Opus Capital Limited 創富融資有限公司

September 30, 2024

To: the Independent Board Committee and
the Independent Shareholders of Qyuns Therapeutics Co., Ltd.

Dear Sir or Madam,

CONTINUING CONNECTED TRANSACTIONS IN RELATION TO THE DEVELOPMENT AND POTENTIAL COMMERCIALIZATION PARTNERSHIP OF QX005N WITH ZHONGMEI HUADONG

INTRODUCTION

We refer to our appointment by the Company to advise the Independent Board Committee and the Independent Shareholders in respect of the terms of the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the proposed annual caps of the Clinical Development and Registration Fee payable by Zhongmei Huadong to the Company for the three years ending December 31 ("**FY**"), 2026 (the "**Proposed Annual Caps**"), details of which are set out in the letter from the Board (the "**Letter from the Board**") contained in the circular of the Company dated September 30, 2024 (the "**Circular**"), of which this letter forms part. Capitalized terms used in this letter shall have the same meanings as those defined in the Circular unless the context requires otherwise.

Reference is made to the announcement of the Company dated July 21, 2024, where the Board announced on July 19, 2024, the Company entered into a Cooperation Agreement with Zhongmei Huadong, a wholly-owned subsidiary of Huadong Medicine whose shares are listed on the Shenzhen Stock Exchange (stock code: 000963.SZ), pursuant to which the Company has granted to Zhongmei Huadong, in the Authorized Territory and in the Authorized Fields, (i) an exclusive right to jointly develop the Subject Product; (ii) the Optional Right to promote the Subject Product; and (iii) a right of first refusal for the transfer of MAH of the Subject Product.

The Subject Product, QX005N, is a monoclonal antibody (mAb) blocking IL-4R α , which has been granted seven IND approvals for indications such as atopic dermatitis ("**AD**"), prurigo nodularis ("**PN**") and chronic rhinosinusitis with nasal polyps.

Under the Cooperation Agreement, Zhongmei Huadong will co-develop the Subject Product together with the Company, including clinical, non-clinical studies as well as registration related work. If Zhongmei Huadong exercises the Optional Right, it will be responsible for the marketing and promotion of the Subject Product in the Authorized Territory, whereas the Company, acting as the MAH in the Authorized Territory, will be responsible for the supply and quality control of the Subject Product and its clinical trial samples, which will be produced by Cellularforce, an indirect non-wholly owned subsidiary of the Company.

The scope of cooperation will cover clinical trials of the following indications: (i) Phase III and related extended treatment studies in adults with AD; and (ii) Phase III and related studies of extended treatment of PN. The development of other indications (including other indications that have already received IND approvals and other potential new indications) will be subject to discussion and unanimous approval by the JDC and written confirmation of both parties.

As at the Latest Practicable Date, Zhongmei Huadong is a substantial shareholder holding approximately 16.17% of the issued share capital of the Company and is therefore a connected person of the Company as defined under the Listing Rules. Accordingly, the entering into the Cooperation Agreement and the sharing of the Clinical Development and Registration Fee would constitute continuing connected transactions under Chapter 14A of the Listing Rules. As the highest of the applicable percentage ratios (other than the profit ratio) in respect of the Proposed Annual Caps exceeds 5%, the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the Proposed Annual Caps) are subject to reporting, announcement, annual review, circular and independent shareholders' approval requirements under Chapter 14A of the Listing Rules.

Mr. Yu Xi, a non-executive Director, is the general manager of investment department at Huadong Medicine, the parent company of Zhongmei Huadong. For good corporate governance practice, Mr. Yu Xi has abstained from voting on the board resolution approving the transactions contemplated under the Cooperation Agreement.

Since the timing of granting the first indication of the Subject Product is unanticipated, the Cooperation Agreement does not have a fixed term. The Company has applied for and was granted a waiver from strict compliance with Rule 14A.52 of the Listing Rules such that the term of the Cooperation Agreement can be of an unspecified term, on the following grounds the same conditions:

(a) The Company has practical difficulties in anticipating the commencement date of commercialization of the Subject Product. The commercialization can only be started after the marketing authorization is obtained. However, the timing of obtaining the marketing authorization depends on the clinical development progress and the marketing authorization application process. As such, the Company is unable to anticipate when will the marketing authorization grant the first indication of the Subject Product.

(b) There are strong commercial reasons for the Cooperation Agreement to be at a longer term. The reason for entering into the Cooperation Agreement is for the Company to jointly develop and to commercialize (in the event the Optional Right is exercised) the Subject Product in the Authorized Territory and in the Authorized Fields. Such cooperation is long term in nature. Imposing a restriction on the term of the Cooperation Agreement for a period of three years would be contrary to the business intention of the parties. In addition, it is not uncommon in the market for the similar cooperation agreement to be entered into with an unspecified term.

(c) The Company is of the view that the term of the Cooperation Agreement is in the interests of the Company and the Shareholders as a whole. As the Subject Product will be one of the Group's core products, it is necessary for the continuation of the marketing of the Subject Product without any material disruption. It ensures that the Company will continue to receive and enjoy the economic benefits derived from the Subject Product.

(d) Notwithstanding the term of the Cooperation Agreement is for an unspecified term, the annual caps for the research and development cost sharing has been set for the three years ending December 31, 2026. Supplemental agreement will be entered into before commercialization to determine the marketing service fee and the annual caps. All the above and the subsequent renewal will be subject to independent shareholders' approval at a general meeting of the Company. Full details, together with the views of the Independent Financial Adviser, will be provided in circulars for shareholders to make an informed decision.

(e) Details of this waiver has been disclosed in this circular to be despatched and the actual transaction amount will be set out in the subsequent annual reports of the Company.

The EGM will be convened for the Independent Shareholders to consider and, if thought fit, approve the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the Proposed Annual Caps).

As at the Latest Practicable Date, Zhongmei Huadong held 35,900,000 shares of the Company, representing approximately 16.17% of the issued share capital of the Company. Huadong Investment, which is wholly-owned by Huadong Medicine, held 1,976,800 shares of the Company, representing approximately 0.89% of the issued share capital of the Company. Accordingly, Zhongmei Huadong and Huadong Investment are required to abstain from voting on the resolution to approve the Cooperation Agreement at the EGM.

As far as the Directors are aware, having made all reasonable enquiries, save as disclosed above, no other Shareholders are required to abstain from voting on the resolutions referred to above at the EGM.

THE INDEPENDENT BOARD COMMITTEE

The Independent Board Committee, comprising three independent non-executive Directors, namely Dr. Zou Zhongmei, Dr. Ling Jianqun and Mr. Fung Che Wai, Anthony, has been established by the Company for the purpose of advising the Independent Shareholders on: (i) whether the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee) are conducted in the ordinary and usual course of business of the Group and are in the interests of the Company and the Shareholders as a whole; (ii) whether the terms of Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including Proposed Annual Caps) are on normal commercial terms and are fair and reasonable so far as the Independent Shareholders are concerned; and (iii) how they should vote on the relevant resolution at the EGM. We have been appointed by the Company to advise the Independent Board Committee and the Independent Shareholders in the same regard.

OUR INDEPENDENCE

As at the Latest Practicable Date, we did not have any relationship with, or interest in, the Company, the Group, Zhongmei Huadong, Huadong Medicine or any other parties that could reasonably be regarded as relevant to our independence. During the two years immediately prior to this letter, we have not: (i) acted in the capacity as a financial adviser or as an independent financial adviser to the Company; (ii) provided any services to the Company; or (iii) had any relationship with the Company. Apart from normal independent financial advisory fees paid or payable (as the case may be) to us in connection with this appointment, no arrangements exist whereby we had received or will receive any fees or benefits from the Company, the Group, Zhongmei Huadong, Huadong Medicine or any other parties that could reasonably be regarded as relevant to our independence. Accordingly, we consider that we are independent pursuant to Rule 13.84 of the Listing Rules.

BASIS OF OUR OPINION

In formulating our advice and recommendation to the Independent Board Committee and the Independent Shareholders, we have reviewed, amongst other things:

(i) the annual report of the Company for FY2023 (the "**2023 Annual Report**");

(ii) the Cooperation Agreement; and

(iii) other information as set out in the Circular.

We have relied on the truth, accuracy and completeness of the statements, information, opinions and representations contained or referred to in the Circular and the information and representations made to us by the Company, the Directors and the management of the Group (collectively, the "**Management**"). We have assumed that all information and representations contained or referred to in the Circular and provided to us by the Management, for which they are solely and wholly responsible, are true, accurate and complete in all respects and not misleading or deceptive at the time when they were provided or made and will continue to be so up to the Latest Practicable Date. Shareholders will be notified of material changes as soon as possible, if any, to the information and representations provided and made to us after the Latest Practicable Date and up to and including the date of the EGM.

We have also assumed that all statements of belief, opinion, expectation and intention made by the Management in the Circular were reasonably made after due enquiries and careful consideration and there are no other facts not contained in the Circular, the omission of which make any such statement contained in the Circular misleading. We have no reason to suspect that any relevant information has been withheld, or to doubt the truth, accuracy and completeness of the information and facts contained in the Circular, or the reasonableness of the opinions expressed by the Management, which have been provided to us.

We considered that we have been provided with sufficient information to reach an informed view and to provide a reasonable basis for our opinion. However, we have not carried out any independent verification of the information provided by the Management, nor have we conducted any independent investigation into the business, financial conditions and affairs of the Group or its future prospects. We also have not considered the taxation implications on the Group as a result of entering into the Cooperation Agreement.

The Directors jointly and severally accept full responsibility for the accuracy of the information disclosed and confirm, having made all reasonable enquiries that to the best of their knowledge and belief, there are no other facts not contained in this letter, the omission of which would make any statement herein misleading.

This letter is issued to the Independent Board Committee and the Independent Shareholders solely in connection for their consideration of the terms of the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the Proposed Annual Caps), and except for its inclusion in the Circular, is not to be quoted or referred to, in whole or in part, nor shall this letter be used for any other purposes without our prior written consent.

PRINCIPAL FACTORS AND REASONS CONSIDERED

In arriving at our opinion in respect of the terms of the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the Proposed Annual Caps), we have taken into consideration the following principal factors and reasons:

1. Information of the Group

The Company, founded in 2015, is a clinical-stage biotech company exclusively focused on biologic therapies for autoimmune and allergic diseases, with a self-developed drug pipeline and an established commercial-scale in-house manufacturing capability. The H Shares of the Company were successfully listed on the Main Board of the Stock Exchange under Chapter 18A of the Listing Rules on March 20, 2024. The Company has two core products, QX002N and QX005N, both of which are self-developed. QX002N is an IL-17A inhibitor and the Company is conducting a Phase III clinical trial for ankylosing spondylitis in China. QX005N is a monoclonal antibody (mAb) blocking IL-4Ra with two phase III clinical trials in progress, for atopic dermatitis and prurigo nodularis, respectively.

2. Information of Zhongmei Huadong

Zhongmei Huadong is a company established in the PRC, a substantial shareholder of the Company and a wholly-owned subsidiary of Huadong Medicine. Zhongmei Huadong is principally engaged in the development, manufacturing and sales of pharmaceutical products. Zhongmei Huadong is also the Group's commercialization partner for joint development and exclusive commercialization of QX001S, one of the Company's key products in China since August 2020.

We note from the Company's prospectus dated March 12, 2024, Huadong Medicine is a leading PRC pharmaceutical company, whose business covers the whole pharmaceutical industrial chain, integrating research and development ("**R&D**"), manufacturing and sales of medicine. The Company regards the collaboration with Huadong Medicine (including Zhongmei Huadong) would enable the Group to leverage their market access, nationwide sales and marketing network of targeting the autoimmune and allergic disease field as well as their extensive experience in chronic disease management, which will be crucial to support rapid commercialization of QX001S.

3. Principal terms of the Cooperation Agreement

As referred to in the Letter from the Board, the principal terms of the Cooperation Agreement are set out below:

Parties:	(1) Zhongmei Huadong; and (2) the Company
Term:	From July 19, 2024 until 15 years after the marketing authorization is granted for the first indication of the Subject Product. The term is automatically renewable for 5 years after the expiration of the above period.
Conditions precedent:	The Cooperation Agreement is conditional upon: (1) full compliance with the Listing Rules with respect to the Cooperation Agreement (and the transactions contemplated thereunder) by the Company; and (2) the Independent Shareholders having passed the resolution at the EGM for approving the Cooperation Agreement (and the transactions contemplated thereunder).

Cooperation arrangement:

During the term of the Cooperation Agreement, the Company will grant to Zhongmei Huadong, in the Authorized Territory and in the Authorized Fields, (i) an exclusive right to jointly develop the Subject Product; (ii) the Optional Right; and (iii) a right of first refusal for the transfer of MAH of the Subject Product. Below sets out the details of these rights.

(a) Exclusive rights to jointly develop the Subject Product:

(i) collaborating with the Company on conducting clinical and non-clinical studies related to the Subject Product; (ii) collaborating with the Company to prepare and submit data or information relating to the Subject Product for obtaining the regulatory approval for clinical trials and to obtain, support or maintain regulatory approval for the Subject Product.

(b) Optional Right:

(i) exclusively promoting the indications of the Subject Product which has obtained marketing authorization; (ii) conducting activities related to market access; (iii) conducting centralized marketing and medical affairs activities related to the Subject Product; and (iv) other rights and obligations as set out in the Cooperation Agreement.

During the period from the effective date of the Cooperation Agreement until six months after the marketing authorization application for the Subject Product has been submitted and accepted by the regulatory authority, Zhongmei Huadong shall decide whether to exercise this Optional Right and shall notify the Company in writing.

(c) Right of first refusal for the transfer of MAH:

In the event that the Company intends to transfer the MAH to a third party or receives an invitation from a third party for such transfer, Zhongmei Huadong shall have the right of first refusal in the transfer of MAH of the Subject Product under the same conditions of cooperation, and both parties shall make their best efforts to negotiate amicably and sign a formal agreement for the transfer. In the event that a third party is willing to participate in the negotiation of the transfer of the MAH, Zhongmei Huadong shall have the right to decide whether to exercise the right of first refusal for the transfer of MAH within 30 Business Days upon receipt of the third-party cooperation proposal.

Under the Cooperation Agreement, both parties will be jointly responsible for the clinical development and registration of the Subject Product. The Company has the exclusive right to develop and market the Subject Product outside the Authorized Territory and the Authorized Fields. Moreover, being the MAH of the Subject Product, the Company will be responsible for the manufacturing, distribution and pharmacovigilance of the Subject Product.

If Zhongmei Huadong chooses to exercise the Optional Right, Zhongmei Huadong will also have a right to sublicense all or part of this right to any third party after obtaining the Company's written consent. No such consent is required if Zhongmei Huadong sublicenses to its Related Parties.

Within 18 months prior to the commercialization of the Subject Product, the Company shall enter into an entrusted production and processing agreement with Cellularforce, and a commercialization supply agreement with Zhongmei Huadong.

To facilitate the cooperation arrangement, two committees will be established, namely the Joint Development Committee (the "**JDC**") and the Joint Supervision Committee (the "**JSC**"), to manage and supervise clinical development and commercialization of the Subject Product, respectively. Each of these committee will comprise of six members, of which each party will appoint three members respectively.

The cost/profit sharing arrangement between the Company and Zhongmei Huadong will be as follows:

(1) Before commercialization of the Subject Product, each party is responsible for 50% of the following clinical development and registration fees (the "**Clinical Development and Registration Fee**"):

a. Clinical expenses which shall include the costs of the following activities involved in the clinical trials of the Subject Product approved by the JDC, including insurance of the Subject Product, patient recruitment, access to clinical trial organization and all related expenses required to conduct clinical trials, conference fees, expert fees, hospitality and travelling expenses, hospital equipment and supplies, reproductive toxicity study expenses, FTE expenses incurred by both parties to support the above activities, services provided by third party service providers, and other relevant expenses incurred in relation to the above activities as approved by the JDC; and

b. Registration fees which shall include all expenses related to registration activities conducted for the purpose of marketing the Subject Product, including evaluation fees and related fees of the National Institutes for Food and Drug Control (中國食品藥品檢定研究院).

The JDC shall develop clinical protocols and budgets throughout the entire clinical trials. The JDC will convene quarterly meetings to confirm the clinical expenses incurred during that quarter.

(2) Upon and after commercialization of the Subject Product, should Zhongmei Huadong exercise the Optional Right, the Company shall pay to Zhongmei Huadong an exclusive marketing service fee (tax inclusive) (the "**Marketing Service Fee**"), which shall be equivalent to Net Sales revenue generated from the sale of the Subject Project x marketing service fee rate. The marketing service fee rate shall be negotiated based on the commercial value of the Subject Product and the parties will enter into a supplemental agreement(s) to agree on the marketing service fee rate before commercialization of the Subject Product. Further announcement will be made when the supplemental agreement is entered into. The Company will comply with the applicable requirements under Chapter 14A of the Listing Rules, including independent shareholders' approval.

Payment terms:

(1) Before commercialization of the Subject Product:

a. All the Clinical Development and Registration Fee incurred shall be paid by the Company in advance.

b. After the Subject Product has achieved the following milestones, Zhongmei Huadong will pay the Company the following registration milestone payment (tax exclusive) within 30 Business Days after the achievement of the relevant milestone, less any expenses for clinical development and registration incurred by Zhongmei Huadong:

Event	**AD in adults**	**PN**
First patient dosing in Phase III clinical study in China	RMB30.0 million	RMB15.0 million
Last patient dosing in Phase III clinical study in China	RMB20.0 million	RMB15.0 million
Independent Review Committee's written confirmation of achievement of the primary clinical endpoint	RMB20.0 million	RMB15.0 million

c. Remaining clinical development fees: Within 30 Business Days after Zhongmei Huadong and the Company having received the Phase III clinical study report, the study of which is conducted with the JDC's approval, officially issued by a research organization for any single indication of the Subject Product, and obtained a positive result compared with the placebo, Zhongmei Huadong shall pay the Company the remaining clinical development fees which is equivalent to 50% of the clinical expenses for the indication confirmed by the JDC less the corresponding milestone payment that Zhongmei Huadong has already made. The remaining clinical development fees of each indication shall be calculated individually.

d. Within 30 Business Days after the Subject Product is granted marketing approval, Zhongmei Huadong shall pay the Company 50% of the registration fees as confirmed by the JDC.

(2) Upon and after commercialization of the Subject Product:

a. Within five days after the end of each month, both parties shall confirm the Net Sales amount received in the previous month and the Company shall pay Zhongmei Huadong the Marketing Service Fee of that month.

b. Within the first month after the end of each sales year, both parties shall confirm the annual Net Sales amount received of the previous sales year and the Company shall pay Zhongmei Huadong for any shortfall of the Marketing Service Fee. If the Company has previously paid excess Marketing Service Fee during the annual review, such excess shall be deducted in the next payment to be made by the Company.

c. In the event of discrepancies in the Net Sales amount between the parties, it shall first be confirmed through negotiation. If no consensus is reached, a mutually agreed annual audit firm may be appointed to conduct a special audit, the result of which is binding on the parties.

d. The Company shall bear the costs of commercial distribution of the Subject Product and taxes and fees in circulation process.

IP Rights: The Company will grant Zhongmei Huadong a non-exclusive license to use the IP rights solely owned by the Company set forth in the Cooperation Agreement, provided that the use of such IP rights shall be limited for the intended marketing and promotion services.

After the Cooperation Agreement becomes effective, any intellectual property rights and technical secrets jointly developed by both parties in relation to the Subject Product (the "**Joint IP Rights**") shall be jointly owned by both parties. Each party will grant to other party an exclusive license under the Cooperation Agreement to the other party to use the Joint IP Rights solely for the purpose of commercialization of the Subject Product. The Company shall have the right to use the Joint IP Rights outside the Authorized Territory at nil consideration.

Termination: The Cooperation Agreement may be terminated by mutual agreement by both parties or either party shall have the right to terminate the Cooperation Agreement immediately upon written notice to the other party upon the occurrence of: (i) the other party becoming insolvent, being adjudicated bankrupt, filing a petition for bankruptcy (whether voluntary or not), transferring assets for the benefit of creditors, other similar relief or losing the financial ability to perform its obligations hereunder; and (ii) the foregoing is not eliminated within 90 days from the date of such occurrence.

In the event that (i) the Subject Product eventually fails to obtain the marketing approval from the National Medical Products Administration (國家藥品監督管理局) (the "**NMPA**"), or (ii) Zhongmei Huadong chooses not to exercise the Optional Right, or (iii) Zhongmei Huadong exercises the Optional Right but the parties are unable to agree on the rate of the Marketing Service Fee, Zhongmei Huadong shall have the right to unilaterally terminate the Cooperation Agreement by giving a 30-day written notice. The Company shall return the payment received in full to Zhongmei Huadong, and shall pay Zhongmei Huadong an interest of 5% per annum on the entire amount paid. Zhongmei Huadong shall return all the project-related information and materials to the Company, and shall cease to have any interest in the project.

When determining the sharing of the Clinical Development and Registration Fee, the parties considered that it is industry practice, on normal commercial terms, and no less favorable than terms available to independent parties for each party to be responsible for 50% of the Clinical Development and Registration Fee. This 50% sharing arrangement aims to ensure that both parties would make balanced dedication and bear balanced risk to the development of the Subject Product, and is determined after arm's length negotiations between the parties with reference to, among other matters, the prevailing industry practice in similar co-development projects. In determining the cost sharing portion amongst the parties, the Board had taken into account the key terms of other similar cooperation arrangements adopted by biotech companies listed on the Stock Exchange. Although the terms of these comparable transactions are not completely identical, it is noted that certain biotech companies with similar cooperation arrangement had also adopted a cost sharing ratio of 50:50. The Board considered that this equal sharing of the Clinical Development and Registration Fee, together with other terms under the Cooperation Agreement, may effectively result in an equitable sharing of the financial exposure with Zhongmei Huadong in respect of the cost to be incurred in the pre-commercialization stage of the Subject Product. Zhongmei Huadong and the Company also enjoy equal power in the JDC and the JSC, which would supervise the parties' contribution to the Subject Product. Therefore, the Board considers that the 50% sharing arrangement is in the interests of the Company because it can utilize the financial support and clinical support for joint development of the Subject Product before Zhongmei Huadong declares to exercise the Optional Right and before the parties determine the formula for the Marketing Service Fee upon the commercialization of the Subject Product. Hence the Company may reduce its financial risk in respect of the development of the Subject Product.

The Board considered that the clinical development and registration milestone payment arrangement is industry practice and on normal and commercial terms. Considering the long span and high cost of Phase III clinical trials of the Subject Product, the Company has requested payment milestones to be split in three stages and associated with the progress of the clinical trials and expenses to be incurred in order to control the risk the Company may face and to enhance certainty of the cooperation, and Zhongmei Huadong has agreed with such milestone payment arrangement. The first payment milestone for AD in adults and PN, namely the first patient dosing in Phase III clinical study in China, has been achieved in May 2024, which indicates the commencement of the Phase III clinical trial. The second payment milestone for AD in adults and PN, namely the last patient dosing in Phase III clinical study in China, indicates the completion of patient enrollment. The last payment milestone for AD in adults and PN, namely the written confirmation by the Independent Review Committee, indicates the achievement of the primary endpoint data read-out of Phase III.

When determining each milestone payment amount, the Company has factored in the expected clinical expenses payable to be incurred that correspond with the occurrence of the relevant milestone event, including but not limited to research center test fee, clinical research coordinator (CRC) service fee, contract research organization (CRO) service fee, labour costs, central laboratory fee and patient recruitment service fee. Upon reaching the last payment milestone event for AD in adults and PN, namely the written confirmation by the Independent Review Committee, the estimated clinical expenses incurred will be no more than RMB230 million. Since Zhongmei Huadong is responsible for 50% of the aforementioned expenses, the total development and registration milestone payment to be shared is around RMB115 million. The Board considered that the milestone payment arrangement would effectively control the risk borne by the Company and ensure the success of the cooperation.

If the Subject Project is not commercialized ultimately, the Company shall return the payment received in full to Zhongmei Huadong, and shall pay Zhongmei Huadong an interest of 5% per annum, which benchmarks against the long-term Loan Prime Rate ("**LPR**") announced by the People's Bank of China of 3.85% when the Cooperation Agreement was entered into with a risk premium, on the entire amount paid. The Board considered such 5% annual interest rate is on normal and commercial terms taking into account the LPR announced by the People's Bank of China with a risk premium, the inherent uncertainties associated with the commercialization of the Subject Product and the inherent risks involved in private credit unsecured lending by Zhongmei Huadong. The Board considered that the above arrangement is on normal and commercial terms and for the interest of the Shareholders as a whole after taking into account that: (i) the Company is the MAH of the Subject Product in accordance with the Cooperation Agreement, who shall undertake all responsibilities for development of the Subject Product (including non-clinical studies, clinical trials, manufacture and distribution, monitoring, and handling of adverse drug reactions) pursuant to Article 30 of the PRC Drug Administration Law (中華人民共和國藥品管理法) that was promulgated and became effective in December 2019; (ii) by utilizing the experience of Zhongmei Huadong gained from other clinical programs, we believe its early involvement at the pre-commercialization stage will enhance the success rate of and facilitate the development of the Subject Product, including assistance with trial protocol optimization and enhancement, communication with principal investigators and experts, and patient recruitment of the clinical trials; (iii) the early payment of Zhongmei Huadong at the pre-commercialization stage can relax the cashflow requirement for the Phase III clinical trials of the Subject Product; and (iv) such terms of annual interest rate are not less favorable than those available from independent parties who may provide financial assistance to the Company.

Our assessment

We have obtained and reviewed the Cooperation Agreement, and note that the Cooperation Agreement establishes a robust framework for collaboration, designed to harness the unique strengths and resources of both parties, thereby maximizing the potential for developing the Subject Product under the clinical trials for Phase III studies associated with AD in adults and PN and commercializing the Subject Project. The Cooperation Agreement delineates the parties' responsibilities clearly, ensuring that both the Company and Zhongmei Huadong are equally committed to the development and commercialization of the Subject Product, which fosters a balanced partnership. We note the transactions contemplated under the Cooperation Agreement are broadly in line with international trends that biotech companies would seek to co-develop candidate medicines with large pharmaceutical companies to not only to reduce R&D costs and risks, but also help the biotech to quickly gain market advantage. It is generally recognized that strategic partners of the large pharmaceutical companies can provide a strong boost to biotech companies' expansion, including expertise and technology, speed, flexibility and a lower cost structure. We note there is an extensive coverage of various forms of partnering deals in the global life science sector on the database maintained at Current Partnering, a leading publisher of life science partnering deal terms and best practice, as well as an online magazine for life science deal makers with website link: https://www.currentpartnering.com/insight/. We found that there is an abundance of diverse partnering/cooperation approaches taken by different international life science companies, with no universal or "one-size-fits-all" approach. When we say diverse approaches, we do not mean that "each term" of the partnering/cooperation projects is different, we mean that "each combination of terms" of the partnering/cooperation projects is very different. Therefore, Independent Shareholders should note that each life science partnering deal has its own unique features so the relevant deal structures and combinations of terms under each deal can only be compared generally to those of the Cooperation Agreement and serve as a reference only.

We note that that the Cooperation Agreement includes cost/profit sharing arrangements between the Company and Zhongmei Huadong, which ensure that both parties are incentivized. The Clinical Development and Registration Fee shall be shared equitably, with the Company initially covering these costs and Zhongmei Huadong reimbursing 50% upon achieving specific predefined milestones. This cost sharing arrangement promotes the interests of both parties and ensures fair risks and costs sharing. Additionally, the inclusion of milestone-based funding and performance metrics adds a layer of accountability, reducing the risks associated with the development of the Subject Product.

Besides, to facilitate the cooperation arrangement, there is the inclusion of the JDC and the JSC in the Cooperation Agreement, which ensures that both parties remain aligned and accountable throughout the product development and commercialization phases. This structured oversight promotes transparency and efficiency, which are crucial for maintaining confidence and maximizing the potential return on investment for both parties. Furthermore, we also noticed that the Cooperation Agreement clearly defines how IP developed during the collaboration will be owned, protected, and utilized, ensuring that both parties can benefit from the innovations resulting from their joint efforts. This clarity in IP rights allocation is essential for fostering innovation while protecting the interests of the Company.

Moreover, upon and after commercialization of the Subject Product, the Cooperation Agreement includes the element of Marketing Service Fee which is directly linked to the Net Sales of the Subject Product, provides Zhongmei Huadong the reward and incentive for its efforts contributing to the commercial success of the Subject Product. This ensures that both parties are financially motivated to achieve successful commercialization, benefitting both parties through potential revenue growth from a well-coordinated and risk-managed partnership. Shareholders should however note, the rate of the Marketing Service Fee will be further negotiated between the parties based on the commercial value of the Subject Product and the parties will enter into supplemental agreement(s) to agree on the rate of the Marketing Service Fee before commercialization of the Subject Product. As there will be possible future payments of Marking Service Fee from the Company to Zhongmei Huadong, a connected person, as and when the Subject Product commercializes, the Company will be required to comply with then prevailing Listing Rules requirements.

Pursuant to the terms of the Cooperation Agreement, the Joint IP Rights jointly developed by both parties in relation to the Subject Product shall be jointly owned by both parties. Each party will grant to other party an exclusive license under the Cooperation Agreement to the other party to use the Joint IP Rights solely for the purpose of commercialization of the Subject Product.

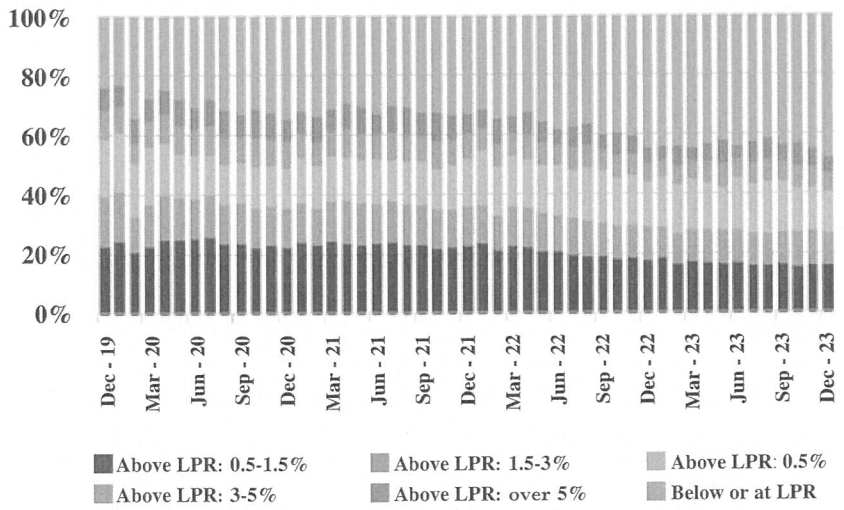
We note that the termination clause of the Cooperation Agreement also includes provisions for a refund of the payment of its portion of the Clinical Development and Registration Fee made by Zhongmei Huadong plus an interest of 5% per annum on the amounts paid by Zhongmei Huadong in the event of unilateral termination by Zhongmei Huadong should (i) the Subject Product eventually fails to obtain the marketing approval from the NMPA, or (ii) Zhongmei Huadong chooses not to exercise the Optional Right, or (iii) Zhongmei Huadong exercises the Optional Right but the parties are unable to agree on the rate of the Marketing Service Fee. In this case, we consider that the collection of Zhongmei Huadong's portion of the Clinical Development and Registration Fee can be regarded as an unsecured loan with an interest rate of 5%, where in the event of the commercialization of the Subject Product fails to meet the expectation of Zhongmei Huadong from a commercial standpoint, Zhongmei Huadong would require to recover such loan from the Company.

Moreover, we are given to understand this clause from two different angles. On the one hand, the Company would nevertheless be required to develop the Subject Product, and Zhongmei Huadong's cost-sharing in the co-development would aid such R&D efforts but should the Subject Product fail to obtain the marketing approval from the NMPA (i.e. item (i) set out above), it means that the Subject Product does not worth the commercialization efforts and the entire Clinical Development and Registration Fee shall be borne by the Company alone. Furthermore, as discussed with the Management, they highlighted that, in accordance with common market practices and the relevant PRC laws and regulations, the marketing service provider of the Subject Product (in this case, Zhongmei Huadong under the Cooperation Agreement), does not take the responsibility for the success of development of the Subject Product. Instead, this responsibility largely rests with the MAH of the Subject Product (in this case, the Company under the Cooperation Agreement). We note the PRC Drug Administration Law revised and implemented in 2019 formally established the drug MAH system. Under this system, the MAHs, not the marketing service provider, shall be responsible for non-clinical research, clinical trials, production and operation, post-marketing research, adverse reaction monitoring, reporting and processing of drugs in accordance with the provisions of the relevant laws and regulations. Independent Shareholders should note however, should the Subject Product successfully proceed to obtain the marketing approval from the NMPA, and Zhongmei Huadong opt to exercise the Optional Right, there shall be no refund of the relevant portion of the Clinical Development and Registration Fee.

On the other hand, if Zhongmei Huadong chooses not to exercise the Optional Right or that it exercises the Optional Right but the parties are unable to agree on the rate of the Marketing Service Fee (i.e. items (ii) and (iii) set out above), although the Company would be required to provide the refund (plus interest) to Zhongmei Huadong, the Company can be released from the Cooperation Agreement and opt to cooperate with a different strategic partner to promote the Subject Product that values the Subject Product and can commercially agree to the rate of the Marketing Service Fee with the Company. In fact, as discussed with the Management, in the latter, the Company can negotiate with the new strategic partner on upfront payments to be cover part of the costs involved in the termination of the Cooperation Agreement thereby providing flexibility to the Company.

In assessing the interest of 5% per annum to be charged on the amounts paid by Zhongmei Huadong in the event of unilateral termination by Zhongmei Huadong, we firstly note as set out in the 2023 Annual Report, the fixed interest rates of the Company's borrowings ranged from approximately 3.3% to 4.2%, and therefore the 5% interest to be charged, if applicable, in the event of a refund to Zhongmei Huadong under the Cooperation Agreement, is just higher than the Company's borrowing interest rates and that of the 5-year LPR of 3.85% quoted by the People's Bank of China when the Cooperation Agreement was entered into. We consider such higher interest rate under the Cooperation Agreement reflects the inherent uncertainties associated with the commercialization of the Subject Product as well as the inherent risks involved in private credit unsecured lending by Zhongmei Huadong, which is neither a bank nor a financial institution. Private credit is essentially non-bank corporate credit provided through bilateral agreements outside of the traditional borrowing channels of debt securities or commercial banks. Independent Shareholders should note that the 5-year LPR of 3.85% quoted by the People's Bank of China is a risk-free benchmark rate and should only be considered as the floor of interest rates available to the Company. Banks would charge a higher interest rate to the Company, let alone Zhongmei Huadong is a private lender, which would propose a higher rate than 3.85%, so the 5%, only being marginally higher than 3.85%, to be charged on the amounts paid by Zhongmei Huadong in the event of unilateral termination by Zhongmei Huadong should be viewed in a positive light. Furthermore, based on the research statistics as shown in Chart 1 below by the National Financial Regulatory Administration (國家金融監督管理總局) (the "**NFRA**") (formerly the China Banking and Insurance Regulatory Commission (中國銀行保險監督管理委員會) and BBVA Research, an independent research firm for research and economic analysis covering different countries in the Americas, Europe and Asia with a team of over 100 analysts producing reports and forecasts for topics such as banking, the digital economy and geostrategy, the middle distribution of the surveyed lending rates by Chinese banks at December 2023 was 3-5% above the LPR. Based on the above, we are of the view that the 5% rate to be charged on the amounts paid by Zhongmei Huadong in the event of unilateral termination by Zhongmei Huadong is fair and reasonable and in the interests of the Company and the Shareholders as a whole.

Chart 1: Statistics of Chinese lending rates over and below LPR



Source: the NFRA and BBVA Research

To further assess the fair and reasonableness of the terms of the Cooperation Agreement from a Hong Kong listed companies perspective, and as part of our work done, we have identified partnering/ cooperation agreements (the "**Comparable Agreements**") which mainly involved the joint R&D, manufacturing and/or commercialization of drug candidate(s), as disclosed in the prospectuses of the companies listed on the Main Board of the Stock Exchange under Chapter 18A of the Listing Rules since 1 January 2023 (the "**18A Research Criteria**"). Based on the 18A Research Criteria, we have exhaustively identified 2 Comparable Agreements and there had not been any adjustment, filtering or removal of samples.

Given that there were only 2 Comparable Agreements based on the 18A Research Criteria, we have, with best endeavour, further expanded our research by conducting a desktop search focus on the published prospectuses, announcements and circulars of all pharmaceutical and biotech companies listed on the Main Board of the Stock Exchange that has disclosed partnering/cooperation agreements mainly involved the joint R&D, manufacturing and/or commercialization of drug candidate(s) that were entered into since 1 January 2010 (the "**General Research Criteria**"). Based on the General Research Criteria, we have identified another 6 Comparable Agreements, which, together with the 2 Comparable Agreements we have identified based on the 18A Research Criteria as discussed in the paragraph above, there are 8 Comparable Agreements in total and there had not been any adjustment, filtering or removal of samples. We have focused our research on six key terms of the Comparable Agreements which we can draw comparison against those of the Cooperation Agreement, namely term of agreement, sharing of R&D expenses, whether there are market service fees (or other revenue/profit sharing arrangements), development milestone payments, payment terms (i.e. upfront payment/prepayment or reimbursement) and whether there are refund arrangements when R&D project fails.

However, one should note there are inherent limitations to our research. Firstly, not all of prospectuses/announcements/circulars have disclosed each and every detail of the key terms of the Comparable Agreements that can draw comparison with those of the Cooperation Agreement. Such lack of disclosures somewhat limits our ability to perform a thorough comparative analysis. Also, each drug candidate in the biotech field is unique, which means that the terms of the Comparable Agreements around them are equally distinctive. The terms of such Comparable Agreements are shaped by a variety of factors, including the specific attributes of the drug candidate and the bargaining power of each party involved. This echoes with our earlier observation that there is no universal or "one-size-fits-all" to partnering/ cooperation approaches.

After considering that (i) the Comparable Agreements are entered into by Chapter 18A companies and also pharmaceutical companies listed on the Main Board of the Stock Exchange with terms mainly involved the joint R&D, manufacturing and/or commercialization of drug candidate(s), which carried the same features as the Cooperation Agreement; (ii) the sample of 8 Comparable Agreement is considered a fair sample larger enough to assess the fair and reasonableness of the terms of the Cooperation Agreement; and (iii) the sample of 8 Comparable Agreement has an adequate coverage of six key terms of the Comparable Agreements which we can draw comparison against those of the Cooperation Agreement, we consider that the research sample of the Comparable Agreements to be fair and representative.

Table 1: Key terms of Comparable Agreements

	Date of Agreement	Company name (stock code)	Name of the R&D partner	Term	Sharing of R&D expense (Company: R&D partner)	Marketing service fee (or other revenue/ profit sharing arrangements)	Development milestone payment	Reimbursement or upfront/ prepayment	Refund arrangement when R&D project fails
1	March 19, 2013	Shanghai Fudan Zhangjiang Bio-Pharmaceutical Co., Ltd. (8231.HK)	Shanghai Pharmaceuticals Holding Co., Ltd.	3 years, renewable	20: 80	Yes	Yearly prepayments, by instalments in accordance with the agreed progress of the project which tracks the actual expenses of the R&D project	Prepayment and reimbursement	Not disclosed
2	September 18, 2015	Shanghai Henlius Biotech, Inc. (2696. HK)	Fosun Pharma Industrial Development Co., Ltd	A long term or for an indefinite term	0: 100	Yes	Upfront milestone payment of RMB50 million, as well as ongoing reimbursement of R&D expenses	Upfront and reimbursement	Not disclosed

	Date of Agreement	Company name (stock code)	Name of the R&D partner	Term	Sharing of R&D expense (Company: R&D partner)	Marketing service fee (or other revenue/ profit sharing arrangements)	Development milestone payment	Reimbursement or upfront/ prepayment	Refund arrangement when R&D project fails
3	March 18, 2016	Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd. (1349.HK)	Shanghai Pharmaceuticals Holding Co., Ltd.	3 years, renewable	20: 80	Yes	Yearly prepayments, by instalments in accordance with the agreed progress of the project which tracks the actual expenses of the R&D project	Prepayment and reimbursement	Not disclosed
4	March 14, 2019	Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd. (1349.HK)	Shanghai Jiaolian Drug Development Co., Ltd	2.7 years, renewable	50: 50	Yes	Yearly, by reimbursement of actual R&D expenses to each other	Reimbursement	Not disclosed
5	May 2019	Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd. (6990.HK)	Harbour BioMed (Suzhou) Co., Ltd.	Not disclosed	50: 50	Yes	Reimbursement payable upon the achievement of specified clinical development and regulatory milestones	Reimbursement	Not disclosed
6	January 18, 2021	ImmuneOnco Biopharmaceuticals (Shanghai) Inc. (1541. HK)	Sunshine Guojian Pharmaceutical (Shanghai) Co., Ltd	Will continue until the completion of the clinical studies	All costs incurred in clinical studies in mainland China will be borne by the partner, except for certain costs to be borne by the company as provided in the agreement	No	Ongoing reimbursement of R&D expenses	Reimbursement	Not disclosed

	Date of Agreement	Company name (stock code)	Name of the R&D partner	Term	Sharing of R&D expense (Company: R&D partner)	Marketing service fee (or other revenue/ profit sharing arrangements)	Development milestone payment	Reimbursement or upfront/ prepayment	Refund arrangement when R&D project fails
7	June 28, 2022 (original agreement) and May 21, 2024 (supplemental agreement)	Shanghai Henlius Biotech, Inc. (2696. HK)	Palleon Pharmaceuticals Inc.	Remain in effect on a licensed product by-licensed product basis until all payment obligations for each licensed product have expired	50: 50 for phase I Majority of R&D expense be borne by the partner for phase II	Yes	Milestones payments are made up of a mixture of upfront fee of US$4m and development milestone payments of not more than approximately US$96.5 million in aggregate based on achievements of each development milestone of the relevant drug	Upfront and prepayment	Not disclosed
8	November 29, 2023	YiChang HEC ChangJiang Pharmaceutical Co., Ltd. (1558.HK)	Sunshine Lake Pharma Co., Ltd.	3 years, renewable	100: 0	Yes	Ongoing reimbursement of R&D expenses	Reimbursement	Transfer the R&D expense invested in the failed project to other agreed innovative drugs project(s)
	July 19, 2024	The Company	Zhongmei Huadong	15 years, renewable for 5 years	50: 50	Yes, to be agreed	Development milestone payments based on achievements of each development milestone of the relevant drug	Prepayment and reimbursement	If the Subject Product eventually fails to obtain the marketing approval, the Company shall return the payment with an interest of 5% per annum on the entire amount paid.

Source: Website of the Stock Exchange.

In order to assess the fair and reasonableness of the terms of the Cooperation Agreement, we have assessed the following key terms of the Cooperation Agreement reference to the Comparable Agreements:

1. Term

The Cooperation Agreement spans 15 years, which is notably longer than the typical duration observed in most of the Comparable Agreements, however we note that the Comparable Agreement between Shanghai Henlius Biotech, Inc. ("**Henlius**") and Fosun Pharma Industrial Development featured a long term or for an indefinite term and we note in the prospectus of Henlius dated September 12, 2019, Frost & Sullivan ("**F&S**"), an independent global market research and consulting company engaged by Henlius as the industry expert, has confirmed that it is a market practice in the pharmaceutical industry for similar cooperation agreement to be entered into for a long term or for an indefinite term, primarily due to the substantial amount of capital committed by the collaboration partners and the risks involved.

2. Sharing of R&D expense

We note almost half of the Comparable Agreement adopted the 50:50 cost sharing model which is consistent with that of the Cooperation Agreement. This balanced expense-sharing structure is both fair and reasonable, ensuring that both parties are equally responsible for the R&D costs. Such sharing arrangements seem to be standard in the industry, even though such feature has not always been explicitly stated in the public documents.

3. Marketing service fee

We note that majority of Comparable Agreements (i.e. 7 out of 8) included a marketing service fee arrangement (or other revenue/profit sharing arrangements). While not all Comparable Agreements disclosed such terms in detailed, their presence indicated that such marketing service fee arrangement under the Cooperation Agreement is consistent with industry norms.

4. Milestone payment

The provision for development milestone payments in the Cooperation Agreement reflects a common deal term prevalent in the Comparable Agreements. Although payment methods of these development milestone are different between the Comparable Agreements as set out in the table above, the development milestone payment based on achievements of each development milestone of the relevant drug under the Cooperation Agreement encourages progressively payments that aligns with the developmental status of the drug candidate. Based on the above table, we note that this development milestone payment term is widely recognized in the industry and reflects a standard practice aimed at fostering collaboration and performance accountability.

5. Payment terms

We note from table above that the payment under Comparable Agreements are mainly through reimbursement or upfront/prepayment and the majority of payment terms under the Comparable Agreements (i.e. 7 out of 8) have included such arrangements of reimbursement. Reimbursements are usually either effected through milestone payments with excess being paid by the relevant parties in regular time intervals or direct reimbursement when actual R&D expenses are incurred.

6. Refund arrangement

We note most of the Comparable Agreements did not explicitly disclose their refund provisions. In the case of YiChang HEC ChangJiang Pharmaceutical Co., Ltd. ("**HEC**"), the Comparable Agreement stipulated that should the relevant R&D project failed, the partner who invested the R&D expenses can transfer the R&D expenses to other agreed innovative drugs project(s). Having considered: (i) the Company would nevertheless be required to develop the Subject Product, and Zhongmei Huadong's cost-sharing in the co-development would aid such R&D efforts but should the Subject Product fail to obtain the marketing approval from the NMPA, the entire Clinical Development and Registration Fee would naturally be borne by the Company alone; (ii) in the event Zhongmei Huadong chooses not to exercise the Optional Right or that it exercises the Optional Right but the parties are unable to agree on the rate of the Marketing Service Fee, although the Company would be required to provide the refund (plus interest) to Zhongmei Huadong, the Company can be released from the Cooperation Agreement and opt to cooperate with a different strategic partner to promote the Subject Product under a newly negotiated commercial arrangement; (iii) the refund interest rate of 5% was considered, with bases, to be fair and reasonable and in the interests of the Company and the Shareholders as a whole as discussed above; and (iv) there exists variations of arrangements to protect the R&D expense spent on failed R&D project(s), as evidenced by the HEC case, we are of view that the refund arrangement under the Cooperation Agreement is fair and reasonable and in the interests of the Company and the Shareholders as a whole.

Based on the above table and the assessment, we note that the Comparable Agreements featured generally similar terms as the Cooperation Agreements including but not limited to sharing of R&D expenses, marketing service fee, milestone payment, and refund arrangements. Although these terms are not exactly identical under different Comparable Agreements, they still suggest that the terms outlined in the Cooperation Agreement are not unusual, as well as aligning well with the industry norms.

Having considered that (i) the transactions contemplated under the Cooperation Agreement are broadly in line with international trends that biotech companies would seek to co-develop candidate medicines with large pharmaceutical companies; (ii) under terms of the Cooperation Agreement, the Clinical Development and Registration Fee shall be shared equitably between the Company and Zhongmei Huadong; (iii) the Cooperation Agreement includes the element of Marketing Service Fee which is directly linked to the Net Sales of the Subject Product, provides Zhongmei Huadong the reward and incentive for its efforts contributing to the commercial success of the Subject Product; (iv) the parties will share the Joint IP Rights; (v) the termination clause provides flexibility for the Company to cooperate with a new strategic partner should Zhongmei Huadong opt out at the commercialization stage of the Subject Product and (vi) from a Hong Kong listed companies perspective, we have reviewed the Comparable Agreements and note that the Comparable Agreements featured generally similar terms as the Cooperation Agreements, we are of the view that the terms of the Cooperation Agreement are on normal commercial terms and are fair and reasonable so far as the Independent Shareholders are concerned.

4. Reasons for and benefits of the entering into of the Cooperation Agreement

Reference is made to the Letter from the Board, Zhongmei Huadong is wholly owned by Huadong Medicine, a leading PRC pharmaceutical company with over 30 years of experience covering the whole pharmaceutical industrial chain, is a suitable business partner for the Group due to their strong development and commercialization capabilities at a national level. The Company believe that this collaboration could utilize Zhongmei Huadong's abundant clinical resources and marketing network in autoimmune and allergic diseases, along with their experience in chronic disease management.

Moreover, the Cooperation Agreement could enable both parties to leverage their strengths and share the value of the Subject Product proportionate to their respective contributions in R&D and sales and marketing. This approach aligns with industry practice and is beneficial for the Group since the cooperation with Zhongmei Huadong will facilitate the full exploration of the potential value of the Subject Product, bring more financial support to the Group and enhance the efficiency of the Company's internal financial resource.

Additionally, the Cooperation Agreement facilitates risks and costs sharing in advancing clinical trials and commercialization of the Subject Product. It enables the pooling of resources and capabilities from both parties to establish a competitive position in relevant markets expeditiously, to accelerate the development of the Subject Product, and to enhance the Group's long-term growth potential and comprehensive competitiveness.

Our assessment

We concur with the Management's view that Zhongmei Huadong, being wholly owned by Huadong Medicine, which is a renowned pharmaceutical company in the PRC with over three decades of experience, with strong market access, nationwide sales and marketing network, presents a suitable partnership opportunity for the Company.

We note that Zhongmei Huadong is a substantial shareholder in the Company, which implicitly presents a sense of long-term cooperation and trust between the parties and with a more amicable and close-knit partnering relationship. As mentioned above, Zhongmei Huadong is also the Group's commercialization partner for joint development and exclusive commercialization of QX001S, one of the Company's key products in China since August 2020, so it is not an initial cooperation but an extension of cooperation between the two parties.

This leading pharmaceutical entity will invest capital and provide essential clinical and registration resources to expedite product development, thereby positioning the Company for a competitive advantage. The Management further indicated that the Cooperation Agreement would utilize Huadong Medicine's clinical resources to accelerate both clinical development and the product launch process. Additionally, the Company will receive a portion of the R&D expenses when each payment milestone is achieved, strengthening and enhancing the efficiency of the Company's internal financial resources.

We note from the 2023 Annual Report, the Company incurred approximately RMB364.4 million of R&D expense for FY2023, of which constituted over 65% of the Group's total expenses during FY2023. As such, we concur with the Management's view that the cost-sharing features of the Cooperation Agreement will strengthen and enhance the efficiency of the Company's internal financial resources, in the event the Subject Product can proceed to commercialization stage.

Furthermore, as mentioned above, the Cooperative Agreement allows both parties to capitalize on their respective strengths and share the value derived from the Subject Product as a results of their contributions in R&D and sales and marketing. This shared value creation model not only mitigates risks but also optimizes resource utilization, thereby driving the developmental efforts of the Group's while expanding the Group's market presence.

Given that (i) Zhongmei Huadong is considered a suitable business partner for the Group due to their strong development and commercialization capabilities at a national level that can offer abundant complementary clinical resources and marketing network during the collaboration; (ii) Zhongmei Huadong's substantial shareholder status in the Company and its past collaboration with the Group presents a sense of long-term cooperation and trust between the parties and with a more amicable and close-knit partnering relationship; (iii) the cost-sharing features of the Cooperation Agreement will strengthen and enhance the efficiency of the Company's internal financial resource, in the event the Subject Product can proceed to commercialization stage; and (iv) the shared value creation model not only mitigates risks but also optimizes resource utilization, thereby driving the developmental efforts of the Group's while expanding the Group's market presence, we are of the view that entering into the Cooperation Agreement is within the ordinary and usual course of business of the Group and is in the interests of the Company and the Shareholders as a whole.

5. Internal control procedures

In respect of the connected transaction, the Company has adopted the following internal control procedures (the "**IC Procedures**") to safeguard the interests of the Shareholders:

(a) Regarding the management of the annual caps for continuing connected transactions for the Clinical Development and Registration Fee, the finance department of the Company and the Board would monitor the actual amount of continuing connected transactions through the connected transactions ledger to ensure that the amount does not exceed the approved annual caps. Once the limit is about to be exceeded, the Company would initiate compliance procedures as required under Chapter 14 of the Listing Rules immediately.

(b) Regarding the transactions under the Cooperation Agreement, the parties would supervise and guide the implementation through establishing the JDC and the JSC.

(c) The Cooperation Agreement has set out the audit mechanism, i.e. if both parties have any disagreement over the clinical expenses or the Net Sales to be generated, they may liaise with internal auditing or third-party professional auditing organizations to conduct special audits to enable the parties to ultimately reach a consensus.

(d) The internal audit department of the Company, under the guidance of the Audit Committee, would conduct special verification on notifiable transactions and connected transactions on a half-yearly basis to ensure compliance with the requirements of the Listing Rules and the Company's internal system.

(e) The Company's auditors will be engaged in accordance with Chapter 14A of the Listing Rules to report on the continuing connected transactions of the Company as to whether there is anything which has come to their attention that causes them to believe that such continuing connected transactions: (i) have not been approved by the Board; (ii) were not, in all material respects, in accordance with the pricing policies of the Group; (iii) were not entered into, in all material respects, in accordance with the relevant agreements governing the transactions; and (iv) have exceeded the annual caps.

(f) The independent non-executive Directors would conduct an annual review (which is subject to the annual review and disclosure requirements under the Listing Rules) to confirm that the the Clinical Development and Registration Fee under the Cooperation Agreement are (a) in the ordinary and usual course of business of the Group; (b) on normal commercial terms or better; and (c) the transactions are conducted in accordance with the Cooperation Agreement, of which the terms are fair and reasonable as well as in the interests of the shareholders as a whole.

We have obtained and reviewed the internal control system in relation to connected transactions of the Group (the "**IC System**") and noted that the internal control procedures are in line with those as set in the Letter from the Board (the "**IC Procedures**").

From the IC Procedures, we note that, for the execution level, the Management will check to ensure that all approval process under continuing connected transactions is strictly complied with in accordance with the IC System and all continuing connected transactions are strictly in accordance with the terms stipulated in related contract or agreement. The finance department will make a continuing connected transactions checklist to confirm all details (including at least the time, amount, names of connected parties, transaction matters and other information of the continuing connected transactions) are comply with related contract or agreement on a monthly basis. The finance department of the Company will also take the lead in monitoring the actual amount of continuing connected transactions through the connected transactions ledger to ensure that the amount does not exceed the approved annual caps. For the Board level, the continuing connected transactions will be subject to annual review and report by the Management on continuing connected transactions that occurred in the previous year to make sure they are conducted in consistent with former approval documents. At the expert level, independent auditors of the Company will conduct annual reviews on the continuing connected transaction for the Clinical Development and Registration Fee on an annual basis. In addition, we also note that the internal audit department of the Company, under the guidance of the Audit Committee, will conduct special verification on notifiable transactions and connected transactions on a half-yearly basis to ensure compliance with the requirements of the Listing Rules and the Company's internal system requirements.

Furthermore, according to the Cooperation Agreement, the JDC and the JSC will be established by the Company and Zhongmei Huadong, to manage and supervise clinical development and commercialization of the Subject Product, respectively. The JDC and the JSC will be responsible for formulating clinical protocols and budgets throughout the entirety of the clinical trials. They will convene quarterly meetings to review and confirm the clinical expenses incurred during each quarter, thus ensuring ongoing oversight and accountability in the execution of the clinical development activities. Additionally, the Cooperation Agreement has set out the audit mechanism, where the Company and Zhongmei Huadong may liaise with internal auditing or third-party professional auditing organizations to conduct special audits to enable the parties to ultimately reach a consensus on any disagreement over the clinical expenses to be generated. This additional structure not only facilitates enhanced governance but also provides an extra layer of control over the Proposal Annual Caps set forth by the Company.

For our due diligence purpose, we have also discussed with Management and understood that the Management is aware of the IC Procedures and will comply with the IC Procedures when conducting the Cooperation Agreement and Proposed Annual Caps.

Given (i) the IC System are in line with the IC Procedures; (ii) the existence of three layers (i.e. execution level, Board level and expert level) of the IC Procedures in place; and (iii) the Management is aware of the IC Procedures and will comply with IC Procedures when conducting the Cooperation Agreement and Proposed Annual Caps, we concur with the Company that it has adopted adequate internal control measures to comply with the Listing Rules requirements with respect to the supervision and monitoring of the Cooperation Agreement and the Proposed Annual Caps.

6. Proposed Annual Caps

Set out below are the Proposed Annual Caps for FY2024, FY2025 and FY2026 (the "**Cap Period**"):

	Proposed Annual Caps		
	FY2024	**FY2025**	**FY2026**
	(RMB'000)	*(RMB'000)*	*(RMB'000)*
Clinical Development and Registration Fee (tax exclusive)	45,000	70,000	135,000

Basis of determination of the Proposed Annual Caps

According to the Letter from the Board, there was no historical figures of transactions that could be made reference to when determining the cap amount. The sharing of 50% of the Clinical Development and Registration Fee between the Company and Zhongmei Huadong is determined after arm's length negotiations between the parties with reference to the prevailing market rates for joint development of the Subject Product. The Directors estimate that for each of FY2024, FY2025 and FY2026, the amount of the Clinical Development and Registration Fee (tax exclusive) payable by Zhongmei Huadong to the Company under the Cooperation Agreement will not exceed RMB45 million, RMB70 million and RMB135 million, respectively (i.e. the Proposed Annual Caps).

In arriving at the above estimated cap for expenses to be incurred before commercialization, the Directors have made reference to the industry practices and budget for clinical studies, and considered: (i) the first payment milestone for AD in adults and PN, namely the first patient dosing in Phase III clinical study in China, has been achieved in May 2024; (ii) the second and third payment milestones for AD in adults and PN, namely the last patient dosing in Phase III clinical study in China and obtaining the Independent Review Committee's written confirmation of achievement of the primary clinical endpoint, shall be completed by the end of 2025; and (iii) the remaining clinical development fees of the estimated sum of no more than RMB135 million, including research center test fee, clinical research coordinator (CRC) service fee, contract research organization (CRO) service fee, labour costs, central laboratory fee and fees of related extended treatment studies of AD in adults and PN, are expected to be paid by Zhongmei Huadong to the Company by the end of 2026. The total Clinical Development and Registration Fee to be incurred under the Cooperation Agreement is expected to be around RMB500 million based on the budget covering the total clinical expenses. The amount of the remaining clinical development fees was deducted from the 50% of the Clinical Development and Registration Fee to be paid by Zhongmei Huadong (i.e. RMB250 million) by the estimated total registration milestone payment under the Cooperation Agreement (i.e. RMB115 million).

If any further Clinical Development and Registration Fee will be incurred after the Cap Period, the Company will re-comply with the applicable requirements under Chapter 14A of the Listing Rules to set annual cap(s).

When determining the formula for the Marketing Service Fee, the parties will make reference to factors including, among others, the reasons and benefits for entering into the cooperation arrangement, the prevailing market practices of the sharing ratio in relation to the cooperation arrangement as well as the proportion of costs to revenue to be incurred by both parties. There will be no Marketing Service Fee incurred from the date of signing the Cooperation Agreement to the commercialization of the Subject Product in the Authorized Territory and in the Authorized Fields.

Our assessment

We have obtained from the Management and reviewed the breakdowns of the total budgeted R&D expenses for the development of the Subject Products for treatment of AD in adults and PN (the "**Budget Break-down**"). From the Budget Break-down, we note that the total amount of the budgeted R&D expenses for both AD in adults and PN of RMB500 million is two times of the aggregated amount of the Proposed Annual Caps for FY2024, FY2025 and FY2026 (i.e. the summation of RMB45 million, RMB70 million and RMB135 million equals to RMB250 million). This is in line with our understanding that the total amount of the budgeted R&D expenses for both AD in adults and PN are to be shared equally by each party to the Cooperation Agreement. In this case and assuming all budgeted R&D expenses will be reimbursed by Zhongmei Huadong during the Cap Period, half of the budgeted R&D expenses would be the aggregated amount of the Proposed Annual Caps for FY2024, FY2025 and FY2026.

We note from the Budget Break-down that the key budgetary elements are made up of research center test fee, clinical research coordinator service ("**CRC**") fee, contract research organization ("**CRO**") service fee, central laboratory fee, patient recruitment service fee, labour costs and an overall buffer of 30% on the estimated gross expenses (the "**Key Budgetary Elements**"). As explained by the Management, the Budget Break-down has been jointly reviewed by members of the JDC representing each of the Company and Zhongmei Huadong. Such joint review can be seen an important part of the internal control in place for the Cooperation Agreement and the transactions contemplated thereunder.

In assessing the reasonableness of the total amount of the budgeted R&D expenses of RMB500 million, we have sought to draw comparison of the estimated cost per patient of the Subject Products to that of the empirical evidence. Given that there are 1,054 patients (i.e. 648 patients for AD in adults and 406 patients for PN) being recruited to take part in the Phase III development of the Subject Products for treatment of AD in adults and PN, according to the Budget Break-down, the estimated cost per patient of the Phase III clinical research is approximately RMB474,383 (equivalent to approximately US$66,909). According to F&S's published research statistics in 2021, the average cost per patient in a clinical trial is generally as follows: the average cost per patient in a Chinese domestic Phase I clinical trial is generally between US$40,000 to US$60,000, and the average cost per patient in Phase II and Phase III clinical trials is generally around US$50,000 to US$70,000. Having considered the F&S research statistics are slightly dated (i.e. 2021), the total amount of the budgeted R&D expenses of RMB500 million appears to be reasonable when compared to empirical experience.

To further assess the reasonableness of the total amount of the budgeted R&D expenses of RMB500 million and since almost 79.7% of the total amount of the budgeted R&D expenses for both AD in adults and PN, we have obtained and reviewed the calculations and bases of determine estimated amounts for the Key Budgetary Elements (which in turn is highly representative (close to 80%) of the entire Budget Break-down) and set out below are our independent work done during the examination of the Key Budgetary Elements:

(1) Research center test fee was calculated based on (i) an estimated number of 648 patients for AD in adults, multiplied by the average fee per patient associated with the research center test contracts that have been signed; and (ii) an estimate number of 406 patients for PN, multiplied by the average fee per patient associated with the research center test contracts that have been signed. We have, on a random basis, obtained and reviewed 10 research center test contracts (5 for each of AD in adults and PN) signed by the Company with different research centers in 2024 for the R&D for AD in adults and PN respectively, and note that the average fee per patient in the Budget Break-down is within range of the average fee per patient of the reviewed research center test contracts.

(2) Each of the CRC fee for AD in adults and PN was determined by taking reference from the quotation provided by Shanghai Medkey Med-Tech Development Co., Ltd. ("**Medkey**"), a CRC service provider, in February 2024. We have obtained and reviewed the quotation provided by Medkey and note that the CRC fee per patient in the Budget Break-down for AD in adults and PN is in line with the quotation provided by Medkey.

(3) Each of the CRO service fee for AD in adults and PN was determined by taking reference from the quotation provided by Hangzhou Tigermed Consulting Co., Ltd. ("**Tigermed**") a CRO service provider, in January 2024. We have obtained and reviewed the quotation provided by Tigermed and note that the CRO service fee per patient in the Budget Break-down for AD in adults and PN is in line with the quotation provided by Tigermed.

(4) Each of the central laboratory fee for AD in adults and PN was determined by taking reference from two latest quotations provided by United-Power Pharma Tech Co., Ltd. ("**United-Power**") in February 2024 and May 2024 respectively. We have obtained and reviewed the two quotations provided by United-Power and note that the central laboratory fee per patient in the Budget Break-down for AD in adults and PN is in line with the quotations provided by United-Power.

(5) Patient recruitment service fee was calculated with 1,054 patients (i.e. 648 patients for AD in adults and 406 patients for PN) multiplied by an estimated average fee per patient. We have, on a random basis, obtained and reviewed 4 different patients recruitment contracts for AD in adults and PN signed by the Company and note that the estimated average fee per patient in Budget Break-down is in line with the average fee per patient in 4 different patients recruitment contracts.

(6) Labour costs for the development of the Subject Products were based on the estimated expenses for employee compensation, travel expenses, conference fees and hospitality expenses to be incurred by both the Company and Zhongmei Huadong during the development of the Subject Products, we note the Management had adopted past operational data to arrive at the estimates.

(7) Lastly but not least, the parties have included an overall buffer of 30% on the estimated gross expenses in the Budget Breakdown, we consider such buffer to be reasonable because as shown in the published research statistics mentioned above that the average cost per patient in Phase II and Phase III clinical trials is generally around US$50,000 to US$70,000, the range of which can be as wide as 40% from the lower bound.

Based on the above independent work done conducted by us, we are of the view that the Key Budgetary Elements have been reasonably determined.

We further note the Proposed Annual Cap for FY2024 of RMB45 million aligns with the payment terms stipulated under the Cooperation Agreement whereby the first patient dosing in Phase III clinical study in China for AD in adults and PN has been completed in May 2024. We have requested and reviewed the support documents to confirm that the completion of such milestone. Such milestone has also been disclosed in the interim results/report of the Company for the six months ended 30 June 2024. As such, the Proposed Annual Cap for FY2024 can therefore be established as the payment terms stipulated under the Cooperation Agreement require the relevant payment of RMB45 million to the Group be effected within 30 Business Days after the achievement of the relevant milestone. Therefore, the Proposed Annual Cap for FY2024 can be considered an actual amount and is no longer an estimate.

For the Proposed Annual Cap for FY2025 of RMB70 million, which aligns with the second and third payment milestones for AD in adults and PN, namely the last patient dosing in Phase III clinical study in China and obtaining the Independent Review Committee's written confirmation of achievement of the primary clinical endpoint, shall be completed by the end of 2025. For the Proposed Annual Cap for FY2026 of RMB135 million, which aligns with the remaining clinical development fees of the estimated sum of no more than RMB135 million, are expected to be paid by Zhongmei Huadong to the Company by the end of 2026.

Independent Shareholders should note this is the best estimate of the timelines by the parties and should the payment milestones be slipped due to the parties' inability to achieve R&D successes, the relevant amount of the Proposed Annual Cap for FY2025 and FY2026 will be rolled over to the following year and so long as the following year has a higher Proposed Annual Cap amount to enable the reimbursement, the Company will comply with the relevant Listing Rules.

Having considered the Proposed Annual Caps have been determined by reference to (i) the Budget Break-down has been jointly reviewed by members of the JDC representing each of the Company and Zhongmei Huadong; (ii) the total amount of the budgeted R&D expenses of RMB500 million appears to be reasonable when compared to empirical experience; (iii) based on the independent work done conducted by us on the Key Budgetary Elements, we are of the view that the Key Budgetary Elements have been reasonably determined; (iv) the total amount of the budgeted R&D expenses for both AD in adults and PN more or less resembles two times of the aggregated amount of the Proposed Annual Caps for FY2024, FY2025 and FY2026; (v) with the first patient dosing in Phase III clinical study in China for AD in adults and PN has been completed in May 2024, the Proposed Annual Cap for FY2024 can be considered an actual amount and is no longer an estimate; (vi) the Proposed Annual Caps for FY2025 and FY2025 align with the second and third payment milestones for AD in adults and PN; and (vii) the Company has adopted adequate internal control with respect to the transactions contemplated thereunder (including the Proposed Annual Caps), we consider that Proposed Annual Caps to be fair and reasonable so far as the Independent Shareholders are concerned.

OPINION AND RECOMMENDATION

Based on the above principal factors and reasons, we are of the view that the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee) are conducted in the ordinary and usual course of business of the Group and are in the interests of the Company and the Shareholders as a whole, the terms of the Cooperation Agreement and the transactions contemplated thereunder (other than the payment of the Marketing Service Fee but including the Proposed Annual Caps) are fair and reasonable so far as the Independent Shareholders are concerned. Accordingly, we recommend the Independent Board Committee to recommend, and we ourselves recommend, the Independent Shareholders to vote in favour of the ordinary resolution to be proposed at the EGM in relation to the Cooperation Agreement.

Yours faithfully,
For and on behalf of
Opus Capital Limited
Cheung On Kit Andrew

Executive Director

Mr. Cheung On Kit Andrew is an Executive Director of Opus Capital and is licensed under the SFO as a Responsible Officer to conduct Type 6 (advising on corporate finance) regulated activity. Mr. Cheung has over 16 years of corporate finance experience in Asia Pacific and has participated in and completed various financial advisory and independent financial advisory transactions.