

DATED the 21day of March 2024

BETWEEN

**BIOPROCESSING TECHNOLOGY INSTITUTE,
A*STAR RESEARCH ENTITIES**

AND

AJINOMOTO CO. INC

=====

AGREEMENT FOR RESEARCH COLLABORATION

=====

AGREEMENT FOR RESEARCH COLLABORATION

THIS AGREEMENT is made on the 21 day of March 2024

BETWEEN

Bioprocessing Technology Institute, A*STAR Research Entities, Company Registration No. 199702110H, having its principal office at 20 Biopolis Way, #06-01, Singapore 138668 (hereinafter referred to as "**BTI**") of the first part;

AND

Ajinomoto Co., Inc., a company incorporated in Japan, of 15-1, 1 Cho-me, Kyobashi, Chuo-ku, Tokyo, Japan (hereinafter referred to as "**COLLABORATOR**" or "**Ajinomoto**") of the second part.

RECITALS

- (A) BTI is a national research institution based in Singapore and funded by the Agency for Science, Technology And Research ("A*STAR") and has considerable knowledge, expertise and experience in, inter alia, the field of cell engineering and bioprocess development.
- (B) COLLABORATOR is a commercial food and biotechnology company and has an interest, expertise and experience in the development and commercialization of cell culture media for biologic medicines and has access to extensive markets.
- (C) BTI and COLLABORATOR wish to collaborate in research and development in the area of interest referred to above by undertaking the Project (as defined below) on the terms and conditions set out below.

NOW IT IS HEREBY AGREED as follows: -

1. DEFINITIONS

In this Agreement, unless otherwise expressly provided, the following terms shall have meanings ascribed to them below.

"Affiliates" means: (i) an organisation, which directly or indirectly controls either Party; or (ii) an organisation which is directly or indirectly controlled by either Party; or (iii) an organisation, which is controlled, directly or indirectly, by the ultimate parent company of either Party. The term "control" as used herein means the possession of the power to direct or cause the direction of the management and the policies of an entity, whether through the ownership of a majority of the outstanding voting security or by contract or otherwise. The term 'Affiliate' with regards to BTI shall include A*STAR, Accelerate Technologies Pte Ltd and all other research institutes and centres funded and managed by A*STAR.

"A*STAR" means the Agency for Science, Technology and Research.

"BTI Project IP" means all IP which was discovered, developed, conceived or reduced to practice solely by BTI or its employees, servants, invitees or agents in the course of the Project.

"Confidential Information" means the terms of this Agreement and any and all information, data, designs, memoranda, models, prototypes, and/or other material whether of scientific, technical, commercial, financial or other nature, furnished to or obtained by a Party from the other Party under this Agreement in written, oral or other tangible form clearly marked or designated as "Confidential" or by words of similar import. Information communicated by a disclosing Party orally or visually shall be summarized

in writing, marked “Confidential” and delivered to the receiving Party within fourteen (14) days of such communication failing which such information shall not constitute Confidential Information.

“**COLLABORATOR Project IP**” means all IP which was discovered, developed, conceived or reduced to practice solely by COLLABORATOR or its employees, servants, invitees or agents in the course of the Project.

“**Effective Date**” means 1 April 2024.

“**Intellectual Property (IP)**” means all Know-How and intellectual property rights (including without limitation patents, copyrights, designs, semiconductor layout designs, and trade secrets) worldwide arising under statutory or common law, and whether or not perfected.

“**Joint Project IP**” means all IP which was discovered, developed, conceived or reduced to practice jointly by BTI and COLLABORATOR or their employees, servants, invitees or agents in the course of the Project.

“**Know-How**” means any methods, techniques, processes, discoveries, inventions, innovations, unpatentable processes, specifications, recipes, formulae, designs, plans, documentation, drawings, data and other technical information which is secret, and identified or identifiable in a tangible form.

“**Party**” means either BTI or COLLABORATOR.

“**Parties**” means both BTI and COLLABORATOR.

“**Pre-Collaboration IP**” means all IP owned or controlled by each Party and which was conceived or reduced to practice either (a) prior to commencement of the work performed pursuant to this Agreement or (b) outside the scope of the work performed pursuant to this Agreement and which is introduced to or disclosed for the Project or otherwise supplied by each Party; and for BTI shall mean the Pre-Collaboration IP which is expressly documented by BTI and made available to COLLABORATOR.

“**Project**” means the research and development activities specified in the Project Plan.

“**Project Plan**” means the statement of work set out in Schedule 1 annexed hereto.

“**Term**” means the period as specified in Clause 4.

2. **STATEMENT OF WORK**

- 2.1 The Parties hereby agree to collaborate in the Project.
- 2.2 The Parties recognize that the Project is research in nature and hence completion within the period of performance, or within the limits of financial support allocated, or the achievement of the deliverables and/or milestones specified in the Project within or outside the time schedule specified therein cannot be guaranteed. The Parties shall exercise reasonable efforts in the performance of the Agreement in accordance with the agreed scope of works.
- 2.3 The Parties agree and declare that the obligations of BTI shall cease (except as otherwise set forth in Clause 13.2) upon the end of the Term.
- 2.4 Each Party shall obtain all relevant ethics and other approvals as may be relevant for its participation in the Project.

3. **CO-ORDINATORS**

- 3.1 The Project shall be supervised and coordinated by Dr Ian Walsh from BTI (hereinafter referred to as "BTI Co-ordinator") and Dr. Chihiro Tsuji from COLLABORATOR (hereinafter referred to as "COLLABORATOR Co-ordinator").
- 3.2 If for any reason the BTI Co-ordinator is unable to continue to serve under the Project, BTI agrees to appoint a successor within thirty (30) days of the unavailability of the BTI Co-ordinator, failing which the provisions of Clause 12.2 shall apply.

4. **PERIOD OF PERFORMANCE**

This Agreement shall come into force on the Effective Date and shall continue for a period of twelve (12) months unless earlier terminated in accordance with the terms of this Agreement or extended by the Parties' agreement in writing.

5. **PROJECT CONTRIBUTIONS**

- 5.1 Each Party will make such contributions in terms of manpower deployment, equipment, facilities, cash funding and other contributions as specified in Schedule 1, or as agreed from time to time by the Parties in writing.
- 5.2 COLLABORATOR shall pay to BTI the sum of Singapore Dollars One hundred and twenty-six thousand (S\$126,000) in accordance with the payment schedule specified in the Project Plan. Payments shall be made without any deduction or set-off whatsoever. The aforesaid sum is exclusive of goods and services tax and any other applicable taxes, and all such taxes shall be borne by COLLABORATOR, provided that each Party shall be liable for its own income tax obligations.
- 5.3 All rights, title and interest in any equipment and consumables purchased by BTI with the funding provided by COLLABORATOR as described in Clause 5.1 above shall vest in BTI.

6. **PUBLICATIONS**

- 6.1 Either Party may publish at any symposia, national, international or regional professional meeting or in any journal, thesis, dissertation, newspaper or otherwise of its own choosing, the findings, methods and results derived from the Project, but always subject to due observance of this Clause 6.
- 6.2 The Party intending to make the publication ("the Publishing Party") shall furnish the other Party ("the Other Party") copies of such proposed publication or presentation in advance of the submission of such proposed publication or presentation to a journal, editor, or other third party. The Other Party shall within thirty (30) days of receipt of the proposed publication or presentation forward its written objections to the same either because there is patentable subject matter that needs protection and/or there is Confidential Information (as defined in Clause 1 herein) or patentable information of the Other Party contained in the proposed publication or presentation. If no objection is made to the proposed publication or presentation within the stipulated time, the Publishing Party shall be free to proceed with the publication or presentation.
- 6.3 Confidential Information identified by the Other Party, which is governed by Clause 7, shall be deleted from the proposed publication or presentation unless the Other Party considers the Confidential Information to be patentable information, in which case it will be treated as set forth in the following sub-Clause.
- 6.4 In the event that the Other Party objects to any such publication or presentation on the basis that the same would disclose patentable information belonging to the Other Party, the Publishing Party shall refrain from making such publication or presentation for a further period of sixty (60) days from date of receipt of such objection in order for the relevant patent application(s) to be filed.

- 6.5 Each Party shall, in any publications it makes in relation to the methods, results and findings of the Project, acknowledge the other Party's contributions to the Project.

7. CONFIDENTIALITY

- 7.1 Each Party agrees, for the Term and for a period of three (3) years after the termination or expiration of the Agreement, to treat the Confidential Information of the other Party as strictly confidential and not to disclose it to any third party for any purpose whatsoever and not make use of the Confidential Information or any part thereof other than for the Project and to treat it with at least the same care and in the same manner as its own secret and valuable information. The receiving Party shall ensure that its employees to whom Confidential Information is disclosed covenant to keep such information confidential to the extent that the receiving Party is bound by this Agreement and that such covenants on the part of employees are strictly observed.

- 7.2 The provisions of Clause 7.1 above shall not apply to any:

- 7.2.1 information which is or was already known to the receiving Party at time of disclosure to it, or
 - 7.2.2 information which after disclosure to the receiving Party under this Agreement is published or otherwise generally available to the public otherwise than through any act, default or omission by the receiving Party of its obligations hereunder, or
 - 7.2.3 information which can be established by tangible evidence was independently developed by the receiving Party without the use of or reference to the disclosing Party's Confidential Information; or
 - 7.2.4 information which is required to be disclosed to governmental or regulatory bodies or to a court of competent jurisdiction pursuant to any written law, provided, however, that such disclosure is limited to that required to be disclosed.
 - 7.2.5 information which is disclosed to the receiving Party by a third party without restriction and without breach of the confidentiality obligations under this Agreement by the receiving Party.
- 7.3 It is agreed that BTI may disclose all or any part of the Confidential Information to its Affiliates on the basis that BTI shall procure that such Affiliates shall also agree to treat the information as confidential.
- 7.4 The receiving Party acknowledges that unauthorized disclosure or use of Confidential Information could cause great or irreparable injury to disclosing Party and that pecuniary compensation would not afford adequate relief or it would be extremely difficult to ascertain the amount of compensation which would afford adequate relief. Therefore, the receiving Party agrees that, in the event of such unauthorized disclosure or use of Confidential Information, the disclosing Party will have the right to seek and obtain injunctive relief in addition to any other rights and remedies it may have
- 7.5 Except for the disclosure of the existence of this Agreement, including the title and identification of the Parties, which information shall not be deemed confidential, neither Party shall disclose the specific terms and conditions of this Agreement without the express permission of the other Party.

8. INTELLECTUAL PROPERTY

- 8.1 COLLABORATOR agrees that if any licenses to third party's IP are required by BTI or COLLABORATOR in the conduct of their scope of work under this Agreement, COLLABORATOR shall be solely and fully responsible for procuring all such licenses and BTI will not be responsible for procuring the same.

- 8.2 All rights, title and interests to Pre-Collaboration IP shall remain with the Party introducing or disclosing the same and shall remain unfettered by this Agreement. Each Party grants to the other Party the right to use its Pre-Collaboration IP for the purposes of the Project during the Term and for no other purposes except as provided in this Agreement.
- 8.2A The Parties do not envisage that any BTI Project IP, COLLABORATOR Project IP or Joint Project IP (collectively, "**Project IP**") will be developed in the course of the Project or under this Agreement. However, in the event that any Project IP is developed in the course of the Project or under this Agreement, all Project IP developed shall be owned and governed by the terms set out in this Clause 8.
- 8.3 All rights, title and interests to BTI Project IP shall be solely owned by BTI. It is agreed that BTI shall be entitled to assign all its rights, titles and interests in the BTI Project IP to A*STAR, and that A*STAR shall be entitled to appoint an Affiliate to undertake all patenting, commercial and/or licensing activities relating to the same on its behalf.
- 8.4 All rights, title and interests to COLLABORATOR Project IP shall be solely owned by COLLABORATOR.
- 8.5 All rights, interests and title to Joint Project IP shall be governed by the following provisions:
- 8.5.1 The Parties shall own the Joint Project IP as joint tenants. COLLABORATOR agrees and accepts that BTI may, at its absolute discretion, assign or otherwise transfer to A*STAR, its share of the legal and beneficial ownership in the Joint Project IP without any reference to COLLABORATOR or any obligation to obtain COLLABORATOR's consent.
- 8.5.2 The Parties shall appoint one of them as the lead party (hereinafter referred to as "IP Lead Party") to undertake the filing, prosecution and maintenance of all applications for the registration of patents, trademarks, designs and copyrights (where applicable) for the protection of the Joint Project IP in the joint names of BTI and COLLABORATOR or their assignees. It is agreed that BTI shall have the first option to be the Joint IP Lead Party.
- 8.5.3 The Parties agree to give the IP Lead Party reasonable assistance in the filing, prosecution and maintenance of all applications for the registration of the Joint Project IP including without limitation patents and will cause to be executed all assignments and other instruments and documents as may be necessary or appropriate.
- 8.5.4 Both Parties shall bear all expenses incurred in the filing, prosecution and maintenance of all applications for the registration of the Joint Project IP equally, unless otherwise expressly agreed in writing. The IP Lead Party shall use reasonable efforts to keep the other Party informed prior to the filing and maintenance of all such applications. The IP Lead Party shall maintain adequate records showing all expenses incurred, which shall be made available to the other Party for inspection on reasonable notice. In the event that the IP Lead Party anticipates the possibility of any extraordinary expenditure of more than Singapore Dollars Twenty-five Thousand only (S\$25,000) arising from the preparation, filing, prosecution or maintenance of any application, it shall provide the other Party with full particulars and shall discuss with the other Party a mutually acceptable course of action prior to incurring, such expenditure. The IP Lead Party shall be entitled to receive reimbursement from the other Party for its share of the expenses within sixty (60) days of the other Party receiving an invoice from the IP Lead Party in respect of such expenses.
- 8.5.5 The other Party shall reimburse the IP Lead Party for its equal share of the expenses incurred in the filing, prosecution of applications and maintenance of

issued applications with respect to the Joint Project IP on a quarterly basis after receiving an invoice from the IP Lead Party for such expenses.

- 8.5.6 Each Party may elect to discontinue its obligation to pay or reimburse expenses associated with any such applications relating to Joint Project IP within any particular country upon sixty (60) days written notice to the other Party, and the Party's obligation to share in the said expenses shall cease immediately after the sixty (60) days' written notice period. Where any Party elects not to seek or maintain any application relating to the registration of the Joint Project IP in any particular country or not to share in the expenses thereof in any country, the other Party shall have the right to seek or maintain such protection in such country in the joint names of both Parties at its expense and will have full control over the prosecution and maintenance thereof. In such event, the Party choosing not to seek or maintain any application relating to the registration of the Joint Project IP or bear its share of the expenses will not lose its title to such Joint Project IP but shall have no further right to commercialise, or license for use on a commercial basis or use patents in respect of the Joint Project IP for commercial purposes or receive any proceeds from the commercial exploitation of the Joint Project IP.
- 8.5.7 Subject to Clause 8.5.6, each Party shall have the free and unfettered right to use, commercialise and license to third parties the Joint Project IP for any purpose without seeking the consent of, and accounting to, the other Party. The aforesaid right to use the Joint Project IP shall extend to all research centres and institutes funded and managed by A*STAR. It is agreed that any new Intellectual Property conceived or reduced to practice by the aforesaid use of the Joint Project IP shall be the property of the Party developing or inventing the same and the owner shall be entitled to deal with the said Intellectual Property at its absolute discretion.
- 8.6 BTI shall not disclose the Report (as defined in the Project Plan) to any third party or use the Report for any purpose, other than for the purpose of this Agreement or the Project, without the COLLABORATOR's prior written consent.

9. COLLABORATION

For the avoidance of doubt, it is agreed that notwithstanding the terms and conditions of this Agreement, each Party will have the following rights:

- (a) to conduct any research or development work in any field (including work relating to the research contemplated under this Agreement) independently of the other Party, whether by itself or in collaboration with any other party subject to each Party observing the provisions of Clause 7 hereof;
- (b) to continue existing commitments or to make new ones; and
- (c) to use, exploit (including sub-licensing) or otherwise take advantage of its Intellectual Property (other than the Joint Project IP which shall be subject to the terms and conditions of this Agreement).

10. WARRANTIES AND LIABILITIES

- 10.1 Each Party represents and warrants that it has the right to enter into this Agreement and provide the materials and services described herein. Except for the foregoing, BTI does not make any representations, conditions or warranties, either express or implied with respect to any information, its Pre-Collaboration IP, the work performed pursuant to the terms of this Agreement, or the BTI Project IP and Joint Project IP developed under this Agreement. Without limiting the generality of the foregoing, BTI expressly disclaims any implied warranty, condition or representation that the said information, its Pre-

Collaboration IP, BTI Project IP and/or the Joint Project IP developed under this Agreement:

10.1.1 shall correspond with a particular description;

10.1.2 is of a merchantable satisfactory quality;

10.1.3 is fit for a particular purpose; or

10.1.4 is durable for a reasonable period of time.

10.2 Nothing in this Agreement shall be construed as:

10.2.1 a warranty by BTI that anything made, used, sold or otherwise disposed of in connection with its Pre-Collaboration IP disclosed or introduced hereunder or that the BTI Project IP or Joint Project IP developed is or will be free from infringement of patents, copyrights, trademarks, industrial designs or other intellectual property rights of any third party; or

10.2.2 an obligation on BTI to bring or prosecute or defend actions or suits against or by third parties for infringement of patents, copyrights, trademarks, industrial designs or other intellectual property or contractual rights, whether in connection with its Pre-Collaboration IP, BTI Project IP or Joint Project IP developed under this Agreement or otherwise.

10.3 No action whether in contract or tort (including negligence) or otherwise arising out of or in connection with this Agreement may be brought by a Party against the other more than three (3) years after the course of action has accrued.

10.4 Save for death or personal injuries caused by negligence, in no event shall BTI, whether as a breach of contract, tort or otherwise, have any liability to COLLABORATOR or to a third party for any indirect, special, incidental, consequential damages, loss of profits or pure economic loss.

10.5 Notwithstanding anything to the contrary, BTI's total and cumulative liability under this Agreement, however arising, shall not exceed One hundred thousand Singapore Dollars.

11. **USE OF NAMES**

Neither Party shall issue any press release relating to this Agreement without obtaining the prior written consent of the other Party. Prior to being released or made, a copy of all press releases which a Party intends to issue or make regarding this Agreement shall be provided to the other Party for approval, which approval shall not be unreasonably withheld.

12. **TERMINATION**

12.1 Either of the Parties shall be entitled to terminate this Agreement immediately by notice in writing to the other Party (but without prejudice to any rights either Party may have against the other arising prior to such termination) if any of the events set out below shall occur. The said events are:

12.1.1 if the other Party shall commit any material breach of any of its obligations under this Agreement and shall fail to remedy such breach (if capable of remedy) within thirty (30) days after being given notice by the first Party so to do; or

12.1.2 if the other Party (being a company) shall go into liquidation whether compulsory or voluntary (except for the purposes of a bona fide reconstruction or amalgamation with the consent of the first Party, such consent not to be unreasonably withheld) or if the other Party shall have an administrator appointed

or if a receiver, administrative receiver or manager shall be appointed over any part of the assets or undertaking of the other Party.

- 12.2 Pursuant to Clause 3.2, BTI shall be entitled to terminate this Agreement if the events specified in Clause 3.2 hereof occur, in which case BTI shall be relieved of its obligations herein (except for the obligations described in Clause 13.2 and any other obligations that are expressed to survive termination of this Agreement) and shall have no liability whatsoever to COLLABORATOR in respect of such termination.

13. CONSEQUENCE OF TERMINATION

- 13.1 The provisions of Clauses 6, 7, 8, 9, 10, 11, 12.2, 13, 14, 16, 17, 18, 19, 20 and 21 shall continue in full force and in accordance with their terms, notwithstanding the expiration or termination of this Agreement for any reason.

- 13.2 Without prejudice to any claims for damages that either Party may be entitled to, upon termination or expiration of this Agreement,

13.2.1 each Party shall promptly return all materials of the other Party in its possession, including, without limitation, Confidential Information of the other Party, upon the request of the other Party; and

13.2.2 where applicable, COLLABORATOR shall pay BTI for all work done by BTI and any non-cancellable commitments incurred by BTI up to and including the date of termination.

14. ASSIGNMENT

- 14.1 Save as expressly provided in this Agreement, neither of the Parties shall assign this Agreement or otherwise transfer its rights or obligations, or any part thereof, under this Agreement without the prior written consent of the other Party.

- 14.2 It is agreed that if at any time after the date of this Agreement the functions and operations of BTI are assigned, merged, transferred into or otherwise forms part of another organization of A*STAR ("the New Entity"), such that the New Entity takes over the whole or substantially the whole of BTI's operations, then it is agreed that BTI may:

14.2.1 at its option, assign this Agreement in its entirety to the New Entity which will then assume all of BTI's rights and obligations hereunder; or

14.2.2 assign all or any part of its rights hereunder to the New Entity.

15. FORCE MAJEURE

- 15.1 Neither Party shall be liable for delays in delivery or performance when caused by any of the following which are beyond the actual control of the delayed Party: (i) acts of God, (ii) acts of the public enemy, (iii) acts or failure to act by the other Party, (iv) acts of civil or military authority, (v) governmental priorities, (vi) hurricanes, (vii) earthquakes, (viii) fires, (ix) floods, (x) epidemics or pandemics, (xi) embargoes, (xii) war, and (xiii) riots (hereinafter referred to as the "Force Majeure Event").

- 15.2 The respective obligations of either Party hereunder shall be suspended during the time and to the extent that such Party is prevented from complying therewith by a Force Majeure Event provided that such Party shall have given written notice thereof, specifying the nature and details of such event and the probable extent of the delay to the other Party.

- 15.3 In case of a Force Majeure Event, the time for performance required by either Party under this Agreement shall be extended for any period during which the performance is prevented by the event. However, the other Party may terminate this Agreement by notice if such an event prevents performance continuously for more than thirty (30) days.

16. DISPUTE RESOLUTION

- 16.1 The Parties agree to attempt to settle any claim or controversy arising out of this Agreement through consultation and negotiation in good faith and spirit of mutual cooperation. Any dispute between the Parties relating to this Agreement will first be submitted in writing to one senior executive from each Party, who will promptly meet and confer in an effort to resolve such dispute. Each Party's senior executive will be identified by notice to the other Party and may be changed at any time thereafter by notice to the other Party. Any agreed decisions of the senior executives will be final and binding on the Parties. In the event the senior executives are unable to resolve any dispute within thirty (30) days after submission to them, either Party may then refer such dispute to arbitration in accordance with Clause 16.2.
- 16.2 Any dispute which cannot be resolved by amicable settlement by the process described in Clause 16.1 above shall be referred to and finally resolved by arbitration in accordance with the Arbitration Rules of the International Chamber of Commerce for the time being in force which rules are deemed to be incorporated by reference to this clause. The tribunal shall consist of a single arbitrator. The language of the arbitration shall be in English. Any award made hereunder shall be final and binding upon the Parties and judgment on such award may be entered into any court of tribunal having jurisdiction hereof.
- 16.3 Notwithstanding Clauses 16.1 and 16.2, the Parties agree that the Parties are entitled to seek injunctive or interim relief in any court of competent jurisdiction to prevent any breach or threatened breach of this Agreement by the other Party.

17. GOVERNING LAW

The validity and interpretation of this Agreement and the legal relation of the Parties to it shall be governed by the laws of England and Wales.

18. NOTICE

- 18.1 Any notice to be given by any Party to this Agreement shall be in writing and shall be deemed duly served if delivered personally or sent by facsimile transmission or by prepaid registered post to the addressee at the address as stated above or (as the case may be) the facsimile number of that Party or at such other address (or facsimile number) as the Party to be served may have notified the other Party for the purposes of this Agreement.
- 18.2 Any notice sent by facsimile shall be deemed served when despatched and any notice served by prepaid registered post shall be deemed served forty-eight (48) hours after despatch thereof. In proving the service of any notice it will be sufficient to prove in the case of a letter that such letter was properly stamped addressed and placed in the post or delivered or left at the current address if delivered personally and in the case of a facsimile transmission was duly despatched to the facsimile number of the addressee given above or subsequently notified for the purposes of this Agreement.

19. ENTIRE AGREEMENT

Unless otherwise expressly specified, this Agreement embodies the entire understanding between the Parties in respect of the Project and any prior or contemporaneous representations, either oral or written, are hereby superseded. No amendments or changes to this Agreement shall be effective unless made in writing and signed by authorized representatives of the Parties.

20. GENERAL

- 20.1 All deliverables, information, and other subject matter made available to COLLABORATOR shall be used for commercial and/or civilian purposes only. COLLABORATOR shall ensure that it and its end-users comply with all applicable laws,

- rules and regulations governing the use, export and disposal of the deliverables, information, and other subject matter.
- 20.2 No exercise or failure to exercise or delay in exercising any right power or remedy vested in any Party under or pursuant to this Agreement shall constitute a waiver by that Party of that or any other right power or remedy.
- 20.3 The Parties shall co-operate with each other and execute and deliver to the other Party such instruments and documents and take such other action as may be reasonably requested from time to time in order to carry out and confirm the rights and the intended purpose of this Agreement.
- 20.4 In the event that any term, condition or provision of this Agreement is held to be a violation of any applicable law, statute or regulation the same shall be deemed to be deleted from this Agreement and shall be of no force and effect and this Agreement shall remain in full force and effect as if such term condition or provision had not originally been contained in this Agreement. Notwithstanding the above in the event of any such deletion the Parties shall negotiate in good faith in order to agree the terms of a mutually acceptable and satisfactory alternative provision in place of the provision so deleted.
- 20.5 This Agreement may be executed in any number of counterparts or duplicates each of which shall be an original but such counterparts or duplicates shall together constitute but one and the same agreement.
- 20.6 The recitals and schedules of this Agreement shall form an integral part of this Agreement.
- 20.7 It is agreed that for the purposes of this Agreement, BTI shall mean the Bioprocessing Technology Institute only and shall not extend to any other research institute, center or division of A*STAR Research Entities. For avoidance of doubt, no research institute, center or division within A*STAR Research Entities (other than BTI) shall have any obligation under this Agreement to the COLLABORATOR or to disclose to or receive from the COLLABORATOR any information unless expressly agreed in writing.

21. THIRD PARTY CONTRACTS ACT

Save for the parties identified in Clauses 7, 8 and 14, the Parties do not intend that any term of this Agreement should be enforceable by virtue of the Contracts (Rights of Third Parties) Act 2001 or otherwise, by any person or entity who is not a party to this Agreement.

22. ELECTRONIC SIGNATURE

The parties hereby agree to electronically execute this Agreement using the electronic signature system "Adobe Sign" (hereinafter referred to as the "System"). Each of electronic files of this Agreement that is downloaded from the System shall be deemed an original, but all of which shall constitute one and the same instrument together with the original electronic file of this Agreement, which is electronically signed and stored in the System.

SCHEDULE 1

PROJECT PLAN

Machine learning derived media components important for glycosylation of antibody production in CHO cells.

1. BACKGROUND

Antibody glycosylation is one of the most important CQA to monitor in bioprocessing operations. The heterogeneity and abundance of mAb glycans are very sensitive to the media components in the cell culture that express the protein drug product.

The Bioprocessing Technology Institute (BTI) propose to work with Ajinomoto Corporation to map the influence of various CHO media components on **mAb N-glycosylation** critical quality attributes (CQAs). The proposed platform leverages Ajinomoto's cell culture media range and expertise in media characterization combined with BTI's Background Intellectual Property (IP) in glycomics and machine learning (ML) with respect to glycosylation.

Objective: Using a model-based framework to **enable the optimization of Ajinomoto's in-house cell culture media.**

Goals: The project will involve the training of algorithms on data that consists of absolute concentrations of media components and the corresponding N-glycan abundances at numerous time points. There are two major goals of the project:

1. we will identify the combinations of media component in Ajinomoto's cell culture media range which affect mAb glycan quality using BTI's *in silico* modeling tools.
2. develop a model-based media design approach to modify basal/feed media rationally towards the desired mAb N-glycosylation.

2. SCOPE OF WORK

Identification of media component combinations for Ajinomoto's in-house cell culture media affecting N-glycans (Phase 1)

As a step towards discovering new molecular levers for cell-culture bioprocessing we will examine if machine learning (ML) models can discover glycosylation relevant media components (GMRCs) in Ajinomoto's in-house cell culture media formulations. Feature selection ML algorithms will be used to establish which GMRCs are important for modelling glycan abundances in CHO in the dataset. The dataset will be created by Ajinomoto by performing in-depth cell culture and analysis of the media components and N-glycan analysis (% relative abundances). The approach is shown in Figure 1.

After ML selection, the GMRCs will then be confirmed that they influence N-glycan abundances by altering, in wet-lab experiments, the levels of the selected GMRCs in basal and feed while keeping the physiochemical parameters constant. Ajinomoto will perform this experimental validation. The experimental reinforced confidence is shown in Figure 1A. The experiment validation will give further confidence that the GMRCs have a 'cause and effect' on N-glycan abundance.

Another important factor that needs to be considered is the possibility that no GMRCs will be found that influence N-glycan abundance in the wet-lab experiments. In this case we would have to consider and discuss how to add additional basal/feed metabolites such as nucleotide sugars to the media (Figure 1B).

Importantly, in this phase of the project we will not determine the absolute metabolite concentrations we should change in basal and feed to improve N-glycosylation. The GMRCs at this stage are only indicators/markers for improving the media. In the second phase of the

project, algorithms that can suggest favorable changes to basal and/or feed will be developed (a new scope will be described for this if we decide to proceed to phase 2).

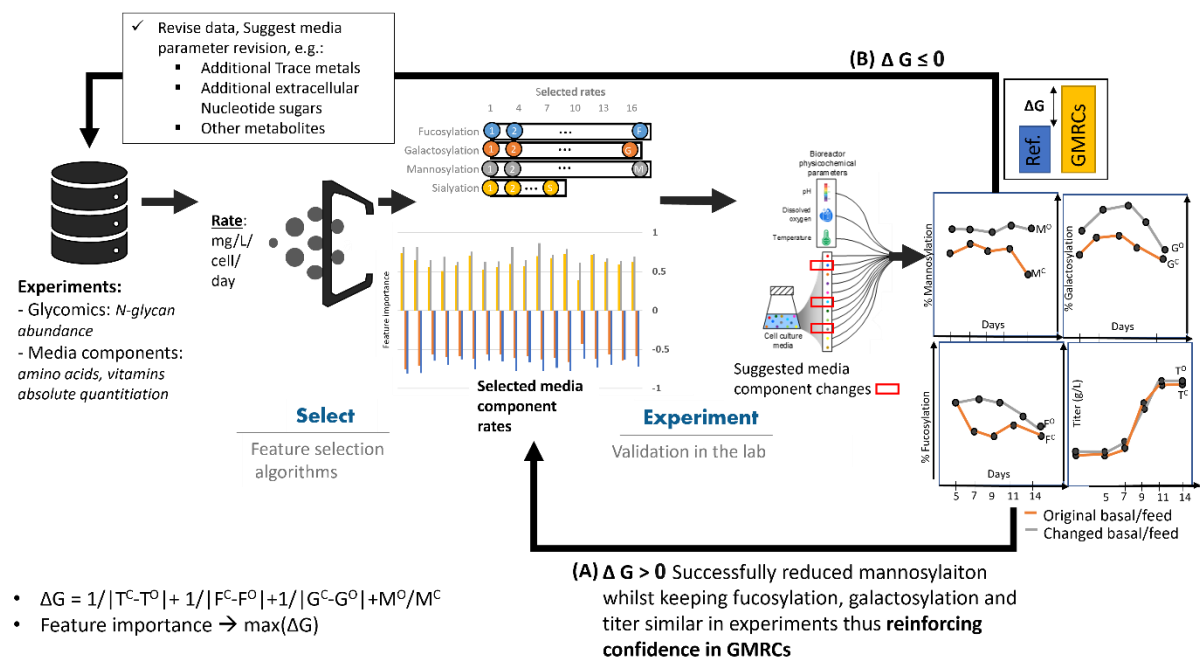


Figure 1. Proposed workflow of phase 1 – feature selection ML. This part of the project involves finding the relevant features in the cell culture media that are important for N-glycan abundance changes. That is, they are markers for N-glycosylation particularly mannosylation. After they are detected, it is important that they experimentally show influencing effects on reducing mannosylation whilst keeping fucosylation, galactosylation and titer similar to the reference media (i.e. $\Delta G > 0$). This can be achieved by altering their concentrations in basal and/or feed. The altered amount/concentration of the media component in basal/feed will not be determined in this phase. We will attempt to maximize $\Delta G = 1/(T^C-T^O) + 1/(F^C-F^O) + 1/(G^C-G^O) + -M^O/M^C$ where T^O , F^O , G^O , and M^O are the titer, fucosylation, galactosylation and mannosylation of the original reference media normalised between [0-1]; T^C , F^C , G^C , and M^C are the titer, fucosylation, galactosylation and mannosylation, normalised between [0-1], when using the computationally determined GMRCs.

Objectives:

- Identification of media components (GMRCs) relevant for controlling glycosylation by feeding regimes. Components may be individual or in combination, e.g. media component A, B and C should be changed at the same time.
- Establish experimental confidence that the GMRCs reduce the abundance of mannosylation and keep the levels of fucosylation and galactosylation at approximately the same levels as the reference media.

3. PROJECT SCHEDULE / TIME FRAME

Task	Q1	Q2	Q3	Q4
Phase 1. N-glycan CQA improvement - Machine learning selection				
Feature selection - detect glycan related media components (GMRCs)				
Ajinomoto assess if changes shortlisted GMRCs effect N-glycan abundance in cell culture				S/G 1

Stop / Go (S/G) situations:

S/G 1: The identified GMRCs do not seem to effect N-glycan abundance in Ajinomoto's experimental validation. Therefore, we would discuss whether to stop the project or continue.

4. DELIVERABLES

BTI DELIVERABLES

1. A report ("**Report**") listing the media markers important for mannosylation abundance changes. The listing will be derived using our in-house ML framework. The listing will include combinations of media components that likely affect mannosylation. Subsequently, the media markers will be reduced, or increased, by Ajinomoto's media formulation team and validated by Ajinomoto if they affect glycan levels.

AJINOMOTO DELIVERABLES

1. Minimal dataset as described in Table 1.

	Conditions	Days	Replicates	Etc.
Cell culture profiling	4	(0), 3, 5, 7, 9, 11, 13, 14	2	VCD, VIA, Titer, Glucose, Lactate, Ammonia, Volume, Temp, pH, DO, Osmolarity
SMA	4	5, 7, 9, 11, 14	2	AA, vitamin, amine, nucleoside, metal
N-glycan profile	4	5, 7, 9, 11, 14	2	AA, vitamin, amine, nucleoside, metal

Table 1. Initial dataset description.

2. Revision of dataset if points raised by BTI on revision is acceptable.
3. Experimental validation of models.

5. CASH AND IN-KIND CONTRIBUTIONS FROM EACH PROJECT PARTY

• Budget Breakdown

Phase 1

<u>In-kind Contribution by BTI</u>		(SGD)
	<u>Manpower</u>	
	Project coordinator 6 months, 10% of time	25 000

<u>In-kind Contribution by Ajinomoto</u>		(SGD)
	<u>Equipment</u>	
	Cell culture and analysis	10 000
	<u>Manpower</u>	
	Conducting cell culture	28 000
	Analysis	14 000
	<u>Consumables</u>	
	Cell culture and analysis	3 000

<u>Cash Contribution by Ajinomoto</u>		(SGD)
	<u>1 x bioprocessing data analytical scientist</u>	
	Research Scientist 6 months, 80% of time.	126,000

- **Payment Schedule**

Issuing of Invoice	Amount in SGD	Payment Due Date
Upon execution of Agreement	\$63,000	30 days from date of invoice
Upon submission of the Report	\$63,000	

6. BACKGROUND INTELLECTUAL PROPERTY

- ***Intellectual Property***

BTI: Yes

- Know how on ML algorithms are optimized to predict the abundance of glycan forms enzymatically released from antibodies using omics data derived from multiple bioreactor runs (TD: BTI/11271; BTI/Z/13300)
- Improved CHO-specific genome-scale metabolic model and N-glycosylation model, simulation methodologies of each model, knowledge on integration of two models into a single multi-scale one (TD number).

Ajinomoto: Yes

- Proprietary range of mammalian cell culture media
- Expertise on cell culture media development (Media complexity, formulation, etc)
- Knowledge on individual media component's solubility and stability

- ***Proprietary Know-How:***

BTI: Yes

Machine learning and mechanistic modelling know-how for improved bioprocessing of biologics

Bioprocessing knowhow – Cell line development, Bioreactor runs, cell culture media feeding and purification.

Ajinomoto: Yes

7. FOREGROUND INTELLECTUAL PROPERTY

Likelihood of protectable IP from this Project?

- **Patentable invention**

Unlikely

- **Other form of IP (e.g.: Proprietary Know-How/Copyright)**

Possible

Likelihood of commercialising/licensing the discovery/invention from this Project?

- **Commercialisation**

Possible







21 Mar 2024 BTI-Ajco RCA

Final Audit Report

2024-03-26

Created:	2024-03-21
By:	Intellectual Property Dept. Ajinomoto (contract_ipd@asv.ajinomoto.com)
Status:	Signed
Transaction ID:	CBJCHBCAABAANUgumADgIIrVQiHE1d09DU-JxDsWYo4e

"21 Mar 2024 BTI-Ajco RCA" History

-  Document created by Intellectual Property Dept. Ajinomoto (contract_ipd@asv.ajinomoto.com)
2024-03-21 - 6:06:13 AM GMT- IP address: 163.58.199.20
-  Document emailed to koh_boon_tong@bti.a-star.edu.sg for signature
2024-03-21 - 6:08:55 AM GMT
-  Email viewed by koh_boon_tong@bti.a-star.edu.sg
2024-03-22 - 8:16:41 AM GMT- IP address: 192.122.132.242
-  Signer koh_boon_tong@bti.a-star.edu.sg entered name at signing as BTKoh
2024-03-22 - 8:17:35 AM GMT- IP address: 192.122.132.242
-  Document e-signed by BTKoh (koh_boon_tong@bti.a-star.edu.sg)
Signature Date: 2024-03-22 - 8:17:37 AM GMT - Time Source: server- IP address: 192.122.132.242
-  Document emailed to Mathew Lau (mathew_lau@bti.a-star.edu.sg) for signature
2024-03-22 - 8:17:41 AM GMT
-  Email viewed by Mathew Lau (mathew_lau@bti.a-star.edu.sg)
2024-03-22 - 8:46:23 AM GMT- IP address: 112.199.161.20
-  Document e-signed by Mathew Lau (mathew_lau@bti.a-star.edu.sg)
Signature Date: 2024-03-22 - 8:47:15 AM GMT - Time Source: server- IP address: 112.199.161.20
-  Document emailed to michael.lish.tq8@asv.ajinomoto.com for signature
2024-03-22 - 8:47:17 AM GMT
-  Email viewed by michael.lish.tq8@asv.ajinomoto.com
2024-03-26 - 7:08:02 AM GMT- IP address: 104.47.23.190
-  Signer michael.lish.tq8@asv.ajinomoto.com entered name at signing as Michael Lish
2024-03-26 - 7:08:22 AM GMT- IP address: 34.98.160.110



Document e-signed by Michael Lish (michael.lish.tq8@asv.ajinomoto.com)

Signature Date: 2024-03-26 - 7:08:24 AM GMT - Time Source: server- IP address: 34.98.160.110



Document emailed to masakazu.sugiyama.qk8@asv.ajinomoto.com for signature

2024-03-26 - 7:08:27 AM GMT



Email viewed by masakazu.sugiyama.qk8@asv.ajinomoto.com

2024-03-26 - 7:19:32 AM GMT- IP address: 52.102.13.5



Signer masakazu.sugiyama.qk8@asv.ajinomoto.com entered name at signing as Masakazu Sugiyama

2024-03-26 - 7:20:15 AM GMT- IP address: 34.98.160.30



Document e-signed by Masakazu Sugiyama (masakazu.sugiyama.qk8@asv.ajinomoto.com)

Signature Date: 2024-03-26 - 7:20:17 AM GMT - Time Source: server- IP address: 34.98.160.30



Agreement completed.

2024-03-26 - 7:20:17 AM GMT



Adobe Acrobat Sign