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I. EXECUTIVE SUMMARY

Company: PeptiDream, Inc.	**Stock Price (¥):** ¥ 5,310
Ticker: 4587 JP	**Market Cap (¥):** ¥665.4 billion
Industry: Pharmaceuticals	**Float:** 74.6%
Report Date: November 7, 2019	**Average Volume:** ¥3.21 billion

PeptiDream: A Sportscar Without Wheels

When wooing retail investors, Chairman Kiichi Kubota likes to compare non-standard peptide drugs to a Jaguar sports coupe (while comparing other drug types to a dump truck and motor scooter). We believe this comparison would be more relevant to PeptiDream if the Jaguar were missing its wheels.

PeptiDream has really cool technology – it can put trillions of different peptides in a single test tube! But we believe the coolness of PeptiDream's technology amounts to at best a very small business opportunity. In other words, the question investors need to ask the company is "So what?"

PeptiDream's technology allows for the creation of vast libraries of peptides - but library size doesn't necessarily correlate with drug development success.[1] The technology can aid in identifying hits to targets of interest, but these hits then need to be modified to produce compounds with drug-like properties, and we believe it is here PeptiDream's peptides have

[1] See infra.

problems. There is no way of knowing for certain why the rate of progression to the clinic is so low, but we heard from a drug discovery expert that translating peptide hits into viable drugs with desirable pharmacokinetic characteristics is challenging because of the specific chemical properties of peptides. (Note that the partner for whom this researcher works is still listed in PeptiDream's materials, despite the researcher describing the partnership as inactive.) Therefore, we view PeptiDream's recent partnerships, such as one with drug delivery technology company PharmaIN Corp, which aims to increase peptide stability and slow their degradation,[2] as an indication that PeptiDream has encountered systemic limitations in advancing its drug candidates to the clinic.

In early 2019, Chairman Kubota told retail investors "PeptiDream cannot possibly fail as long as the projects that that you see here stay on track".[3] We believe that a substantial number of those projects and their corresponding partnerships are effectively dormant or dead. We assume Chairman Kubota knows this too. Meanwhile, senior management has spent the past six years cashing out ¥31.4 billion of stock,[4] part of which likely funded CEO Patrick Reid's ¥1.9 billion beachfront estate in Maui.[5] And though co-founders Kiichi Kubota and Hiroaki Suga each speak glowingly about PeptiDream, they have sold ¥2.9 billion of stock in just the last six months.[6] For these and other reasons, we think PeptiDream will fail to meet investors' expectations by large margins.

Summary

Muddy Waters Capital is short PeptiDream, Inc. because we believe it is more stock story than substance, and the market is deluded as to its potential for commercializing drugs. PeptiDream touts its 19 major partnerships and 101 discovery programs, but half of its partnerships are likely effectively dormant or dead. We see it being highly unlikely that the company's own development attempts ever yield significant revenue. PeptiDream's recent shift in focus to developing its own pipeline recalls once-beloved Sosei Group Corporation ("***Sosei***"), which has lost significant market cap over the past three years. We forecast PeptiDream will have at most one drug commercialized by 2027, versus investor expectations of eight to 15 by then.

To even remotely justify investor expectations, PeptiDream would likely need to succeed in meeting drug development milestones at rates many times industry norms. But to date, PeptiDream has underperformed these industry norms, despite being in operation since 2006.

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[2] http://contents.xj-storage.jp/xcontents/45870/7cc267eb/b31e/45c9/9202/3aa661f1e395/20190605161410843s.pdf

[3] A researcher attended a January 28, 2019 investor meeting in Sapporo and reported Chairman Kubota saying as he presented slide 32 "The people at Nomura and on our IR team tell me not to say this, but PeptiDream cannot possibly fail as long as the projects that that you see here stay on track" / 「このままプロジェクトが推移していくと、当社は『絶対に』つぶれません」

[4] Source: Bloomberg. Share sale proceeds are calculated as amount of shares sold multiplied by the closing price for PeptiDream stock as of the trade date.

[5] Reid is listed as the sole member of a company called Kura Capital. Kura Capital bought the above-referenced property in 2016. See https://hbe.ehawaii.gov/documents/business.html?fileNumber=163869C5 and https://qpublic.schneidercorp.com/Application.aspx?AppID=1029&LayerID=21689&PageTypeID=4&PageID=9251&KeyValue=380020250001

[6] Source: Bloomberg. Share sale proceeds are calculated as amount of shares sold multiplied by the closing price for PeptiDream stock as of the trade date.

Even as the Company has struggled to commercialize drugs, Chairman Kiichi Kubota tours Japan ginning up retail investor interest in the stock in every prefecture in Japan.

Despite the "cool" factor of peptides, PeptiDream's technology is not unique. Nor is the number of pharmaceutical companies with which it has at one time or another signed agreements noteworthy for a drug development platform. We have identified 13 other peptide drug development companies. Six of these companies have drugs in Phase 2 or beyond, compared to PeptiDream, which has failed to get a drug to Phase 2 after 13 years. To illustrate the greatly unrealistic expectations baked into PeptiDream's share price, the market caps of the five publicly traded peptide drug development companies equal 46% of PeptiDream's market cap…Combined!

Effectively Dead and Dormant Partnerships

In at least six English press releases since November 2018,[7] PeptiDream states that it has established partnerships with 19 leading pharmaceutical companies, and that all of these partnerships are "active and ongoing."[8] This is misleading at best. We believe a significant number of these partnerships – possibly over half – are close to dormant or dead. PeptiDream's drug discovery track record has been dismal. In 13 years, its platform has generated only two drugs that have entered clinical trials. Only two compounds have reached Phase I, one of which appears to have uncertain commercialization prospects; and, the other appears to be a diagnostic that will likely yield no revenue for PeptiDream. Our conclusions are based on our own research, as well as work done by two external research firms we engaged.

The activity level at PeptiDream's partnerships is key to its ability to succeed. PeptiDream enters into research and development contracts with "Discovery Partners" to identify peptide drug molecules against defined targets that are a focus of drug development for the Discovery Partner. PeptiDream receives a small upfront fee, research funding, and the biological targets of interest from the Discovery Partner, and PeptiDream utilizes its PDPS platform to identify "hits" against the target. PeptiDream receives payments when development milestones are met on these programs (e.g. lead identification, entry into preclinical studies) and is eligible for royalties on drug sales if the compound reaches the market. Partners may also license PeptiDream's platform, in which case the company receives payments over the course of implementation, as well as annual fee income. The total value of milestone payments for a product making it all the way from discovery to market has been disclosed by PeptiDream to be in the region of ¥5.4 billion, with low-single-digit royalties on product sales.[9]

PeptiDream investor relations confirmed that milestone announcements are key indicators of activity levels in partnerships. He conceded that if there has been no announcement, then generally, the partnership is not active. As shown below, there are 18 partnerships that were announced through the end of 2017.[10] Only nine of them have announced milestones or activity

[7] See for example press release of November 2018: http://contents.xj-storage.jp/xcontents/45870/0ba7bd40/e45a/4ea9/bb63/a205699d645a/20181116113209697s.pdf
[8] The Japanese versions omit the "active and ongoing" language.
[9] Source: Disclosed in call with PeptiDream IR representative.
[10] Source: PeptiDream's website and press releases.

since March 31, 2017. This implies that half of the partnerships currently have little to no activity.

Our external researchers' work supports the view that a significant number of partnerships lack activity.

Figure A: PeptiDream's Partnerships by Signing Date and Most Recent Reported Activity[11]

Company	Signed	Activity within current and previous financial years (July 2017 to date)
Amgen	2010	None
Mitsubishi Tanabe	2010	None
BMS	2010	Initiation of trial for Dx Feb 2018
Daiichi Sankyo	2012	None
GSK	2012	None
AstraZeneca	2012	None
Novartis	2012	New peptide-drug conjugate agreement June 2019. No news on milestones.
Ipsen	2013	None
Lilly	2013	Milestone Dec 2017
Sanofi	2015	None
Kyorin	2015	None
Genentech/Roche	2015	Expansion of discovery alliance June 2018. No news on milestones.
Merck	2015	Milestones Nov 2017, Apr 2018, Dec 2018; Tech transfer milestone June 2019
Teijin	2015	Milestone Feb 2018
Shionogi	2016	Tech transfers complete April 2019/May 2018; new peptide-drug conjugate agreement Jan 2019; 2 milestones Dec 2017
Asahi Kasei	2016	Milestones Oct 2017, November 2018
Janssen	2017	None
Bayer	2017	Milestone June 2019
Santen	2018	Agreement signed September 2018

Technology does not necessarily equal a viable business. Peptide drug discovery experts with whom we have spoken acknowledged that PeptiDream's technology finds "hits" against selected targets, but they appear not to translate into development of viable drug candidate molecules. A researcher at a partner speculated that the reason for the lack of drugs in clinic could be due to the difficulties in developing large macrocyclic peptides with the pharmacokinetic properties to be viable drugs. In any event, we believe that if no clinical candidates are produced in a discovery program within three to four years from starting screening, then that program should be considered a failure. Only one of the 14 partnerships that are at least four years old has led to a drug in clinical trials. We believe this broadbased lack of success is the primary reason for the inactive partnerships.

We speculate that partners do not formally terminate partnerships for reasons including a desire to save face for PeptiDream, and partners' senior management not focusing on the state of the PeptiDream partnership due to its small size.

[11] Source: PeptiDream's website and press releases.

We engaged two research firms to investigate the state of PeptiDream's various partnerships. One of the firms is a recognized leader in global pharmaceutical industry research. The research processes involved speaking with people at partners, sell-side analysts, and PeptiDream. It was difficult to get much detail on the partnerships, because they are generally not highly visible. (This is due in part to the size differences between PeptiDream and its partners, as opposed to partnership progress.)

On the whole, the investigators' work supports our view that a significant number of the partnerships have low levels of activity. However, the firms' assessments occasionally contradicted one another with respect to specific partnerships. Their work sometimes produced assessments of ongoing activity at partnerships at which there have been no recent milestone announcements. We therefore feel it is fair to say that while we lack conviction with respect to assessments of some particular partnerships, on the whole, it is clear that the company has not made it clear to investors that many of the partnerships have stalled.

Research firm A is a global pharmaceutical research firm. It assessed the activity level of 12 of PeptiDream's partnerships and graded confidence in its assessments as low, low-medium, medium, or medium-high. Firm A had confidence of medium or higher for 10 of the partnerships. Four of the 12 partnerships were assessed as low activity (each with medium-high confidence). Six of the 12 partnerships were assessed as high activity, but generally without high confidence levels. The assessed partnership activity levels are as follows:

Figure B: Research Firm A's Assessed Partner Activity Levels

Partner	**Confidence**
Low Assessed Activity	
Amgen	Medium-High
GSK	Medium-High
AstraZeneca	Medium-High
Ipsen	Medium-High
Medium Assessed Activity	
Mitsubishi Tanabe	Low
Sanofi	Medium-High
High Assessed Activity	
Daiichi Sankyo	Medium
Kyorin	Medium
Novartis	Medium
Genentech / Roche	Medium
Janssen	Medium-High
Bayer	Low-Medium

Research firm B is a local Japanese research firm (multi-industry). It attempted to assess the strength of the respective partners' commitment levels to the PeptiDream partnerships. Disregarding the portions of the assessments that are based on sell-side analysts, the research indicated the following with respect to seven of the partnerships:

- Santen – a PeptiDream source characterizes Santen's commitment as strong, and stated that Santen management is excited about its potential. This partnership agreement was signed recently (in September 2018), so we would expect Santen's commitment to still be strong. We understand that the likely rationale for Santen to enter into a partnership is that the delivery mechanism is likely to be through eyedrops, which could improve the success rate.

- Shionogi – a PeptiDream source characterizes Shionogi's commitment as strong. Two milestones were announced in December 2017.

- Bayer – a public relations source at Bayer chacterized the commitment as strong, but a source at the Japanese subsidiary, Bayer Yakushin Ltd., stated that the partnership is low visibility. It is possible that the partnership is more visible at Bayer headquarters than at its Japan operation. The divergent assessments are in line with the "low-medium" confidence that Research Firm A assigned to its assessment of high activity. The partnership was announced in 2017 and there was a milestone announced in June 2019.

- Sanofi – a public relations source at Sanofi stated that the partnership has the solid commitment of Sanofi's management as a drug discovery platform. This is not out-of-line with Research Firm A's assessment of medium activity with medium confidence, despite the lack of any announced milestones.

- GSK – a Japan-based GSK source opined that the partnership is no longer on the company's radar. This is consistent with Research Firm A's assessment of low activity (medium-high confidence), and no milestones since the partnership was announced in 2012.

- Novartis – a Japan-based source (Novartis Pharma K.K.) opined that the partnership is low activity. However, the partnership appears in corporate materials prepared by the Novartis parent, Novartis International AG. It is possible that the partnership is more visible at Novartis International than at its Japan subsidiary. The favorable interpretation is consistent with Research Firm A's assessment of high activity (medium confidence). There have been no announced milestones since the partnership was formed in 2012.

- Mitsubishi Tanabe – the compounds generated with PeptiDream's technology have reportedly had problems in connection with absorption, distribution, metabolism, excretion, and toxicity ("ADMET"). This appears to be inconsistent with Research Firm A's assessment of medium activity (low confidence), but is not out-of-line with no announced milestones since the partnership was formed in 2010.

PeptiDream could, of course, make the states of these partnerships clearer to investors. Instead, as we discuss infra, PeptiDream obscures its lack of success by limiting the useful information it provides investors. What limited program information there is from the last 18 months supports our view that a significant number of partnerships are inactive. At first glance, PeptiDream's program tables (shown below) make clear that new programs are being added at initial stages,

with numbers growing at the "Target-to-Hit", "Hit-to-Lead", and "Lead-to-Preclinical" stages. A superficial reading of this would focus on the implication that PeptiDream has continued to sign new agreements and has expanded its in-house research. Indeed, this is the table Chairman Kubota showed investors when he remarked that "PeptiDream cannot possibly fail as long as the projects that that you see here stay on track." Investors should look beyond the rosy proclamations.

From this data, PeptiDream appears to have never removed any program from the pipeline. Many of these programs – particularly the ones started years ago – are unlikely to be actively pursued in the future.

Figure C: PeptiDream's Pipeline Progress June 2017-June 2019. Data from PeptiDream Financial Results Reports[12]

	June 2017		June 2018		June 2019
Total # Programs	**60**		**84**		**101**
Target-to-hit	25	+11	36	+9	45
Hit-to-Lead	23	+11	34	+5	39
Lead-to-Preclinical	8	=	8	+2	10
Clinical candidate	3	+1	4	+1	5
Phase 1	1	+1	2 (1 diagnostic)	=	2 (1 diagnostic)
Phase 2	0		0		0
Phase 3	0		0		0

Growth in total programs and progress at earliest stages

Limited progress over time into subsequent stages of development

Even PeptiDream's biggest successes demonstrate the overall inability of the company to generate meaningful revenue from its technology. To date, PeptiDream has only announced that two programs have made it past the key hurdle into Phase 1 development. Both programs are collaborations with BMS, and neither looks promising for PeptiDream.

BMS Compounds Demonstrate PeptiDream's Lack of Progress in Drug Discovery

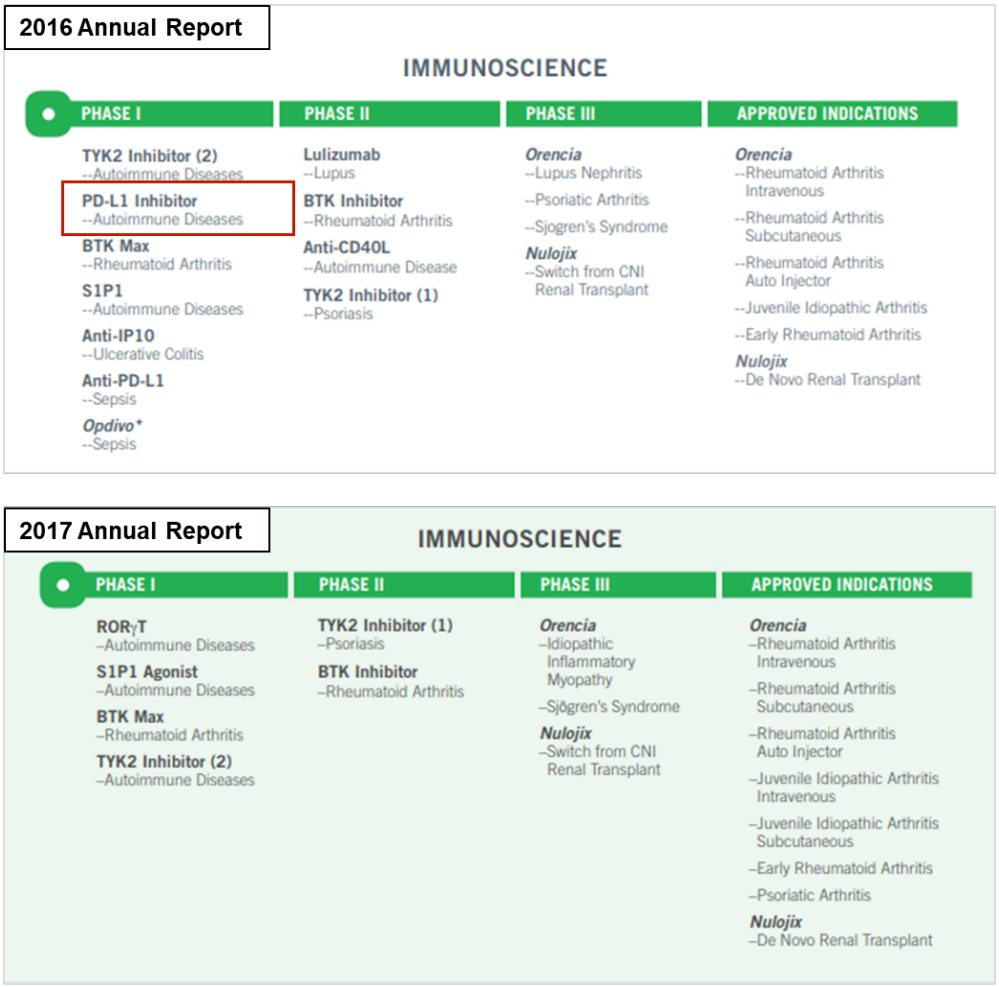
Two compounds discovered in its partnership with BMS illustrate the difficulty PeptiDream has in generating meaningful revenue from its platform. We believe that neither drug will ever yield material revenue for PeptiDream.

In 2016, PDPS identified two compounds in partnership with BMS: a PD-L1 inhibitor and a diagnostic (an imaging agent).[13] The PD-L1 inhibitor has unclear development prospects, and we understand that PeptiDream is not entitled to economics on the diagnostic from BMS because their agreement only covers therapeutics.

[12] We calculate target-to-hit programs by taking the difference between the total number of programs and the sum of all other disclosed program categories.
[13] BMS-986189 and PD-L1-PET, respectively.

In June 2016, PeptiDream announced that BMS had commenced a Phase 1 clinical trial for the PD-L1 inhibitor.[14] BMS's 2016 annual report showed the PD-L1 inhibitor in its list of pipeline drugs; however, the 2017 annual report omitted the PD-L1 inhibitor. Below is a comparison of the two annual reports.

Figure D: Pipeline Information in BMS Annual Reports 2016 vs 2017 Showing Removal of PD-L1 Inhibitor



In addition, the United States National Library of Medicine's entry for the Phase I trial of the PD-L1 inhibitor shows that the trial concluded in December 2016.

Figure E: Entry for the Phase 1 trial of BMS's PDL-1 antagonist peptide[15]

Official Title:	Randomized, Double-Blinded, Placebo-Controlled, Single Ascending Dose Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Pharmacodynamics of BMS-986189 in Healthy Subjects
Actual Study Start Date :	April 18, 2016
Actual Primary Completion Date :	December 14, 2016
Actual Study Completion Date :	December 14, 2016

[14] http://contents.xj-storage.jp/xcontents/45870/e1ad69c6/2e65/4bb3/b328/40ed5b780727/20160615140723355s.pdf
[15] https://clinicaltrials.gov/ct2/show/NCT02739373

When investors noticed the change in BMS's annual report, PeptiDream issued press releases defending the company's position in English and Japanese. The English version asserted that the program for the "Phase I development candidate… believed by some to be the product jointly developed by PeptiDream and BMS", must still be active because BMS had not notified it of failure.[16] The Japanese release, on the other hand, asserted flatly that the project deleted from BMS's annual report was not the drug candidate from the PeptiDream partnership.[17] This assertion does not make sense based on the available information about the drug candidate.

We question whether it is appropriate that the PD-L1 inhibitor remains listed in PeptiDream's pipeline, where the company claims "promising efforts continue in optimizing oral bioavailability"[18] despite the troubling chronology from BMS's reports and the almost three-year time gap since the Phase 1 trial concluded.

In February 2018, PeptiDream announced that development of the BMS imaging agent had hit a milestone. Although little information was released about the BMS imaging agent, it could be used to predict and monitor patient response to cancer therapies targeting the PD-L1 receptor (such as BMS's drug Opdivo) through non-invasive PET imaging.[19] [20] BMS initiated a clinical trial of the imaging agent. However, we understand that BMS focuses on therapeutic pharmaceutical products and does not currently sell any diagnostic agents. We believe that BMS is instead developing the agent as a tool for use in its own research; for example, to help select and monitor patients in clinical trials. Regardless, a PeptiDream investor relations representative shared with an investor that the partnership agreement with BMS only covers therapeutic compounds. (According to IR, PeptiDream is trying to renegotiate the contract to include diagnostic agents as well.[21]) We therefore conclude that BMS is unlikely to pay royalties or other fees to PeptiDream for the imaging agent.

The BMS imaging agent illustrates that even when PeptiDream identifies a potentially useful compound, the structures of its partnerships might not lead to a return for investors. There is a risk that a number of the partnership agreements (beside BMS) allow partners to develop drugs without compensating PeptiDream. PeptiDream is entitled to compensation for viable drugs developed with its platform technology, but some of the Pharma Partners may be using the technology merely to understand targets better. There might be situations in which PeptiDream's platform has identified hits and provided information about the binding of the peptide to the target, but the partner would be using the information to instead develop a different type of drug (such as a small molecule). Some of PeptiDream's partners might believe their agreements do not entitle PeptiDream to revenues in this situation.

[16] http://contents.xj-storage.jp/xcontents/45870/dc8ad06b/68c4/4467/a1f2/75beb33255c8/20170507173717410s.pdf
[17] http://contents.xj-storage.jp/xcontents/45870/57c4e560/eeb6/4d9f/92f2/f0c716c9b029/20170507173328816s.pdf
[18] http://contents.xj-storage.jp/xcontents/45870/1b3d70cf/920a/49d6/87cd/479749f3a3b9/20190808180848287s.pdf
[19] Conversation with sell-side analyst, August 2018
[20] PD-L1 testing is currently carried out through widely available laboratory tests on tumor samples taken from patients.
[21] Source: Disclosed in call with PeptiDream IR representative

In-House Development is Unlikely to Succeed

PeptiDream's shift to an in-house drug development strategy is reminiscent of Sosei, which similarly pivoted to developing its own drugs before its stock price collapsed. Based on its performance to date, we believe PeptiDream should be valued as just another development-stage platform company without drugs in clinic.

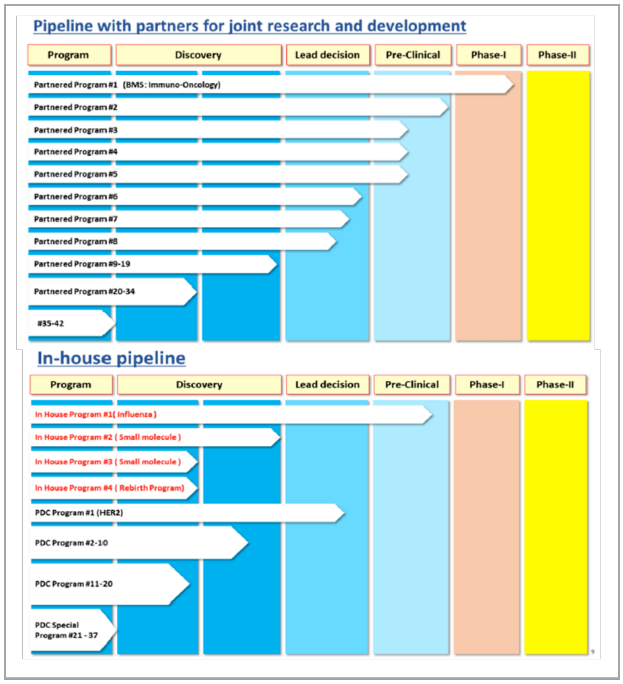
PeptiDream has yet to successfully out-license any of its in-house projects. In an April 2014 press release, the company provided an update on its proprietary development program for influenza and stated that it expected to file an application to begin human trials in 2015. No further news was announced on the program until February 2018, when PeptiDream announced the completion of preclinical studies, with the delay allegedly caused by challenges in manufacturing product for use in the trials. PeptiDream investor relations now says to expect a licensing announcement in fiscal 2020. In a rare bout of skepticism, analysts have suggested PeptiDream is facing challenges identifying an interested partner, as effective influenza products, including generic versions of Tamiflu and recently launched Xofluza, are already available.

We believe that an in-house pipeline focus for the Company will continue to show the limitations of PeptiDream's development platform, as it will likely report disappointing lack of progress quarter after quarter – just as Sosei did. Indeed, both companies are followed by the same analyst pool, which seems to accept the rosy estimates of pharmaceutical executives without any critical thought. These same analysts were largely bullish on Sosei, until reality intervened.

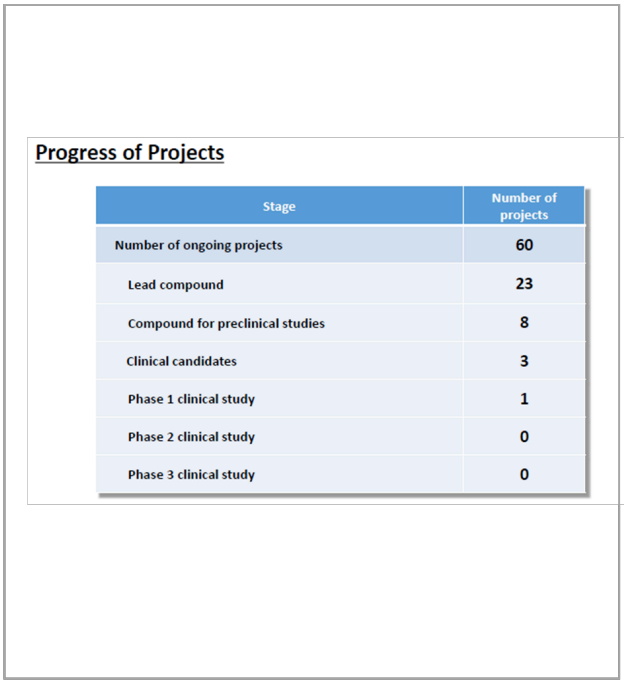
PeptiDream Obfuscates its Failures through Increasing Opacity

PeptiDream attempts to obscure the details of its track record and prospects. The company presents revenue on its portfolio of programs lumped together as generic "programs," with no detail on how the programs break down between the different business segments, or even which programs are in-house versus partnerships. While confidentiality agreements place some restrictions on what PeptiDream may disclose, the company could provide at least high-level details on the number of programs in different business segments. In fact, PeptiDream used to furnish such information, but now no longer does. In our experience, when companies' disclosures become more opaque, it's usually to obscure bad news from investors.

Figure F: Change in Information Provided on Pipeline Programs After Feb 2017



Financial Results H1 FY2017, Feb 2017
Includes split of partnered vs. in-house pipeline



Progress of Projects

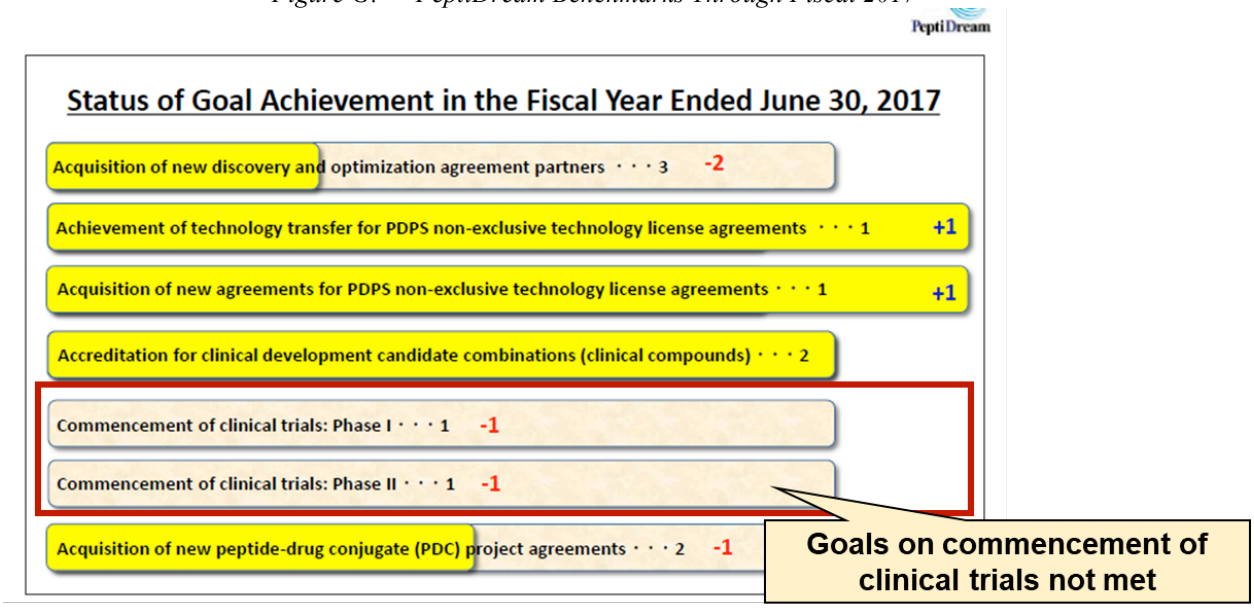
Stage	Number of projects
Number of ongoing projects	60
Lead compound	23
Compound for preclinical studies	8
Clinical candidates	3
Phase 1 clinical study	1
Phase 2 clinical study	0
Phase 3 clinical study	0

Financial Results FY2017, August 2017
No details by segment provided

PeptiDream also obfuscates by refusing to set goals for the business. In the past, the Company would set development goals, but discontinued this practice because it never met them. In 2016, the Company stated that it aimed to commence one Phase 1 and one Phase 2 clinical trial in the financial year ending June 2017.[22] In the Company's presentation of 2017 financial results, it then reported that it had missed these goals and two others relating to the signing of new agreements (see Figure G below).

[22] Source: PeptiDream FY2016 Financial Results Presentation

Figure G: PeptiDream Benchmarks Through Fiscal 2017[23]



PeptiDream then stated that it would no longer set similar short-term goals because these "included items outside the Company's control, such as approval for clinical development candidate combinations and the commencement of clinical trials, and were judged to not be appropriate as targets set for a single fiscal year." We believe the company's real reason for not publicly setting annual goals is that management is greatly concerned about PeptiDream's ability to achieve even marginally ambitious results in a reasonable timeframe.

The development process of the BMS Compounds discussed above also demonstrates PeptiDream's lack of candor about its progress. Even though the therapeutic PDL-1 inhibitor is in an unclear state of development, it continues to show up in PeptiDream's disclosed pipeline.

Perhaps PeptiDream has no choice but to inflate the size of its pipeline: it is a prisoner of its medium-term forecast, first issued in 2017. That forecast now calls for one drug to be approved and on the market by June 2022, with ten drugs advancing to the clinic by that time.

[23] Source: PeptiDream Financial Results Presentation FY 2017

Figure H: 2022 Medium-Term Targets[24]

Medium-term targets (by the end of June, 2022)	
1. Bringing to market new drugs (approval and sales)	1 or more
2. Number of companies with which the Company has discovery and optimization agreements	25 or more
3. Number of companies to which the Company reaches PDPS non-exclusive technology license agreements	8 or more
4. Number of projects for which clinical trials begin	10 or more
5. Number of employees at the end of June 30, 2022	170 or more

These targets are fast approaching their due dates, and they defy not only PeptiDream's own track record, but also industry success rates and our forecasts.[25] Despite these overwhelming odds, CEO Patrick Reid continued to make overly confident representations in a recent shareholder communication. In a move characteristic of PeptiDream's emotional appeals to retail investors, he said PeptiDream is "strongly moving forward" toward these "eminently achievable" June 2022 targets.[26]

PeptiDream's Bold Claims and Increased Spending Try to Buy Time For Future Success

To perpetuate PeptiDream's reputation for innovation, company executives advance prospects that are entirely divorced from the current realities of the business. The Japanese version of PeptiDream's FY2018 presentation presents the idea that the company's technology will help develop multiple forms of animal medicines as well as pesticides.[27] None of the company's major partnerships disclose these goals, if indeed such a focus exists. Further, in a May 2019 interview given by PeptiDream's Investor Relations Director Toshiyuki Iwata for *Nikkei xTrend*, Iwata asserted that, "In the near future, the operating margin will reach around 80%."[28] The article's author explained that Iwata believes PeptiDream will be able to take a Google-, Amazon-, Facebook-, or Apple-like position in the trillion-dollar pharmaceutical market. PeptiDream's reality in that fiscal year was much less optimistic: the company posted an FY2019 operating margin of 50%.[29] Meanwhile, the company expects to make a negative operating margin once again in the second half of calendar year 2019, citing increased R&D expenses.[30]

The sole advancement to clinical candidacy that PeptiDream announced in FY2019 was a compound developed by Kleo Pharmaceuticals, which is heavily financed by PeptiDream. So far, PeptiDream has not only contributed an upfront payment to Kleo, but it paid in $10 million

[24] http://contents.xj-storage.jp/xcontents/45870/1b3d70cf/920a/49d6/87cd/479749f3a3b9/20190808180848287s.pdf
[25] See infra.
[26] http://contents.xj-storage.jp/xcontents/45870/9932c227/0b22/4406/9b31/83f32b81ad5f/20190927110027135s.pdf
[27] http://contents.xj-storage.jp/xcontents/45870/5eabb2ae/4190/4f08/9c79/4c71fff76e9c/20190924171546010s.pdf
[28] https://xtrend.nikkei.com/atcl/contents/18/00136/00004/?i_cid=nbpnxr_index
[29] http://contents.xj-storage.jp/xcontents/45870/5d5f1b18/4b1b/4071/8c29/acfd0fd52d79/20190808102640495s.pdf
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out of the $21 million Kleo raised in its 2018 Series B fundraising.[31,32,33] PeptiDream is, in effect, funding Kleo's increasing research expenses while bearing its own platform costs. This expensive development effort suggests the waning of a high-margin business model focused on monetizing PDPS—and it highlights PeptiDream's seeming desperation to advance compounds past discovery.

Moreover, in announcing a recent partnership with drug delivery expert PharmaIN, PeptiDream emphasized that PharmaIN's technology can "improve the solubility of the peptide payload", protect "the peptide payload from degradation, thereby increasing stability", and that it "slowly releases the peptide payload resulting in a significantly longer circulation half-life".[34] We view these touted advantages in a different way: as a tacit admission that PeptiDream's own technology has not produced drug candidates that have performed well in the clinic to date.

PeptiDream has also trumpeted other "strategic" partnerships and peptide-drug conjugate agreements to distract from its lack of clinical success. These developments include a research expansion into beauty products with cosmetics company Pola Orbis; antibody purification with chemical company JSR Corporation; and the use of "quantum-inspired" technology from Fujitsu in order to improve PDPS discovery.[35,36,37] None of these aforementioned initiatives address the fact that the company's peptides seems to have difficulty progressing to trials. Worryingly, they suggest a lack of strategic focus amid a business shift from asset-light big pharma licensing—which underpins PeptiDream's astronomical valuation—, to non-core product areas and capital-intensive R&D.

PeptiDream includes the below slide in its presentation to Japanese investors. It compares non-standard peptides to a Jaguar F-Type sports car, while it analogizes antibody drugs and small molecule drugs to a dump truck and a motor scooter. We think this analogy would be more appropriate if PeptiDream's Jaguar were missing its wheels.

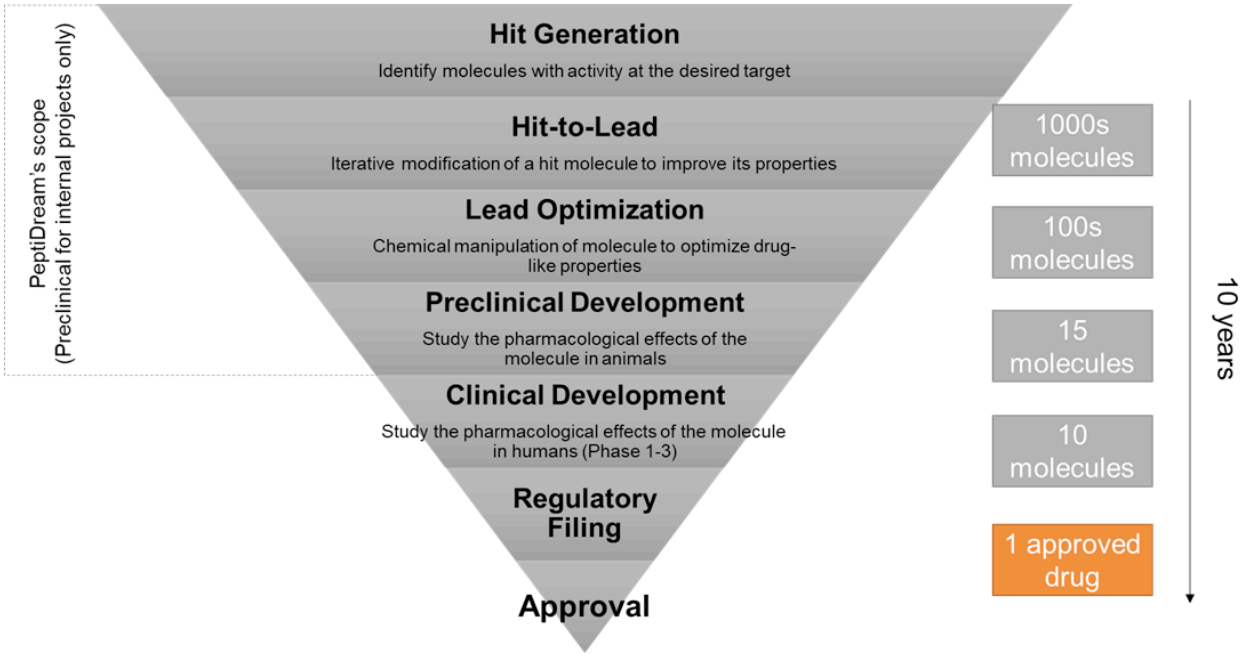
[31] http://contents.xj-storage.jp/xcontents/45870/3a1cb536/613a/460f/ba8b/f116e0ab2a06/20170718163419477s.pdf
[32] http://contents.xj-storage.jp/xcontents/45870/a2f3f025/627f/4ad5/b512/ad07dcca9f95/20190618152317832s.pdf
[33] https://www.prnewswire.com/news-releases/kleo-pharmaceuticals-secures-21-million-to-advance-novel-small-molecule-cancer-immunotherapies-300749133.html
[34] http://contents.xj-storage.jp/xcontents/45870/7cc267eb/b31e/45c9/9202/3aa661f1e395/20190605161410843s.pdf
[35] https://ir.po-holdings.co.jp/news_en/news/news-1360097446261277914/main/0/link/20190327_peptide_E.pdf
[36] http://contents.xj-storage.jp/xcontents/45870/3487fb4a/fef0/4928/9e4f/defceac682c7/20190920093142583s.pdf
[37] http://contents.xj-storage.jp/xcontents/45870/58ced46c/bb1c/4cc7/b106/3fdd9354e3ea/20190920092252638s.pdf

PeptiDream is Likely to Fall Far Short of Analysts' Intellectually Dishonest Expectations

We forecast that PeptiDream will have no more than one commercially successful drug through 2027. In contrast, the sell-side analysts who follow PeptiDream have predicted a number of successful products, ranging from a difficult-to-believe eight to a ludicrous 15. Sell-side analysts justify their price targets through contortions of logic, such as assuming development success rates six times the industry norm – even for a company with PeptiDream's dismal track record.

For any pharmaceutical company, the probability of progressing through the successive stages of drug development is low, and failure can occur at each stage. Typically, hundreds of compounds are screened to hone down to one or two lead compounds go into preclinical testing. Of these, fewer than one in ten typically make it market (see Figure I).

Figure I: Overview of Drug Discovery Process and PeptiDream's Areas of Focus



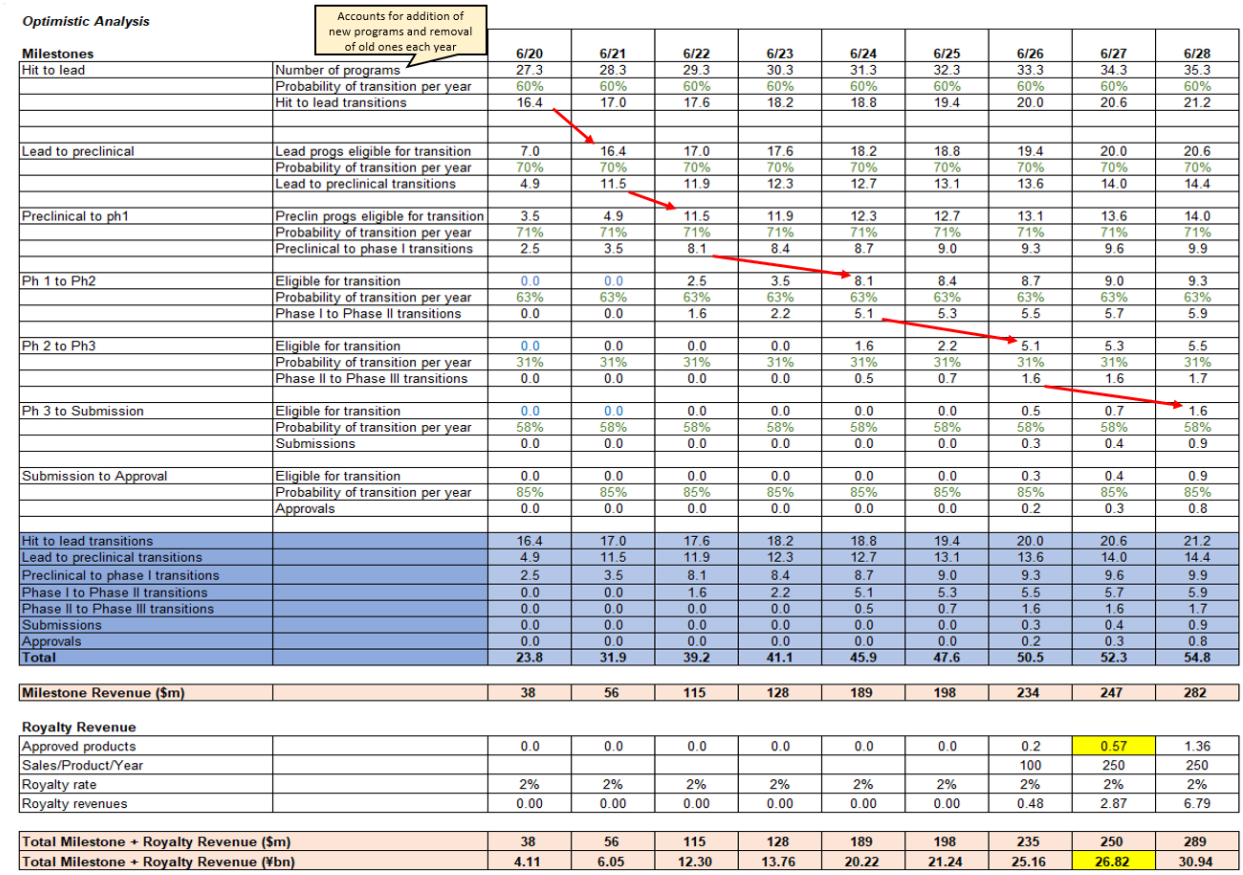
We have forecast future revenue from milestone payments and royalties under two scenarios, based on estimating revenue as products transition through development phases. Assuming (a) PeptiDream continues to operate in a similar way in the future and maintains a similar number of partnerships over the next 10 years, and (b) the likelihood of transitioning from one development phase to the next is based on standard industry success probabilities, we can designate a probable range of the number of products likely to reach the market (see Figures J and K).

Figure J: Assumptions Used in "Optimistic" Modeling Revenue Scenarios

				Milestone Payments ($m) *Source: Estimates based on info shared in PeptiDream IR call; Calls with analysts*			Average milestone fees across segments ($m)	Starting Programs *Source: PeptiDream Jun 2019 financial results report*
	Probability	Time in Phase (years)	Reference	Collabs	Outlicense	Tech Transfer	(weight equally)	
Target to hit	NA	NA	NA: Analysts assume no fees for this	0	0	0	0.0	45
Hit to lead optimization	60%	1	AZ NRD paper	2.5	0	0	0.8	39
Lead optimization to preclinical	70%	1	Valuation in LS chap	2.5	0	2.5	1.7	10
Preclinical to phase 1	71%	2	AZ NRD paper	5	10	5	6.7	5
Phase 1 to Phase 2	63%	2	BIO analysis	10	30	10	16.7	
Phase 2 to Phase 3	31%	2	BIO analysis	10	30	10	16.7	
Phase 3 to Submission	58%	2	BIO analysis	10	50	10	23.3	
Submission to Approval	85%	0	BIO analysis	10	80	10	33.3	

Scenario	% Starting Programs Assumed Active	Growth Per Year in New Programs
Optimistic	70%	1

Figure K: Illustration of Modeled Revenue Over Time for Optimistic Scenario



Optimistic Analysis

Accounts for addition of new programs and removal of old ones each year

Milestones		**6/20**	**6/21**	**6/22**	**6/23**	**6/24**	**6/25**	**6/26**	**6/27**	**6/28**
Hit to lead	Number of programs	27.3	28.3	29.3	30.3	31.3	32.3	33.3	34.3	35.3
	Probability of transition per year	60%	60%	60%	60%	60%	60%	60%	60%	60%
	Hit to lead transitions	16.4	17.0	17.6	18.2	18.8	19.4	20.0	20.6	21.2
Lead to preclinical	Lead progs eligible for transition	7.0	16.4	17.0	17.6	18.2	18.8	19.4	20.0	20.6
	Probability of transition per year	70%	70%	70%	70%	70%	70%	70%	70%	70%
	Lead to preclinical transitions	4.9	11.5	11.9	12.3	12.7	13.1	13.6	14.0	14.4
Preclinical to ph1	Preclin progs eligible for transition	3.5	4.9	11.5	11.9	12.3	12.7	13.1	13.6	14.0
	Probability of transition per year	71%	71%	71%	71%	71%	71%	71%	71%	71%
	Preclinical to phase I transitions	2.5	3.5	8.1	8.4	8.7	9.0	9.3	9.6	9.9
Ph 1 to Ph2	Eligible for transition	0.0	0.0	2.5	3.5	8.1	8.4	8.7	9.0	9.3
	Probability of transition per year	63%	63%	63%	63%	63%	63%	63%	63%	63%
	Phase I to Phase II transitions	0.0	0.0	1.6	2.2	5.1	5.3	5.5	5.7	5.9
Ph 2 to Ph3	Eligible for transition	0.0	0.0	0.0	0.0	1.6	2.2	5.1	5.3	5.5
	Probability of transition per year	31%	31%	31%	31%	31%	31%	31%	31%	31%
	Phase II to Phase III transitions	0.0	0.0	0.0	0.0	0.5	0.7	1.6	1.6	1.7
Ph 3 to Submission	Eligible for transition	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.7	1.6
	Probability of transition per year	58%	58%	58%	58%	58%	58%	58%	58%	58%
	Submissions	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	0.9
Submission to Approval	Eligible for transition	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	0.9
	Probability of transition per year	85%	85%	85%	85%	85%	85%	85%	85%	85%
	Approvals	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.8
Hit to lead transitions		16.4	17.0	17.6	18.2	18.8	19.4	20.0	20.6	21.2
Lead to preclinical transitions		4.9	11.5	11.9	12.3	12.7	13.1	13.6	14.0	14.4
Preclinical to phase I transitions		2.5	3.5	8.1	8.4	8.7	9.0	9.3	9.6	9.9
Phase I to Phase II transitions		0.0	0.0	1.6	2.2	5.1	5.3	5.5	5.7	5.9
Phase II to Phase III transitions		0.0	0.0	0.0	0.0	0.5	0.7	1.6	1.6	1.7
Submissions		0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	0.9
Approvals		0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.8
Total		**23.8**	**31.9**	**39.2**	**41.1**	**45.9**	**47.6**	**50.5**	**52.3**	**54.8**
Milestone Revenue ($m)		**38**	**56**	**115**	**128**	**189**	**198**	**234**	**247**	**282**
Royalty Revenue										
Approved products		0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.57	1.36
Sales/Product/Year								100	250	250
Royalty rate		2%	2%	2%	2%	2%	2%	2%	2%	2%
Royalty revenues		0.00	0.00	0.00	0.00	0.00	0.00	0.48	2.87	6.79
Total Milestone + Royalty Revenue ($m)		**38**	**56**	**115**	**128**	**189**	**198**	**235**	**250**	**289**
Total Milestone + Royalty Revenue (¥bn)		**4.11**	**6.05**	**12.30**	**13.76**	**20.22**	**21.24**	**25.16**	**26.82**	**30.94**

Below are summaries of projections from three sell-side analysts. All of these are tremendously intellectually dishonest in our view. Assumptions in two key areas appear to be significantly over-optimistic: (1) number of projects and (2) success rate of each development stage.

Figure L: Analyst Projections for PeptiDream

	Report Date	**Projected Revenue FY 6/2027**	**Projected number of launched products by 2027**
Analyst A	Jan 2018	¥65.2bn ($575m)	8
Analyst B	May 2018	¥84.4bn ($745m)	9
Analyst C	Discussion August 2018	NA	15

Despite PeptiDream's lack of results from its partnerships so far, analysts bizarrely project that the number of Discovery Partnerships will grow, that such partnerships will be expontentially

more productive than in the past, and that the Company's in-house discovery will suddenly explode with viable new products.

An investor spoke to Analyst A to better understand the basis of his assumptions. Analyst A assumes that PeptiDream will continue to sign new Discovery Partnerships in the next three years, for a total of 27 by the end of Fiscal Year 2022, and up to 30 by Fiscal Year 2025. The most obvious flaw here is that PeptiDream's own optimistic expectations in its latest guidance are for only 25 Discovery Partnerships by Fiscal Year 2022.[38] Given PeptiDream's track record of missing its targets on number of Discovery Partnerships (see Figure G above), to predict a number of partnerships above the Company's own goals appears deeply unrealistic.

Furthermore, Analyst A assumes an average of one new project per Discovery Partnership, including existing partnerships, for the next 10 years, with no attrition in number of partnerships over time. Given that partnerships with many Discovery Partners are likely already inactive, this significantly overstates the number of potential partnerships, and seemingly forecasts growth from Discovery Partnerships with little or no current activity.

With respect to in-house projects, Analyst A assumes that PeptiDream will out-license one in-house project per year for the next ten years. The non-existent output of PeptiDream's in-house development thus far seemingly belies this assumption.

Most damningly, Analyst A projects success rates at each drug development milestone well in excess of the industry averages. Analyst A justifies his "optimistic adjustment[s]" based on claims that "peptide-based therapeutics and in-licensed projects for pharma companies have higher chance of survival."[39] These boosts end up yielding a projected success rate of drug development that is nearly **six times** that of the industry![40] Amazingly, Analyst A has also made his assumptions marginally more optimistic over time, despite PeptiDream's lack of progress to date.

Using standard industry success rates, our base case implies a revenue miss against analyst expectations of more than 60%, while an aggressive case in the Company's favor would yield a revenue miss in excess of 50%. Analysts seem to be looking at the current share price, and doing their projections backward from there.

[38] FY2018 Financial Results Presentation
[39] Analyst A report
[40] The cumulative industry success rate is 2.9%, while the cumulative success rate Analyst A projects for PeptiDream is 16.5%.

Figure M: Analyst A vs. Standard Industry Assumptions for Development Success Rates [41]

Phase	Analyst A Assumed Probability of Success	
	New	Old
Lead ID	95%	95%
Lead ops to Preclinical	90%	95%
Preclinical to Phase 1	79%	80%
Phase 1 to 2	75%	75%
Phase 2 to 3	46%	46%
Phase 3 to file	72%	72%
Approval	92%	92%
Approval (second region)	92%	92%

Source: Analyst A estimates

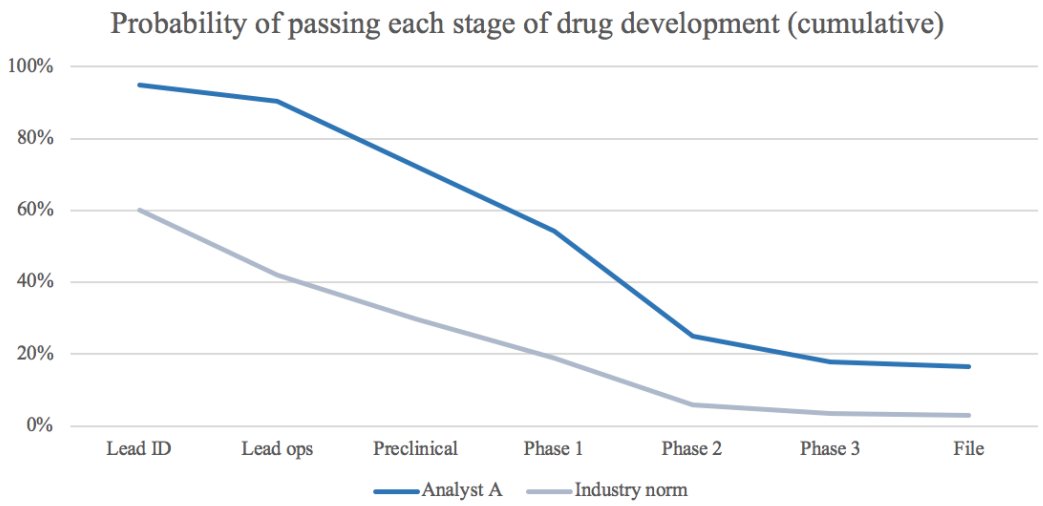
Standard Industry Assumptions

Industry Ave.
60%
70%
71%
63%
31%
58%
85%

Combined industry average probability of reaching preclinical stage from Lead ID is **half** of analyst estimate

Combined industry average probability of reaching market from preclinical stage is **one third** of analyst estimate

Overall industry average probability of reaching market from Lead ID is **one sixth** of analyst estimate



[41] Industry assumptions are based on values derived from analysis of historical success rates across the pharmaceutical industry. Literature on pharma industry success rates sourced from Valuation in Life Sciences, A Practical Guide, Boris Bogdan and Ralph Villiger; Clinical Development Success Rates 2006-2015, Biotechnology Innovation Organization; Impact of a five-dimensional framework on R&D productivity at AstraZeneca, Morgan et al., Nature Reviews Drug Discovery (2018)

Figure N: Comparison of Analyst A Forecast, Our Optimistic Case and Base Case

	Assumptions	**Projected Milestone & Royalty Revenue FY 6/2027**	**Projected # launched products by 2027**
Analyst A	As described above	¥58bn[42]	8
MWC Optimistic Case	Standard industry success probabilities applied to current pipeline Conservative assessment of number programs assumed inactive Moderate continued growth in number of programs over time	¥27bn	0-1
MWC Base Case	Realistic assessment of number programs assumed inactive Limited growth in number of programs over time	¥20bn	0

As intellectually dishonest as Analyst A's projections appear, those of Analyst B and C seem more egregious, since they predict even higher revenues and commercialized products counts.

PeptiDream Has a Number of Peptide Discovery Competitors Who Are Far Surpassing It

A comparison with other peptide-based discovery platforms shows that PeptiDream's valuation is ludicrous. Although the Company presents its PDPS technology as a one-of-a-kind value proposition, it competes with at least 13 other peptide drug developers, six of which have drugs in Phase 2 or even further. While PeptiDream currently generates revenue, we believe that development success is the only measure that matters. On that count, PeptiDream is a laggard.

Figure O, below, outlines the many peptide drug discovery companies that operate in a similar space to PeptiDream. While the competitors are generally more focused on in-house development than PeptiDream is, it is notable that the valuations of these companies are a fraction of PeptiDream's ¥618 billion market capitalization (at the time of table compilation). Despite the seemingly greater success some of them have enjoyed, PeptiDream's market cap is more than 2x the market caps of the five listed companies— Ra Pharmaceuticals, Protagonist Therapeutics, Bicycle Therapeutics, Polyphor, and Aileron Therapeutics—*combined*.

The range of competition also indicates that PeptiDream is not a pharmaceutical company's only option if it is looking to partner on development of peptide-based drugs. Indeed, some of PeptiDream's Pharma Partners are also partnered with other competitors. One expert we spoke to

[42] Estimated based on split of milestone, royalty and license fees from Analyst A Initiating Coverage in Sep 2016

opined that the more focused approaches pursued by these competitors may be more likely to produce successful drugs than PeptiDream's large library approach.

Although PeptiDream has the technology to synthesize trillions of different peptides, experience has shown that the size of the library is not the key factor in developing commercially viable pharmaceuticals.[43]

Figure O: Selected Companies with Similar Technology to PeptiDream by Year of Founding

Company	Founded	Technology	Business Model	Market Cap	Clinical stage of most advanced peptide drug	Number of industry partnerships
Polyphor	1996	Peptidic and non-peptidic macrocycle chemistry	Focus on in-house development - mixed commercialization and out-licensing strategy. Previously had a platform services business but terminated in 2017 as "not financially self-sustainable"	CHF92.2 Mn ($92.9 Mn)	Phase 3	None
PepScan	1999	Peptide synthesis	Services for peptide drug discovery including synthesis, libraries, screening. Fee for service and other arrangements	Private	NA	Janssen (J&J), Zeland, Isogenica, AstraZeneca, Crucell, Adimab, Phylogica, Immunovo, Complix, MedImmune plus "multiple" undisclosed partners
Ambrx	2003	Non-natural amino acids in biologic molecules (e.g. monoclonal antibodies)	In-house development and collaborations	$45 Mn funding in 2016	Phase 2	4: BMS, Lilly, Astellas, Zhejiang Medicine Co
Aileron Therapeutics	2005	Stapled peptides	In-house development	$15.7 Mn	Phase 2	None
PeptiDream	2006	Natural/non-natural cyclic peptides	In-house discovery, platform licensing, development, and collaborations	¥665 Bn ($6.1 Bn)	Phase 1	19 + 9 "strategic partnerships"
Protagonist Therapeutics	2007	Constrained peptides	In-house development and collaborations	$317.0 Mn	Phase 2	One with Janssen (J&J)
RA Pharmaceuticals	2008	Natural/non-natural cyclic peptides	In-house development through ph3. Collaboration with Merck.	$2.2 Bn	Phase 3	One collaboration with Merck
Apeptico	2008	Peptide discovery and development	In-house development through ph3. Platform licensing	Private Has raised €6.4 Mn to date	Phase 2	Two
Bicycle Therapeutics	2009	Bicyclic peptides	In-house development	$159.3 Mn	Phase 1	4 partnered programs: Thrombogenics, AstraZeneca, Bioverativ, Cancer Research UK
Lanthio Pharma	2010	Stapled peptides	In-house development and collaborations	Bought out for EUR20 Mn by MorphoSys in 2015	Phase 1	NA
Ensemble Therapeutics	2013	Synthetic cyclic peptides	In-house development and collaborations. Closed in 2017. No molecules ever made it into the clinic.	Private Raised $43.5 Mn in equity from launch to close.	Preclinical	5 partnered programs prior to closing (Novartis, BMS, Genentech, Alexion, Boehringer Ingelheim)
Circle Pharma	2014	Orally available macrocyclic peptides	In-house discovery; collaboration with Pfizer	Private $6.5m Series A in 2018	Discovery	One collaboration with Pfizer
Encycle Therapeutics	2015	Synthetic cyclic peptides	In-house development and collaborations	Acquired for up to $80 Mn by Zealand Pharma A/S in 2019	Preclinical	4: Merck, Pfizer, AstraZeneca, GSK
SyntheX	2016	Peptide screening and synthesis	In-house development	Private $6.2m seed round in 2017	Preclinical	NA

[43] Conversation with peptide chemistry leader at a large pharmaceutical company, July 2018