3) Increasing vaccination rate. China's HPV vaccination rate is relatively low. According to the International Papillomavirus Society and Cancer Foundation of China, the awareness rate of HPV in China is only 30%, while the vaccination rate is less than 1%. However, with the continuous increased awareness for and acceptance of vaccination, especially after COVID-19, it is expected that more and more people in China will undergo early inoculation of HPV vaccines.

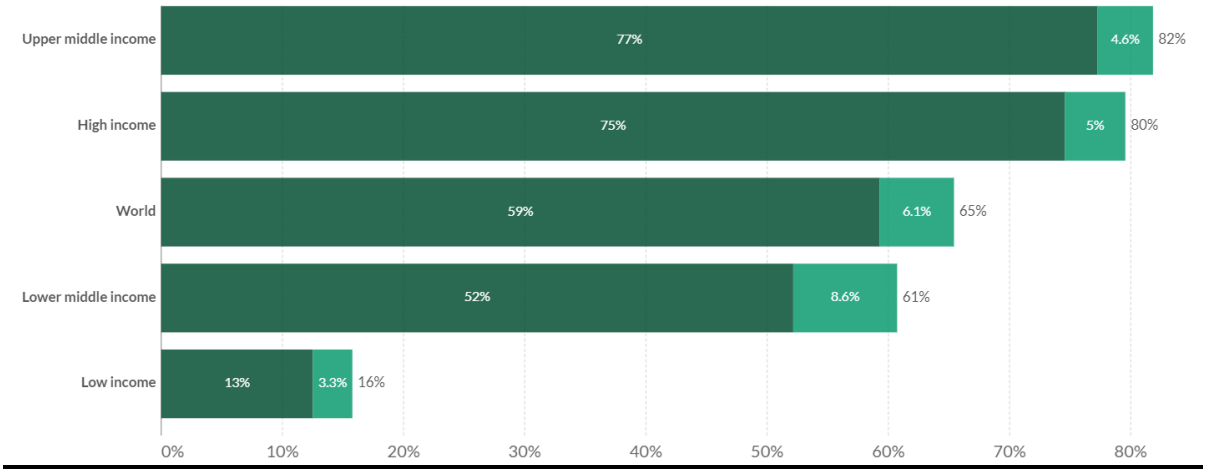
4) Domestic substitution. Currently, China's HPV vaccine market is primarily dominated by imported products. Nevertheless, several PRC companies are developing HPV vaccines, some of which have reached ph III clinical trials or obtained marketing approval. These domestic vaccines and vaccine candidates are proven to have non-inferior efficacy and safety profile compared to imported products, while their prices are generally cheaper. As such, it is expected that these domestic HPV vaccines will account for a larger market share going forward. In addition, the R&D of innovative adjuvants is expected to drive the upgrade of HPV vaccine candidates to achieve better clinical performance, thus facilitate the growth of the HPV vaccine market.

Overview of COVID-19 vaccine market

As of May 4, 2022, there have been ~514.8mn confirmed COVID-19 cases globally, including approximately 6.3mn reported deaths, as per worldometer. As of May 3, 2022, high-income and upper middle-income countries have achieved vaccination rate more than 80% on average, whereas that of low-income countries remain as low as ~16%.

According to F&S, at least 89.2% of the global population will need to be vaccinated with a vaccine of 70% efficacy to reach herd immunity, indicating a considerable demand of COVID-19 vaccines.

Figure 62: Relative between vaccination status and income (as of May 3, 2022)

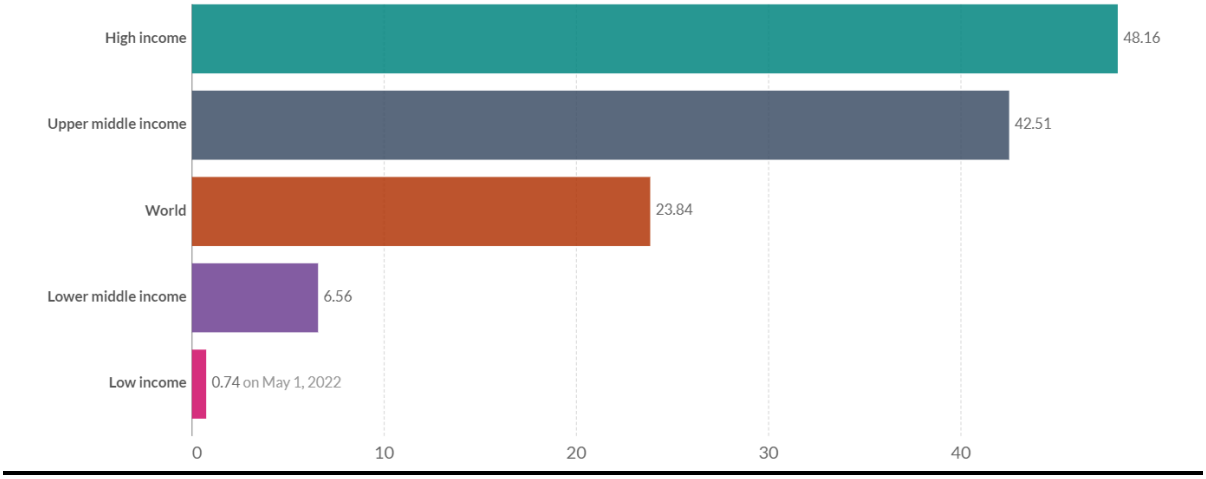


Source: Our World in Data, CMBIGM
Note: alternative definitions of a full vaccination, e.g. having been infected with SARS-CoV-2 and having 1 dose of a 2-dose protocol, are ignored to maximize comparability between countries.

On Sep 22, 2021, the FDA amended the EUA for the Pfizer-BioNTech COVID-19 vaccine to allow for use of a single booster dose for certain populations. On Oct 20, 2021, the FDA amended the EUA for the Moderna COVID-19 vaccine and the EUA for the Janssen COVID-19 vaccine (Johnson & Johnson) to allow for use of a single booster dose for certain populations. On Mar 29, 2022, FDA also authorized a second booster dose of either the Pfizer-BioNTech or the Moderna COVID-19 vaccines for older people and certain immunocompromised individuals.

To date, several mutant strains of SARS-CoV-2 have emerged, generates vaccination of the booster dose vaccines. The rate of people receiving COVID-19 vaccine boosters in high income countries is now far lagged behind the number getting their first two shots, according to our world in data. As of May 1st, only 0.74% of population has been vaccinated with booster in low-income countries, indicating huge market opportunity for easy-storage, cost-effective recombinant COVID vaccines.

Figure 63: COVID-19 vaccine booster doses administered per 100 people (as of May 3, 2022)



Source: Our World in Data, CMBIGM

There are five technical pathways COVID-19 vaccines could adopt, including recombinant protein vaccines, inactivated vaccines, viral vector vaccines, mRNA vaccines and DNA vaccines.

Figure 64: Key features of various types of COVID-19 vaccines

Platform	Target	Authorized COVID-19 Vaccine	Advantages	Disadvantages
Protein-based Subunit Vaccines	S protein	Yes	• No infectious virus needs to be handled; • Production can be rapidly scaled-up to large quantities using well-characterized manufacturing processes; • Adjuvants can be used to increase immunogenicity.	• Global production capacity might be limited; • Antigen and/or epitope integrity needs to be confirmed.
Inactivated Vaccines	Whole virion	Yes	• Straightforward process used for several licensed human vaccines; • Existing infrastructure can be used; • Has been tested in humans for SARSCoV-1; • Adjuvants can be used to increase immunogenicity.	• Large amounts of infectious virus need to be handled, which may lead to biosafety issue; • Antigen and/or epitope integrity needs to be confirmed.
Adenovirusbased Viral Vector Vaccines	S protein	Yes	• No infectious virus needs to be handled; • Strong preclinical and clinical data for many emerging viruses, including MERS-CoV.	• Vector immunity might negatively affect vaccine effectiveness (depending on the vector chosen).
mRNA Vaccines	S protein	Yes	• No infectious virus needs to be handled; • Vaccines are typically immunogenic; • Rapid production possible.	• Safety issues with reactogenicity have been reported; • Delivery and storage challenge such as tight temperature control and avoidance of shock and vibration.
DNA Vaccines	S protein	No	• No infectious virus needs to be handled; • Easy scale up, low production costs; • High heat stability; • Tested in humans for SARS-CoV-1 virus; • Rapid production possible.	• Vaccine needs specific delivery devices to reach good immunogenicity; • No approved vaccines for human use developed using this platform.

Source: Company data, CMBIGM

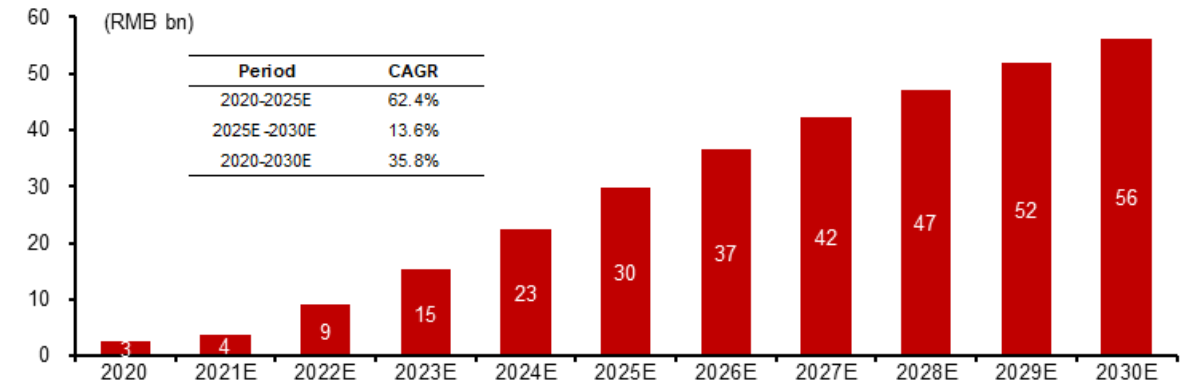
To date, there were at least 24 COVID-19 vaccines on the market, including five recombinant protein vaccines and 52 candidates in phase III or later stage globally. There are in total 146 COVID-19 vaccines candidates under clinical development, including 47 recombinant protein vaccines. Among all of the recombinant protein COVID-19 vaccines under commercialization or clinical trial, ReCOV is the only one that targets a specific combination of NTD and RBD as an immunogen.

Overview of shingles vaccine market

Shingles is caused by reactivation of latent infection of varicella-zoster virus (VZV). This reactivation occurs when immunity to VZV declines due to aging or immunosuppression. Herpes zoster can occur at any age but most commonly affects the elderly population. Active shingles are infectious through direct contact with fluid. Symptoms of shingles usually include rash, pain, itching in infected areas.

Driven by growing awareness of shingles and the increasing availability of shingles vaccine products, China's shingles vaccine market is expected to grow from RMB2.6bn in 2020 and to reach RMB56.2bn in 2030E at a 2020-2030E CAGR of 35.8%, as per F&S.

Figure 65: China shingles vaccine market, by production value (2020-2030E)

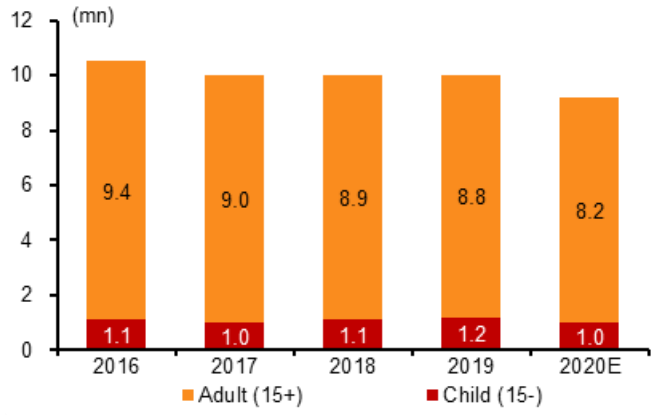


Source: F&S, CMBIGM

Overview of adult tuberculosis (TB) vaccine market

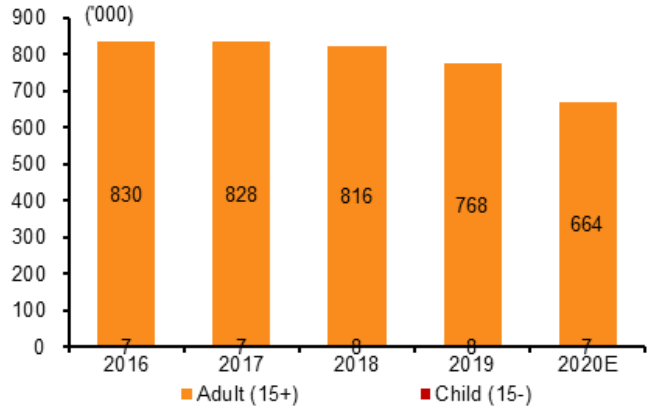
Tuberculosis (TB) is a communicable disease caused by bacterium called mycobacterium tuberculosis, which can spread in the air, such as by coughing. According to the WHO, TB ranks the first among infectious diseases by number of deaths in 2019 globally. There were 10mn of new active TB cases worldwide in 2019, 90% of which were adults. China is among the WHO-listed 30 high TB burden countries with the third highest incidence of 775,800 cases in 2019.

Figure 66: Global incidence of active TB (2016-2020E)



Source: WHO, China CDC, F&S, CMBIGM

Figure 67: China incidence of active TB (2016-2020E)



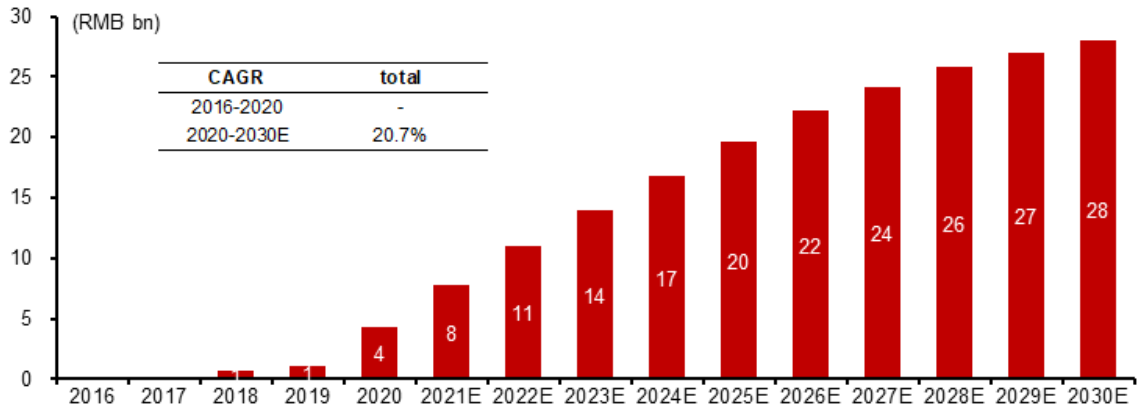
Source: WHO, China CDC, F&S, CMBIGM

Overview of influenza (flu) vaccine market

Influenza is a contagious respiratory illness caused by influenza viruses that infect the nose, throat, or the lungs. It may develop severe complications vulnerable group such elderly people aged over 65, children or people with chronic medical conditions. We think annual flu vaccination is by far the best way to prevent flu infection, according to CDC. There were approximately 1.1mn new influenza cases and 70 deaths in China in 2020, according to the National Bureau of Disease Control and Prevention.

Ever since the approval of first Quadrivalent Influenza Vaccine ("QIV") by NMPA in 2018, China's QIV market has grown to RMB4.3bn in 2020, which is expected to reach RMB28.0bn by production value in 2030E, at a 2020-2030E CAGR of 20.7%, according to F&S.

Figure 68: China QIV Market, by production value (2016-2030E)



Source: NICPBP, F&S

Overview of HFMD vaccine market

HFMD is a mild, contagious disease caused by viral infection. HFMD is mostly common in children under five years old, causing sores in the mouth and rashes on the hands and feet. HFMD has the fourth highest incidence in China among notifiable infectious diseases, with more than 760,000 cases reported in 2020.

Common viruses of HFMD include Enterovirus 71 (EV71), Coxsackievirus A16 (CA16), Coxsackievirus A10 (CA10) and Coxsackievirus A6 (CA6), causing approximately 90% of HFMD cases in China. EV71 inactivated vaccine is by far the only HFMD vaccine approved globally and in China. In China, EV71 only caused 44% of the HFMD cases. China's EV71 vaccine market in terms of production value amounted to RMB2.7bn in 2020, which is expected to reach RMB4.6bn in 2030E, according to F&S. With the development of recombinant protein quadrivalent vaccine that can address EV71, CA16, CA10 and CA6, China's HFMD vaccine market will experience rapid growth in the future.

Financial Analysis

Vaccine sales to start from 2022E

To factor in the risk in drug development, we apply different probability of success (PoS) to our sales forecasts. We expect Recbio to file EUA of its first product, ReCOV, in 2022E. We forecast ReCOV to contribute sales from 2022E and expect risk-adjusted revenue of RMB155mn/ RMB1,789mn/ RMB1,474mn in FY2022E/ 23E/ 24E. We forecast Recbio to submit BLA applications of its HPV vaccine candidates, REC603, REC601, and REC602, to the NMPA by 2025E and to file BLA of its shingles vaccine candidate REC610 in 2024E.

Figure 69: Risk-adjusted revenue forecasts (2022 - 26E)

(YE 31 Dec) RMB mn	2022E	2023E	2024E	2025E	2026E
HPV 9-valent vaccine (REC603)	**0**	**0**	**0**	**0**	**250**
New adjuvant HPV 9-valent vaccine (REC604b)	**0**	**0**	**0**	**0**	**205**
HPV bivalent vaccine (REC 601)	**0**	**0**	**0**	**0**	**251**
New adjuvant 4-valent HPV vaccine (REC604a)	**0**	**0**	**0**	**0**	**75**
Recombinant Covid-19 vaccine (global) (ReCOV)	**155**	**1,789**	**1,401**	**796**	**0**
Recombinant shingles vaccine (REC610)	**0**	**0**	**0**	**412**	**1,884**
Adult tuberculosis vaccine (REC607&606)	**0**	**0**	**0**	**28**	**274**
4-valent influenza vaccine (REC617)	**0**	**0**	**74**	**740**	**1,421**
4-valent hand, foot and mouth vaccine (REC605)	**0**	**0**	**0**	**137**	**479**
Others	**0**	**0**	**0**	**0**	**0**
Total revenue	**155**	**1,789**	**1,474**	**2,113**	**4,839**

Source: Company data, CMBIGM estimates

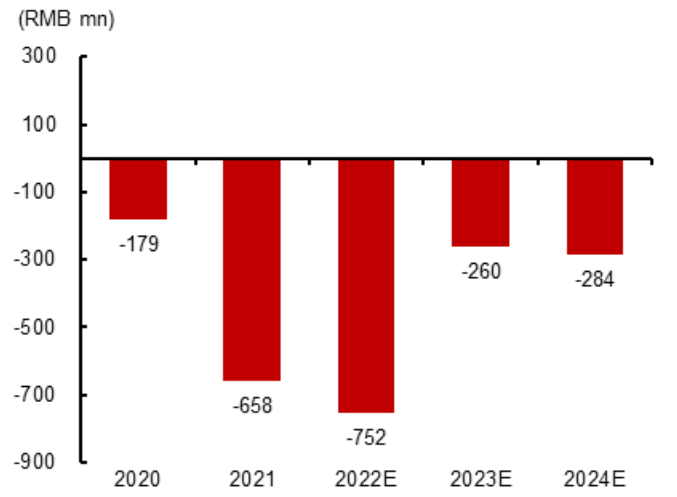
Recbio recorded net losses of RMB179mn/ RMB658mn in FY20A/ 21A. We expect the Company to continue incur net losses of RMB752mn / RMB260mn/ RMB284mn in FY22E/ 23E/ 24E.

Figure 70: P&L forecasts (2019-23E)

(YE 31 Dec) RMB mn	2020	2021	2022E	2023E	2024E
Revenue	**0**	**0**	**155**	**1,789**	**1,474**
YoY				*1051.98%*	*-17.58%*
Cost of sales	0	0	-54	-608	-487
% of revenue			*-35.00%*	*-34.00%*	*-33.00%*
Gross profit	**0**	**0**	**101**	**1,181**	**988**
GPM			*65.00%*	*66.00%*	*67.00%*
Other income and gains	10	28	26	27	22
% of revenue			*16.74%*	*1.48%*	*1.48%*
Selling & marketing expense	0	-3	-20	-590	-472
% of revenue			*-12.88%*	*-33.00%*	*-32.00%*
Administrative expenses	-18	-143	-180	-198	-218
% of revenue			*-115.90%*	*-11.07%*	*-14.77%*
Research and development costs	-131	-473	-650	-600	-500
% of revenue			*-418.54%*	*-33.54%*	*-33.91%*
Other expenses	-3	-10	0	0	0
% of revenue			*0.00%*	*0.00%*	*0.00%*
Finance costs	-37	-56	-29	-79	-104
% of revenue			*-18.57%*	*-4.41%*	*-7.04%*
Profit (Loss) before tax	**-179**	**-658**	**-752**	**-260**	**-284**
% of revenue			*-484.16%*	*-14.53%*	*-19.24%*
Income tax expense	0	0	0	0	0
% tax rate			*0.00%*	*0.00%*	*0.00%*
Profit (Loss) for the year	**-179**	**-658**	**-752**	**-260**	**-284**
Minority Interests	0	0	0	0	0
Net profit attributable to shareholders	**-179**	**-658**	**-752**	**-260**	**-284**
NMP			*-484.16%*	*-14.53%*	*-19.24%*

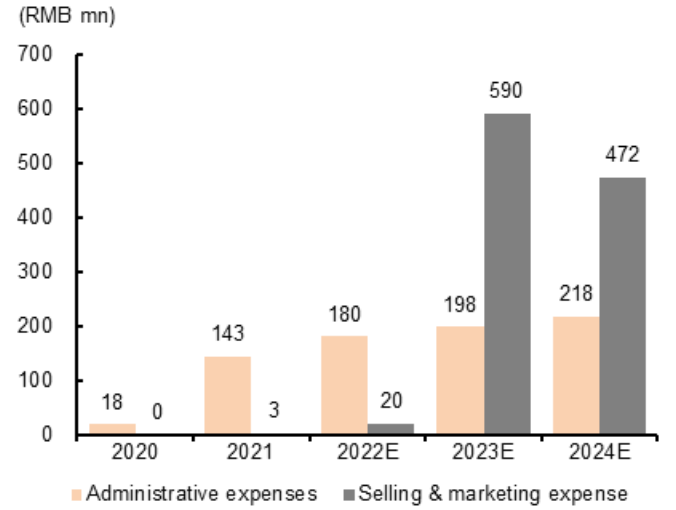
Source: Company data, CMBIGM estimates

Figure 71: Net profit forecasts (2020-24E)



Source: Company data, CMBIGM estimates

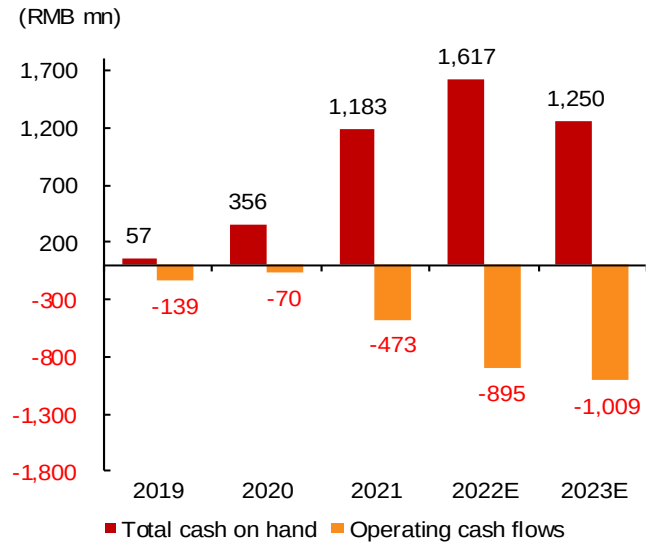
Figure 72: SG&A expenses forecasts (2020-24E)



Source: Company data, CMBIGM estimates

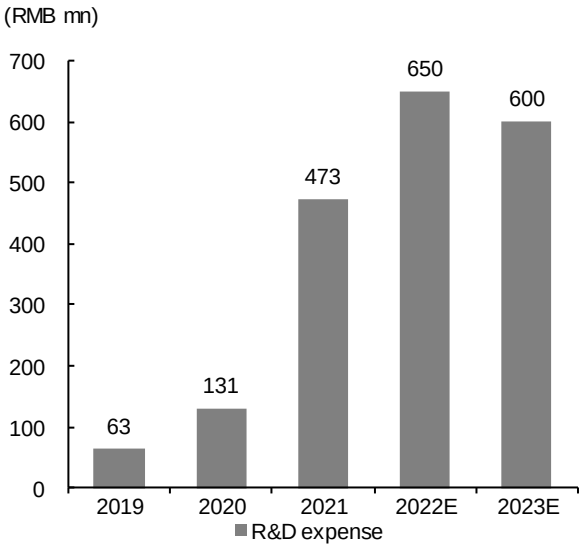
We forecast R&D expenses to climb from RMB131mn/ RMB473mn in FY20A/ 21A to RMB650mn/ RMB600mn/ RMB500mn in FY22E/ 23E/ 24E, mainly due to initiation of new clinical trials and progress of existing clinical trials.

Figure 73: Cash and operating cash flows (2020-24E)



Source: Company data, CMBIGM estimates

Figure 74: R&D expenses (2020-24E)



Source: Company data, CMBIGM estimates

Valuation

Initiate at BUY with TP of HK$38.79

As a pre-revenue company, Recbio relies on future cash flows of vaccine sales. We derive our target price of HK$38.79 based on a 14-year DCF model (WACC: 12.5%, terminal growth rate: 2.0%).

Figure 75: Base case risk-adjusted DCF valuation (terminal growth rate: 2.0%)

DCF Valuation (in Rmb mn)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	-744	-203	-197	185	745	2,040	3,455	4,757	5,373	5,666	5,936	5,972	5,955	5,897
Tax rate	0.0%	0.0%	0.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
EBIT*(1-tax rate)	-744	-203	-197	157	634	1,734	2,937	4,043	4,567	4,816	5,046	5,076	5,062	5,012
+ D&A	39	51	58	65	71	77	83	88	93	98	103	108	112	116
- Change in working capital	-190	-858	173	-321	-1,380	-2,186	-2,021	-1,337	-255	-187	-142	-51	25	85
- Capex	-300	-300	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200
FCFF	**-1,195**	**-1,309**	**-165**	**-299**	**-876**	**-575**	**799**	**2,594**	**4,205**	**4,528**	**4,807**	**4,932**	**4,998**	**5,013**
Terminal value														**48,765**

Terminal growth rate	**2.0%**
WACC	**12.5%**
Cost of Equity	15.7%
Cost of Debt	6.0%
Equity Beta	1.10
Risk Free Rate	3.0%
Market Risk Premium	11.5%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%
Terminal value (RMB mn)	9,393
Total PV (RMB mn)	15,008
Net debt (RMB mn)	-540
Minority interest (RMB mn)	-0
Equity value (RMB mn)	**15,548**
# of shares (mn)	483
Price per share (RMB)	32.19
Price per share (HK$)	**38.79**

Source: CMBIGM estimates

Figure 76: Sensitivity analysis (HK$)

Terminal growth rate	WACC				
	11.5%	12.0%	12.5%	13.0%	13.5%
3.0%	50.50	45.72	41.51	37.78	34.46
2.5%	48.51	44.04	40.08	36.56	33.41
2.0%	46.72	42.52	**38.79**	35.45	32.46
1.5%	45.12	41.15	37.61	34.44	31.58
1.0%	43.66	39.91	36.54	33.51	30.77

Source: CMBIGM estimates

Financial Statements

Income statement

YE Dec 31 (RMB mn)	FY20A	FY21A	FY22E	FY23E	FY24E
Revenue	**0**	**0**	**155**	**1,789**	**1,474**
Cost of sales	0	0	-54	-608	-487
Gross profit	**0**	**0**	**101**	**1,181**	**988**
Other income and gains	10	28	26	27	22
Selling & marketing expense	0	-3	-20	-590	-472
Administrative expenses	-18	-143	-180	-198	-218
Research and development costs	-131	-473	-650	-600	-500
Other expenses	-3	-10	0	0	0
Finance costs	-37	-56	-29	-79	-104
Profit before tax	**-179**	**-658**	**-752**	**-260**	**-284**
Income tax expense	0	0	0	0	0
Net profit (loss)	**-179**	**-658**	**-752**	**-260**	**-284**
Minority Interests	0	0	0	0	0
Profit attributable to shareholders	**-179**	**-658**	**-752**	**-260**	**-284**

Cash flow summary

YE Dec 31 (RMB mn)	FY20A	FY21A	FY22E	FY23E	FY24E
Profit before tax	**-179**	**-658**	**-752**	**-260**	**-284**
Depreciation of PP&E	7	15	34	47	54
Depreciation of right-of-use assets	6	8	5	5	4
Working capital changes	64	-19	-190	-858	173
Other operating activities	32	181	8	57	87
Net cash from operating activities	**-70**	**-473**	**-895**	**-1,009**	**35**
Purchase of PP&E	-138	-238	-300	-300	-200
Other investing activities	-120	307	21	22	17
Net cash from investing activities	**-259**	**69**	**-279**	**-278**	**-183**
Interest paid	0	0	-29	-79	-104
Proceeds from shares issued	0	0	638	0	0
Other financing activities	680	1,229	1,000	1,000	0
Net cash from financing activities	**680**	**1,229**	**1,609**	**921**	**-104**
Net change in cash	351	825	434	-367	-252
Cash at the beginning of the year	7	356	1,183	1,617	1,250
FX changes	-3	-8	0	0	0
Cash at the end of the year	**356**	**1,173**	**1,617**	**1,250**	**998**

Balance sheet

YE Dec 31 (RMB mn)	FY20A	FY21A	FY22E	FY23E	FY24E
Non-current assets	**338**	**625**	**886**	**1,134**	**1,276**
Property, plant and equipment	129	416	682	935	1,081
Right-of-use assets	58	55	50	46	42
Goodwill	9	9	9	9	9
Other intangible assets	22	22	22	22	22
Other non-current assets	120	122	122	122	122
Current assets	**709**	**1,295**	**1,827**	**2,713**	**2,200**
Inventories	8	24	45	492	387
Prepayments, other receivables and other assets	20	88	88	88	88
Financial assets at fair value through profit or loss ("FVTPL")	326	0	0	0	0
Cash and bank balances	356	1,183	1,617	1,250	998
Current liabilities	**57**	**139**	**47**	**441**	**354**
Trade payables	2	17	27	300	240
Other payables and accruals	51	115	12	133	107
Lease liabilities	4	8	8	8	8
Non-current liabilities	**1,998**	**107**	**1,107**	**2,107**	**2,107**
Interest-bearing bank borrowings	0	50	1,050	2,050	2,050
Redemption liabilities on owners' capital	1,953	0	0	0	0
Lease liabilities	22	19	19	19	19
Deferred income	18	32	32	32	32
Defer tax liabilities	6	6	6	6	6
Total equity	**-1,009**	**1,673**	**1,559**	**1,299**	**1,015**
Minority interest	0	0	0	0	0
Shareholders' equity	-1,009	1,673	1,559	1,299	1,015

Key ratios

YE Dec 31	FY20A	FY21A	FY22E	FY23E	FY24E
Profit & loss ratios (%)					
Gross margin	N/A	N/A	65	66	67
EBITDA margin	N/A	N/A	-454	-8	-9
Pre-tax margin	N/A	N/A	-484	-15	-19
Net margin	N/A	N/A	-484	-15	-19
Effective tax rate	0	0	0	0	0
Balance sheet ratios					
Current ratio (x)	12	9	39	6	6
Inventory days	N/A	N/A	300	295	290
Trade receivable days	N/A	N/A	180	180	180
Trade payables	N/A	N/A	180	180	180
Net debt to total equity ratio (%)	Net cash	Net cash	Net cash	64	106
Returns (%)					
ROE	N/A	-39	-48	-20	-28
ROA	-17	-34	-28	-7	-8

Source: Company data, CMBIGM estimates

Investment Risks

Facing competition

The development and commercialization of vaccines is highly competitive. There is intense and rapidly evolving competition in the biotechnology, disease prevention and vaccine fields. Recbio competes with a variety of multinational biopharmaceutical companies and developed vaccine companies, as well as vaccine research centers at universities and other research institutions.

Failures in clinical development activities

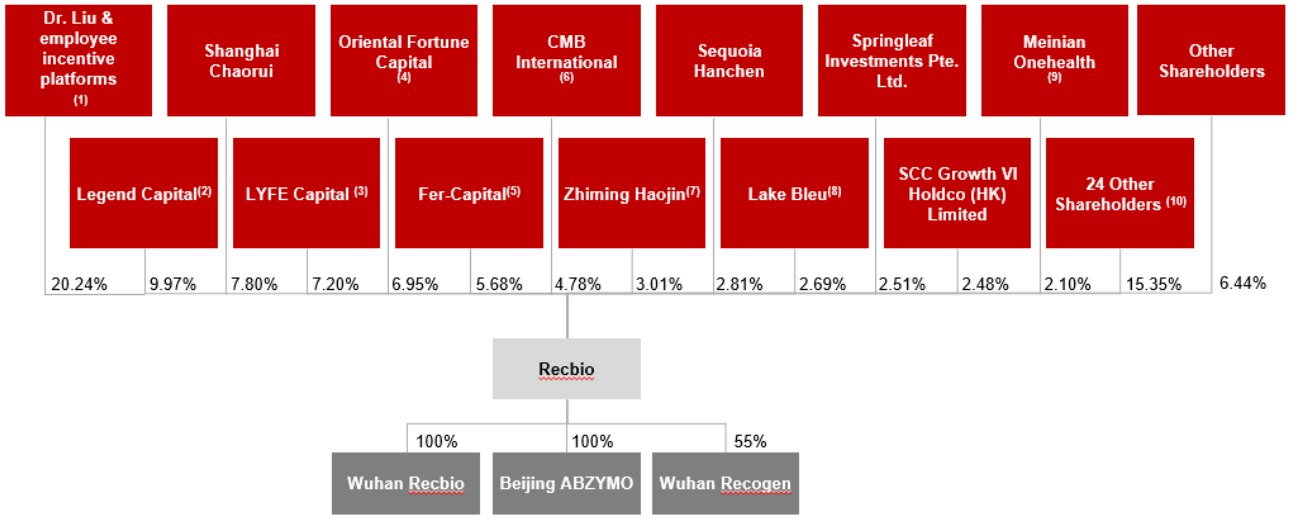
Vaccine development involves a lengthy and expensive process with uncertain outcomes and results of earlier clinical trials may not be predictive of results of later-stage clinical trials. Clinical testing is expensive and can take many years to complete, while its outcomes are inherently uncertain. Vaccine candidates during later stages of clinical trials may fail to show the desired outcomes in safety and efficacy despite having progressed through early-stage clinical trials, and of the level of scientific rigor in the study, design and adequacy of execution. Recbio exclusively focus on developing vaccine candidates with the potential to become transformative vaccines, but the Company cannot guarantee success for any of their vaccine candidates.

Risks relating to government regulation

A number of governmental agencies or industry regulatory bodies in China impose strict rules, regulations and industry standards governing vaccine and biotechnology research and development activities, which apply to Recbio. In addition, the Company is also subject to laws and regulations with respect to our overall operations. Recbio may be unable to comply with such laws and regulations as they continue to change and evolve, or due to differences in national, provincial or local laws and regulations, or their implementation or enforcement. The failure to comply with such regulations could result in the termination of ongoing research, administrative penalties imposed by regulatory bodies or the disqualification of data for submission to regulatory authorities.

Appendix: Company Profile

Figure 77: Shareholder structure (Post Global Offering)



Source: Company data, CMBIGM

Notes:

1) Dr. Liu, as the sole general partner of these employee ownership platforms, is able to exercise the voting rights of the Shares held by each of Taizhou Yuangong, Lianyungang.
2) Representing the shares held by Junlian Shengyuan, Junlian Yongshuo, Healthy Prestige Limited and Union Season Holdings Limited.
3) Representing the shares held by LYFE Niagara River Limited, Shanghai Jiyue and Shanghai Jixuan.
4) Representing the shares held by Fuhai Xincai Phase II, Fuhai Juanyong II, Fuhai Juanyong III, Qianhai Kekong Fuhai, Fuhai Youxuan II and OFC Small and Medium.
5) Representing the shares held by Shenzhen Yingkejin, Woyang Health, Woyang Phase II and Shenzhen Luewei, all of which are managed by Shenzhen Fer-Capital Investment Co., Ltd.. Fer-Capital is an associate of FENG Tao, and thus a core connected person of Recbio.
6) Representing the shares held by Zhaoyin Modern, Nanjing Zhenyuan and Nanjing Zhaoyin Gongying.
7) Representing the shares held by Ganzhou Haojin Zhiyuan and Haojin Zhitong.
8) Representing the shares held by LBC Sunshine Healthcare Fund II L.P. and Hengcui Investment LPF.
9) Representing the shares held by Jiangsu Jiequan and Jiangsu Zhongwei Tengyun.
10) Wuhai Recogen was owned as to 55%, 40% and 5% by the Company, Shenzhen Rhegen and Wuhan Aiweige, respectively, as of Mar 11, 2022.

Figure 78: Management profile

Name	Age	Date of Joining	Position	Roles and Responsibilities
Liu Yong (刘勇)	48	Mar 7, 2011	Chairman of the Board, Executive Director and General Manage	Overall management of business strategy, corporate development and R&D of our Group
Chen Jianping (陈健平)	43	Mar 1, 2018	Executive Director and Vice General Manager	Management of daily operations of R&D activities and the strategic development
Li Bu (李布)	45	Apr 1, 2020	Executive Director and Vice General Manager	Management of daily operations of administrative, human resources, purchasing and IT departments and the strategic development
Zhou Hongjun (周红军)	40	Aug 1, 2020	Vice General Manager	Management of quality system, production and technology
Chen Qingqing (陈青青)	38	Apr 6, 2021	Vice General Manager, CFO, and secretary of the Board	Management of financing activities, investor relationship, internal control, corporate governance, finance and legal department
Zhou Lei (周雷)	35	Mar 22, 2019	Finance Controller	Financial management

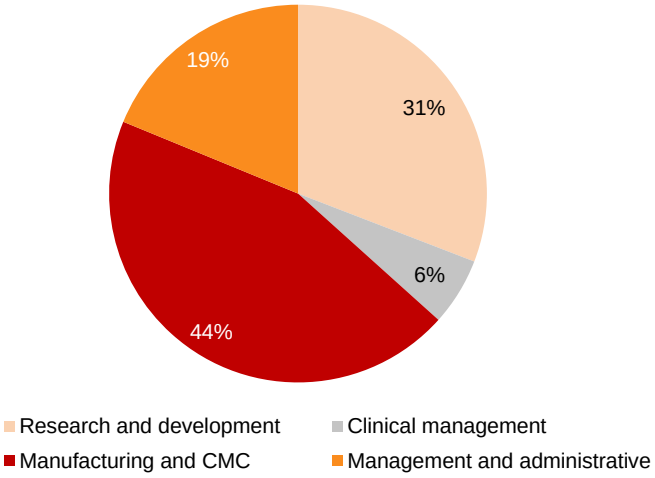
Source: Company data

Figure 79: Employee structure

Function	# of staff	% of Total
Research and development	133	31%
Clinical management	25	6%
Manufacturing and CMC	192	45%
Management and administrative	81	19%
Total	**431**	**100%**

Source: Company data (as of 11 Mar 2022)

Figure 80: Employee number breakdown



Source: Company data (as of 11 Mar 2022)

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