UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

March 18, 2022

Anatoly Dritschilo
Chief Executive Officer
Shuttle Pharmaceuticals Holdings, Inc.
One Research Court, Suite 450
Rockville, MD 20850

Re: Shuttle Pharmaceuticals Holdings, Inc.
Draft Registration Statement on Form S-1
Submitted September 16, 2019
CIK No. 0001757499

Dear Dr. Dritschilo:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Amendment No. 1 to Draft Registration Statement Submitted February 11, 2022

Summary Financial Information, page 12

1. Please revise the financial information presented here to also include loss per share calculations.

Research and Development-Net of contract expense reimbursements, page 44

2. Please revise to disclose the costs incurred during each period presented for each of your key research and development products/projects. If you do not track your research and development costs by project, please disclose that fact and explain why you do not maintain and evaluate research and development costs by project. Provide other quantitative or qualitative disclosure that provides more transparency as to the type of

research and development expenses incurred (i.e., by nature or type of expense) which should reconcile to total research and development expense on the Consolidated Statements of Operations.

Financial Statements
Note 2- Summary of Significant Accounting Policies
Fair Value of Finanicial Statements, page F-10

3. We note your disclosures stating, "In drawing its conclusions, management considered various relevant factors, including the work of an independent third-party valuation firm engaged to provide a valuation analysis as of June 30, 2019, which indicated a valuation of $12.61 per common share. Management ultimately determined, and the valuation firm concurred, that the Market Approach method was the most appropriate valuation methodology under the circumstances." Please tell us your reliance on a third-party and how you considered filing a written consent of this entity as an exhibit to your registration statement. Refer to Rule 436 and Section 7 of the Securities Act and Question 141.02 of the Compliance and Disclosure Interpretations on Securities Act Sections, which can be found at https://www.sec.gov/corpfin/securities-actsections.

Note 8- Stockholders' Equity
Equity Incentive Plan, page F-17

4. We note your disclosure stating that your 2018 Equity Incentive Plan provides for equity incentives to be granted to your employees, executive officers, or directors and to key advisers and consultants, which may be in the form of stock options, restricted stock awards, other stock based awards, or any combination of the foregoing. As it relates to the 773,453 shares granted under your 2018 equity Incentive Plan, please expand your disclosure to include all of the information required by ASC 718-10-50-2, as applicable to you.

Amendment to Form S-1 filed February 11, 2022

Cover Page

5. We note your response to comment 1 indicating that you are not registering any shares for resale. However, your registration statement references 500,000 shares being sold by your selling shareholders. Please revise your fee table to include the shares being offered by your selling shareholders and file the fee table as an exhibit to your registration statement. Please see Item 601(b)(107) of Regulation SK. Additionally, we note your cover page indicates your intention to offer securities on a delayed and continuous basis. Given that you are conducting a firm commitment offering, please explain why you have indicated that you are relying on Rule 415.

Prospectus Summary, page 1

6. Please revise your summary to present a balanced view of your company and its current stage of development by focusing on the most material aspects of your company, eliminating the predictive assumptions and clearly stating that you have no FDA approved products, disclosing that you are several years away from applying for a new drug application, have never generated any product revenue and received an audit report that raised substantial doubt about your ability to continue as a going concern. For example:

   - Eliminate the description of your product candidates as "first-in-class." The description applies to a product that has received FDA approval;
   - Remove your statement that you intend to follow the FDA's fast-track development program for developing Ropidoxuridine as it is not appropriate to assume the required evidence of efficacy from trials that you have not yet conducted;
   - Remove statements predicting positive results and future partnerships, such as "Positive results from proof-of-concept studies will enable collaborative partnerships with other pharmaceutical companies for Phase III clinical trials";
   - Ensure that you discuss the risks and obstacles you face in developing your product candidates with the same level of detail as you use to discuss the positive aspects of your operations.

7. Move the detailed scientific explanations of the mechanism of action of your candidates and discussions of clinical trial results to the Business section where the disclosure can be placed in the proper context.

8. We have reviewed your revisions in response to our prior comment 4 and reissue. There are still multiple numerous references to the safety and efficacy throughout your disclosure. Efficacy and safety are determinations that are solely within the authority of the FDA. You may present clinical trial end points and objective data resulting from trials without concluding efficacy, and you may state that your product candidates are well tolerated, if accurate. Please revise any statements referencing safety and efficacy throughout your document, including but not limited to the following:

   - on page 44, "The clinical development of Ropidoxuridine has shown drug safety, bioavailability and a maximum tolerated dose has been established for use in Phase II clinical trials."
   - on page 48, "These results support the safety and potential efficacy in combination with radiation and provide the foundation for design of Phase Ib/II clinical trials in brain tumors and Phase II clinical trials in sarcomas or un-resectable pancreatic cancers, with all three disease sites being eligible for orphan disease designations."
   - on page 49, "suggesting that a combination of SP-1-303 with an immune checkpoint blocker may enhance the therapeutic efficacy in hormone responsive breast cancer."

9. Please provide a textual discussion explaining the graphic appearing at the bottom of page 2. It appears to depict two product candidates and the potential disease indications you intend to develop the candidates to address but it is not clear what the arrows are intended to depict. Additionally, it does not indicate provide any indication of what remains to be done to develop the product candidate.

10. Please revise your disclosure to clarify whether you have filed an IND for your Phase I study of Extended Bio-availability Ropidoxurdine (IPdR/TPI) and, if accurate clarify that SP-1-161 and SP-1-303 are in pre-clinical stages of development.

11. We note your statement on page 4 indicating that you "intend to perform clinical studies to support the FDA's efficacy and safety findings (IND-enabling studies) for the - IPdR/TPI combination..." Please explain your reference to the FDA's efficacy and safety findings. If this is a reference to the approval to conduct a Phase I clinical trial, please delete the reference to the FDA's efficacy and safety findings. The FDA continues to assess safety and efficacy throughout the entire development process and it is not appropriate to interpret FDA approval of your Phase I trial as an FDA finding related to safety and/or efficacy.

Development Strategy, page 6

12. Please clarify the meaning of "CTEP," and "MTD" and explain the significance of Temodar.

Market Opportunity, page 6

13. Please revise your table on page 6 to explain the significance of the asterisks and to explain the the headers "RT Cases Annually" and "RT Cases (estimated)." Do the RT Cases estimated relate to a different time period? What is the basis for the estimate?

Pre-IPO Bridge Financing, page 8

14. Please explain the timing of your plan to use funds from this offering to repay two accredited investors, who will use such proceeds to exercise their warrants and sell their shares in this offering. It appears that the shares they are planning to sell in this offering will not be outstanding at the time of your offering.

Business
Our Pipeline, page 48

15. We note that your table indicates you have completed Phase I in your development of Ropidoxuridine. However, the description of your product candidate indicates that your Phase I clinical trial results provide the foundation for the design of Phase Ib/II clinical trials. Your pipeline table should depict when an entire phase of development has been completed, as opposed to one of multiple trials in a phase of development. Please tell us why you believe it is appropriate to indicate that you have completed Phase I testing when you are planning to conduct a Phase Ib/II trial.

16. Please revise your table to clarify which product candidates Class II HDAC6 Selective, Class I - ER+ Targeting and Dual Functional Pan HDAC are and identify the indications you are seeking to treat with your candidates.

17. Please expand your business section to explain the Cell Lines and Cell Products and Patient Metabolite testing kit.

18. We note your description of Ropidoxuridine discloses the results of fourteen of the eighteen participants in the study, please revise to describe the results of the other four participants.

Our Product Candidates, page 60

19. We note your disclosure indicates you have received an SBIR contract from NIH to fund a Phase I trial with Brown University to determine the maximum tolerated dose in patients with advanced gastrointestinal cancers. This disclosure appears to related to the Phase I trial that has been completed. Please revise to update your disclsoure.

Strategic Agreements, page 60

20. The significance of the identified strategic agreements is unclear. Please revise to your descriptions to provide additional information. For example:

- With respect to the agreement with Georgetown, we note that Georgetown acted as a subcontractor for the work you conducted pursuant to two SBIR contracts. Please clarify whether the intellectual property you have the option to license is related to those subcontract agreements, including whether the intellectual property was developed by Georgetown in the course of conducting such work or if Georgetown University used it's own previously developed intellectual property in performing the subcontracted work. If you develop candidates related to the African-American prostate cancer health disparities project or the metabolomic biomarker project, is such development dependent on intellectual property owned by Georgetown University?
- With respect to the material transfer agreement with Georgetown University, please clarify whether your HDAC inhibitor platform technology is dependent on this

agreement. If so, please describe the material terms of this agreement, including payment terms as well as your rights and obligations under the agreement.

21. Please describe all material provisions of your agreement with Propagenix, including identifying your product candidates that are dependent on the agreement, and quantifying any amounts paid, potential future milestone payments and royalty provisions.

The SBIR Program, page 63

22. Please clarify the material terms of each of your SBIR contracts, including funding received to date, potential future funding and what you need to accomplish to qualify for the future funding. Additionally, clarify the ownership of any intellectual property developed during the course of the program. To the extent the NIH receives any rights to the intellectual property, please clarify.

23. Please clarify your strategy for commercializing prostate cancer cell lines and and predictive biomarkers. For example, your table on page 48 references a testing kit, but there is no disclosure about plans to develop a testing kit.

Collaborative Arrangements, page 64

24. We note your response to our prior comment 12, stating that all relevant references to Doranidazole have been removed from the prospectus. However, there are still several references to Doranidazole throughout your disclosure. Please remove them or advise.

Executive Compensation, page 81

25. Please update your Summary Compensation Table.

Related Party Transactions, page 83

26. Please revise your descriptions of the related party transactions to also include the identify the related party.

Signatures, page II-3

27. We have reviewed your response to our prior comment 24 and reissue. Please ensure that the requisite signatures and dates are provided when you amend your registration statement.

You may contact Kevin Kuhar at 202-551-3662 or Tracie Mariner at 202-551-3744 if you have questions regarding comments on the financial statements and related matters. Please contact Jordan Nimitz at 202-551-5831 or Suzanne Hayes at 202-551-3675 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Megan Penick, Esq.