

2022 Duke-UNC-TMC
Case Competition

Strategic Guide for Better Blue Bio

Three Scientists and an Accountant

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Executive Summary

Client Situation

Client: **Better Blue Bio (BBB)**

BBB-032:

Postpartum depression (PPD) treatment, Phase II clinical trials

Seeking a partner to help fund the R&D



Key Objectives & Conclusions

- **Total PPD Market**
 - Large (**250K**), stable, addressable patient population
- **Potential Market Capture** of BBB
 - Projected **10% penetrance** in Y5 on market
 - Few PPD-specific therapies are on market (**1**) or in development (**3**)
 - Most viable route to market: establish **anchor partnership**



Est. Peak Revenue

\$165
Million
(USD)

in 2032
Y5 on Market



PPD Market Identification



- Disease Characteristics
- Market Size
- Market Segmentation
- Target Market

Market Capture by Better Blue Bio



Market Economics

- Growth Rate
- Market Share
- Revenue Projections
- Profit Projections



Competitive Landscape

- Current
- Future
- Dynamics



Route to Market

- Clinical Trial
 - Feasibility
 - Regulations
 - Timeline
- Partnerships

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PPD is a major depressive episode that occurs following childbirth

HAMD-17 Assessment

- Insomnia or hypersomnia
- Interest (anhedonia)
- Worthlessness
- Fatigue
- Decreased cognition/concentration
- Unintentional weight loss
- Psychomotor (restlessness or slowness)
- Suicidal ideation**

WHY?

NO SINGLE CAUSE

Increased stress
Metabolic changes
Hormonal imbalance

- Young maternal age
- Recent stressful event
- Limited social and economic support
- Tobacco during pregnancy
- Prior history of depression



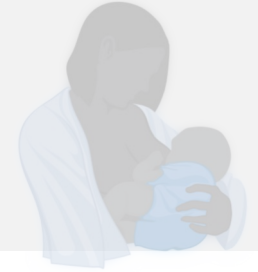
- More than **85%** of new mothers experience **postpartum blues**
- PPD affects **~11.5%** of **mothers** in the first year following childbirth
- PPD affects **~8%** of the **fathers** within the first year following childbirth

Current treatment options leave needs of many patients unmet

Common barriers
to seeking
PPD help

Untreated PPD?

20% of motherhood deaths
are caused by suicide



Primary standard of care is not PPD specific

Mild-to-moderate
Psychotherapy

Moderate-to-severe

Psychotherapy



Pharmacotherapy
e.g., Selective Serotonin
Reuptake Inhibitors (SSRI)

- Transcranial magnetic stimulation
- Omega-3 fatty acid supplements

Remission rate < 60%



Only one specific PPD
therapeutic

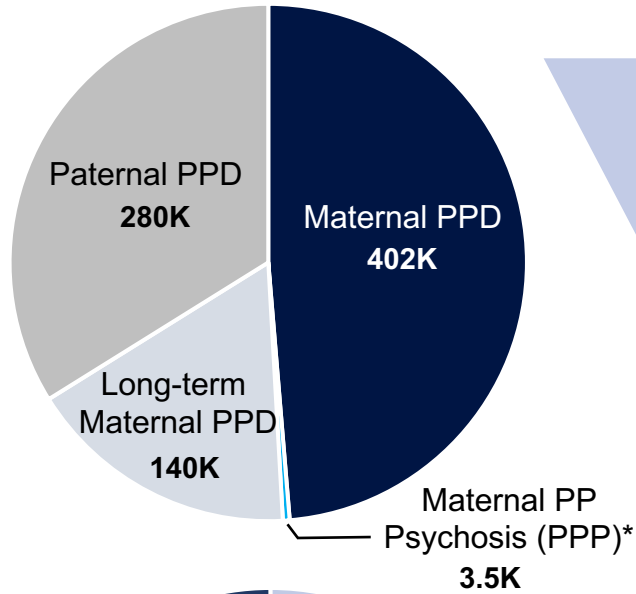
Brexanolone- Sage Therapeutics, Inc.

Continuous IV infusion for **60**
hours at **medically**
supervised setting

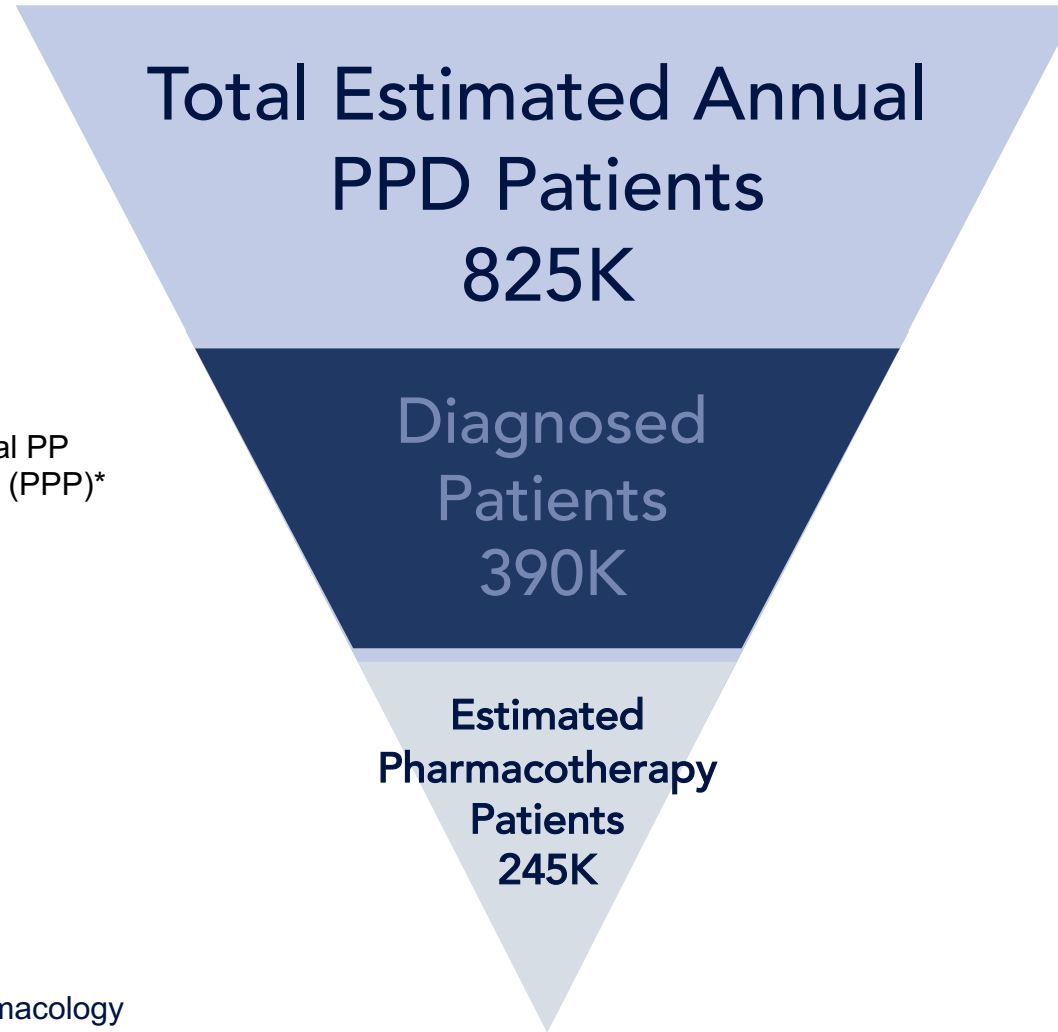
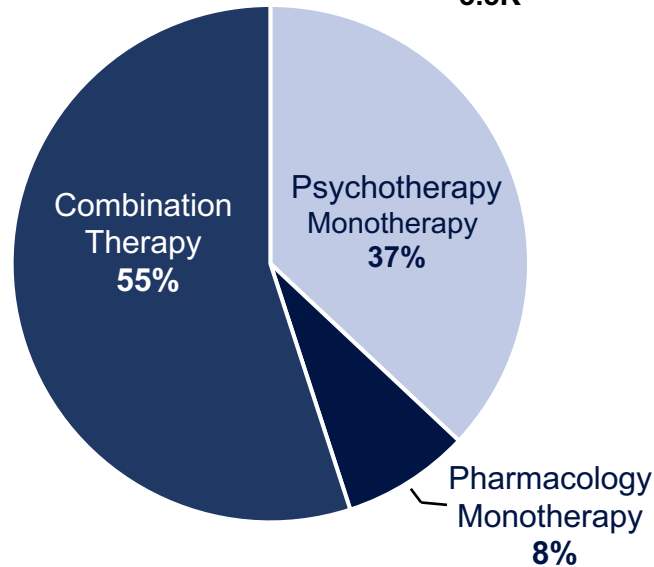
Costly treatment - **\$39,000**

Large and stable maternal and paternal PPD market

Patient Populations
(in thousands)



Treatment Options
(% of Patients)



546K Female PPD Patients (66%)
Mild-to-Moderate, Severe PPD (49%)
PP Psychosis* (0.4%)
Long-term PPD (17%)

330K Diagnosed (~50%*)

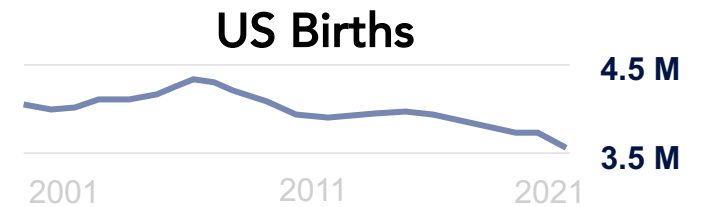
210K Use Pharmacotherapy (~63%*)

280K Male PPD Patients (34%)

56K Diagnosed (~20%)

35K Use Pharmacotherapy (~63%*)

*Assumed all PPP patients diagnosed and treated with pharmacotherapy



References: 8-18, 27; Appendix 1

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- Competitive Landscape**
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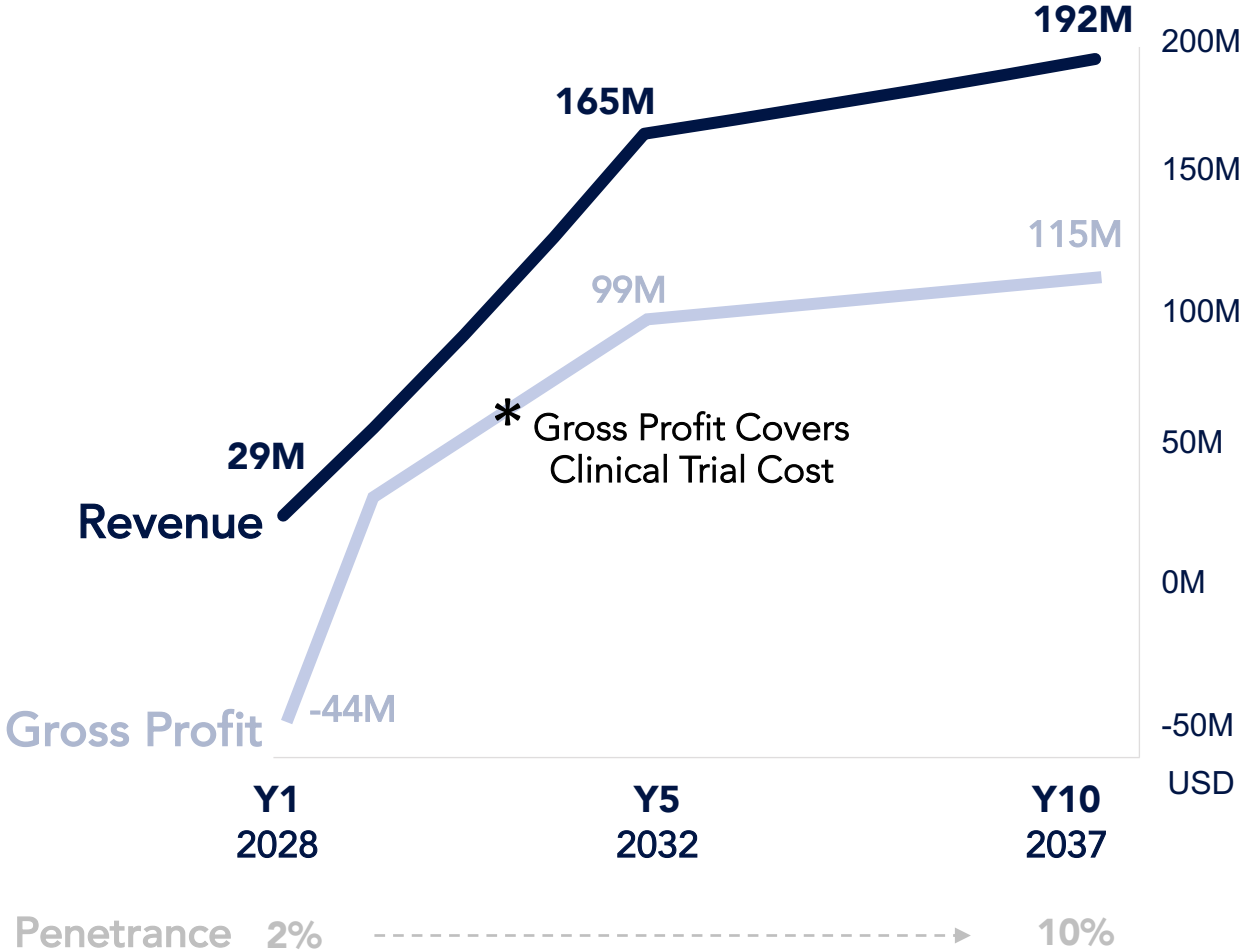
- Route to Market**
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PPD market growth will lead to rapid revenue growth

US Postpartum Depression
Market Size 2020-2030
CAGR 30%



BBB-032 FDA-Approval by 2027
Market Launch in 2028



Treatment Cost
Brand Name SSRIs \$5853/annually
BBB-032 price \$6000/treatment (9 doses)

Estimated Peak Revenues
\$165M by Y5 (2032)
\$192M by Y10 (2037)

References: 2,4,7, 19, 26, 27; Appendix 2-4, 7

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- Competitive Landscape**
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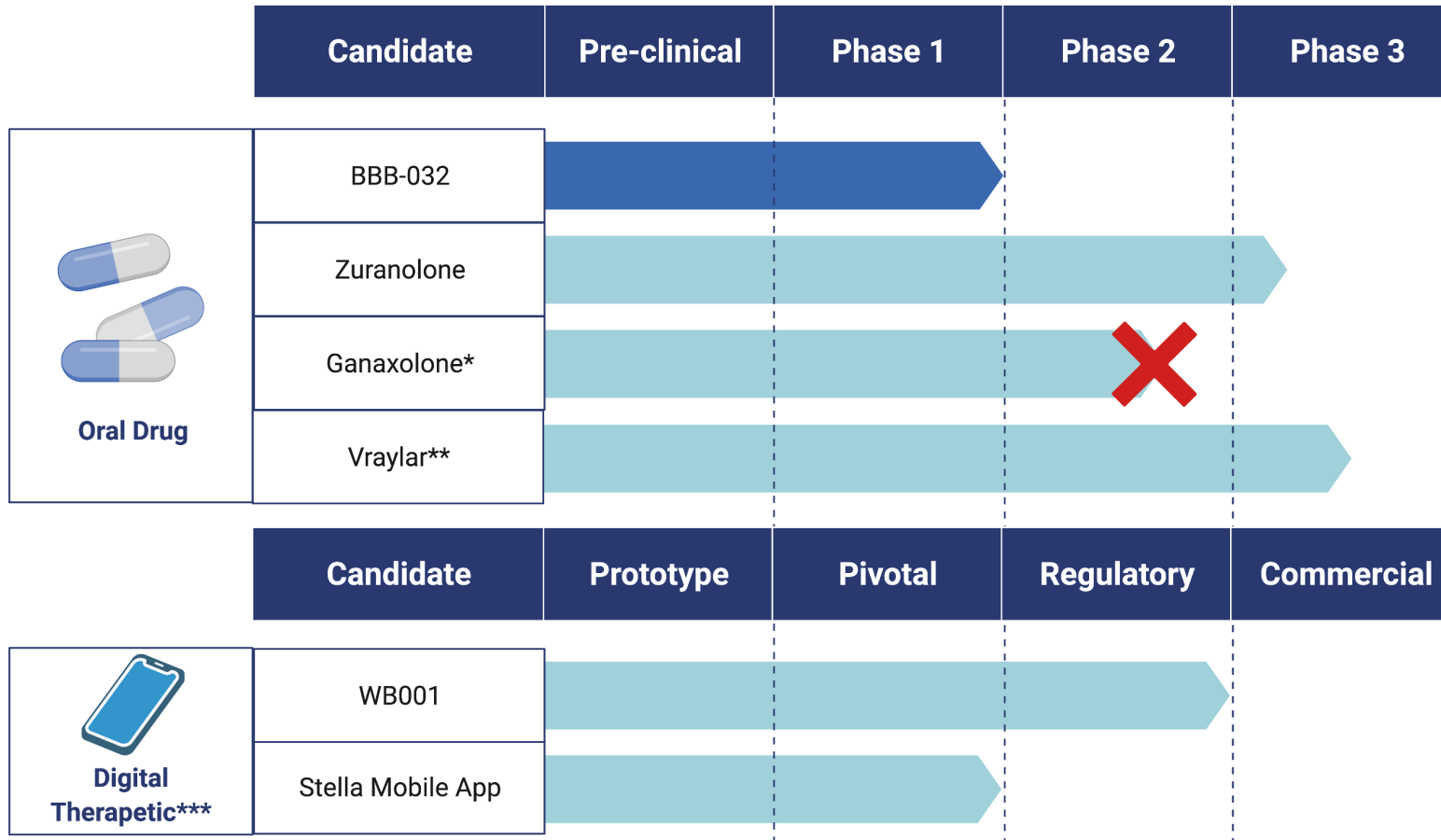
- Route to Market**
- Clinical Trial
 - Feasibility
 - Regulations
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Current PPD Market dominated by SSRIs for general depression

Company	Brand	Drug	Drug Class	Indication	Oral Availability?	Release Date
Sage Therapeutics	Zulresso	brexanolone	GABA _A modulator	PPD	No	2019
Sebelo	Pexeva/ Brisdelle	peroxatine	SSRI	MDD, anxiety, PTSD, OCD	Yes	2014
Eli Lilly	Cymbalta	duloxetine	SSNRI	MDD, anxiety	Yes	2002
GSK	Paxil	peroxatine	SSRI	MDD	Yes	1992
Viartis	Zoloft	sertraline HCl	SSRI	MDD, PTSD, and others	Yes	1999

- Oral availability expected to be driving variable of market share
- PPD specific treatments anticipated to disrupt market as they become readily available

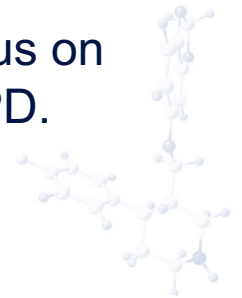
BBB-032 has opportunity as oral treatment for PPD



*Ganaxolone failed Phase II trial in 2019. No further PPD studies sought.

**Vraylar is an SSRI currently marketed for MDD. Seeking additional indication.

***Applications focus on therapy for mild PPD.



Better Blue Bio positioned to compete with Sage Therapeutics

Better Blue Bio

BBB-032

Seeking partner entering Phase II trial

Oral drug with onset of action in just 3 days

Est. Treatment costs \$6,000
Est. \$29M in revenue for Y1 2028

Window of efficacy to be determined

Minimal transient adverse events

Sage Therapeutics

Zulresso

Entered market March 2019

IV drug administered in facility over 60 hours

Treatment costs \$39,000
\$6.3M in revenue for 2021

Effective for up to 30 days. May be “bridge” to other treatments

Infusion may cause sleepiness and sudden loss of consciousness

Zuranolone

Partnered with Biogen for Phase II trial. Anticipating commercialization in 2022-23

Oral drug with onset of action in under 2 weeks

Unknown Treatment Cost
Est. Y1 on market 2023

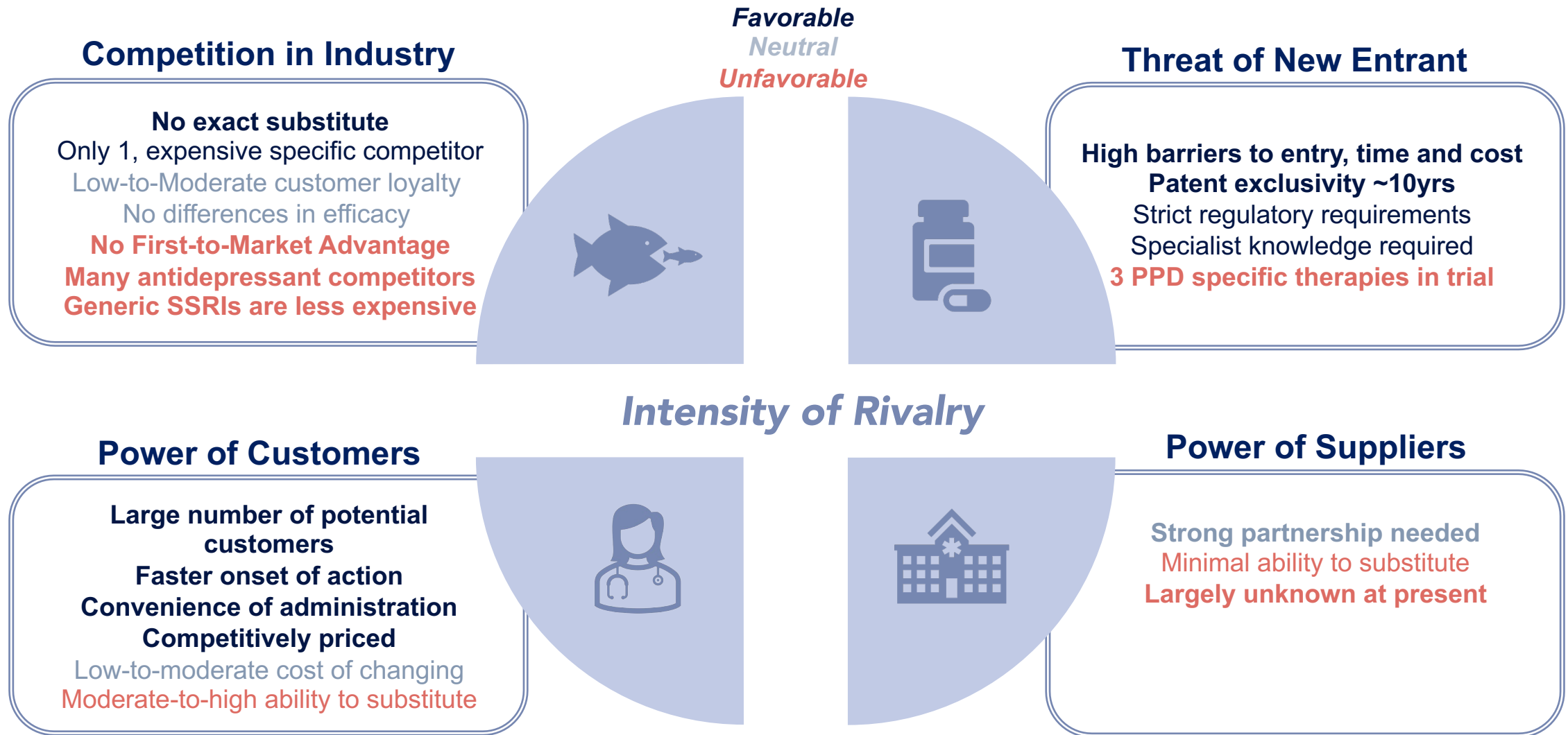
Short window of efficacy is a concern

Similar to other antidepressants

Favorable - **Neutral** - **Unfavorable**

References: 32-33

Competition in the industry is the focus of competitive dynamics



References: 26-35

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~50% of drug discovery and development is completed

Partnership would share remaining R&D process to market lucrative solution

8+ years for Research through Phase 1 Completed

<9 years for Phase 2 to Approval Remaining

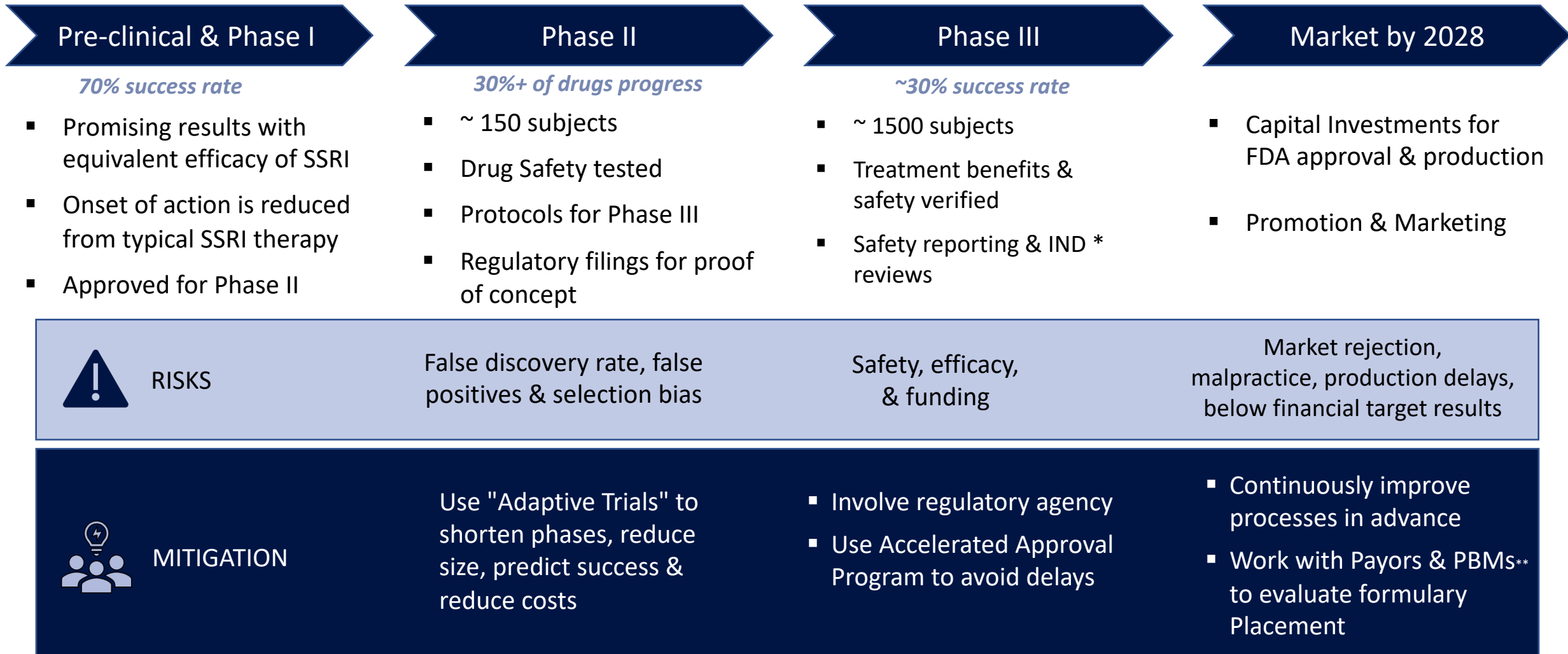


Estimated total R&D costs of **\$61.5M**, with **\$57.5M** remaining for market ready product

<u>Research and Development</u>		
Phase 1	Testing in healthy subjects (1.6 years)	\$4M invested
Phase 2	Testing in individual with disease (2.9 years)	\$13M
Phase 3	Larger scale testing in individuals with the disease (3.8 years)	\$20M

References: 2, 3, 4, 21; Appendix 5-6

Based on regulatory & clinical risks, Better Blue Bio should develop a discipline process for speed-to-market



* IND - Investigational New Drug

** Pharmacy Benefit Manager

References: 1, 3, 5, 6, 22; Appendix 5-6

Partnering can ease challenges of entering the market

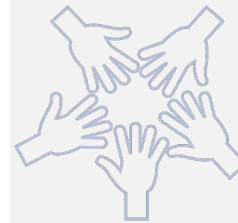
Traditional Life Science Partnering Strategies



- **Strategic Investment**
- **Co-Development**
- ✓ **Technical Capabilities**
 - ✓ **Capacity**
 - ✓ **Culture Fit**

Contract Manufacturing Organizations (CMOs)

Outsourcing had grown to account for **>22%** of pharmaceutical manufacturing!



Opportunistic Partnership

- **Joint Venture**
- **License Agreement**
- **Co-Marketing**

Partnership

Is an answer to allocate capital for future innovation

33%

Higher ROI for Alliances vs. M&A

Favorable market landscape and opportunity for BBB-032



- Market Identification: Target Market **250K** annual PPD patients
- Economics: Peak Revenue **\$165M (USD)** by 2032
- Competitive Landscape: **Favorable**, limited PPD-specific pharmacotherapeutics
- Route to Market: Quickly establish **partnership** (CMO)

4 Key Consideration Areas:

Partnership(s)

Price

Onset of action

Convenience

Potential Risks & Mitigation Strategies for Better Blue Bio

Potential Risks

- Performs better in some segments

Mitigation Strategies

- Focus on the most efficacious segments

Potential Risks

- Insufficient funds
- Low/Long patient recruitment
- Slow speed of approval

Mitigation Strategies

- Quickly find partner
- Use trial center with good history of recruitment

Market Segments

Competitors

Clinical Trial Feasibility

Stakeholder Buy-In

Potential Risks

- New PPD specific therapies further in trials
- Large SSRI market share

Mitigation Strategies

- Competitive pricing with brand name SSRIs
- Strong marketing focused on quick onset of action

Potential Risks

- Low doctor/patient buy-in as efficacy is comparable
- Low payor/insurance coverage

Mitigation Strategies

- Emphasize superior onset of action and reduced cost



Three Scientists and an Accountant – Our Team



Sharon Stevens
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Biochemistry



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Developmental Biology



Catherine Patton,
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Final-Year MBA candidate
Finance & Leadership



Thank You

References 1

1. FDA Approval Process. (2022). US Food & Drug Administration. Retrieved from, <https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fda-drug-approval-process-infographic-horizontal>
2. Kennedy, K. (2021, August). Brand name pharmaceutical manufacturing in the US. Industry report 32541A. IBISWorld.
3. Optum. (2022). *Rush to judgement? 5 warning signs that faster FDA approvals may increase risks, costs*. Optum.com. Retrieved from, <https://www.optum.com/business/resources/library/drug-approval-process.html>
4. Ledesma, P. (2020, January 2). *How much does a clinical trial cost?* Clinical Trial Costs. SOFPROMED. Retrieved from, <https://www.sofpromed.com/how-much-does-a-clinical-trial-cost>.
5. Kruczek, N. (2020, January 8). Navigating drug formularies in pharmacy benefit management. Pharmacy Times. <https://www.pharmacytimes.com/view/navigating-drug-formularies-in-pharmacy-benefit-management>
6. Pretorius, S. and Grignolo, A. (2016, August 1). *Phase III trial failures: costly, but preventable*. *Applied Clinical Trials Online*. <https://www.appliedclinicaltrials.com/view/phase-iii-trial-failures-costly-preventable>
7. Keown, (2022, January 4). *Drug price increases for 460 drugs in 2022*. BioSpace. Retrieved from, <https://www.biospace.com/article/a-new-year-means-price-increases-for-many-prescription-drugs/#:~:text=In%20January%202020%2C%20the%20prices,rise%20in%20prices%20across%20companies>.
8. Eldar-Lissai A, et al., Cost-Effectiveness of Brexanolone Versus Selective Serotonin Reuptake Inhibitors for the Treatment of Postpartum Depression in the United States. *J Manag Care Spec Pharm*. 2020 May;26(5):627-638. doi: 10.18553/jmcp.2020.19306. Epub 2020 Mar 19. PMID: 32191592.
9. Scarff JR. Postpartum Depression in Men. *Innov Clin Neurosci*. 2019 May 1;16(5-6):11-14. PMID: 31440396; PMCID: PMC6659987.
10. Viguera A. Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis. UpToDate. Dec 14, 2021.
11. Viguera A. Severe postpartum unipolar major depression: Choosing treatment. UpToDate. Oct 10, 2019.
12. Viguera A. Mild to moderate postpartum unipolar major depression: Treatment. UpToDate. Dec 14, 2021.
13. Hamilton BE, et al., Births: Provisional Data for 2019. NVSS Vital Statistics Rapid Release. Report No. 008 May 2020.
14. Osterman MJK, et al., Births: Final Data for 2020. NVSS National Vital Statistics Reports. Vol 70, No 17. Feb 7, 2022.
15. Putnick DL, et al., Trajectories of Maternal Postpartum Depressive Symptoms. *Pediatrics*. 2020 Nov;146(5):e20200857. doi: 10.1542/peds.2020-0857. PMID: 33109744.
16. Cleveland Clinic. [Postpartum Depression](#). Accessed 4/4/2022.
17. National Institute of Mental Health. [Postpartum depression facts](#). Accessed 4/4/2022.
18. National Institutes of Health. [Postpartum depression may last for years](#). Accessed 4/4/2022.
19. Mira Health. [How Much Do Antidepressants Cost Without Insurance in 2021?](#) Sept 15, 2021.
20. GlobalNewsWire. [CNS Drugs Take 20% Longer to Develop and 38% Longer to Approve vs. Non-CNS Drugs](#), According to the Tufts Center for the Study of Drug Development. Accessed 4/4/22.
21. Applied Clinical Trials. [New Research Emerges to Challenge Steep Costs of Clinical Trials](#). July 5, 2020. Accessed 4/4/2022.
22. Berezow, A. American Council on Science and Health. [Clinical Trial Success Rates By Phase And Therapeutic Area](#). June 11, 2020.
23. Esquire KW, et al., McGuireWoods LLP. *Understanding Life Science Partnership Structures*. American Health Lawyers Association. March 2009
24. Aylor Ben, et al., Creating More Powerful Partnerships in Pharma Manufacturing., BCG, September 10, 2018.
25. Baral Subin & Ural Arda., How exosystem participation drives more value for life sciences deals., EY., Jan 10, 2022.
26. DelveInsight. (2021). *Postpartum Depression- Market Insight, Epidemiology and Market Forecast -2030*. <https://www.delveinsight.com/report-store/postpartum-depression-market>
27. Postpartum Products Market Share, Size, Trends, Industry Analysis Report, By Products; By Distribution Channel (Hospital Pharmacy, Retail Store, E-Commerce, Wholesales/Distributor, Direct Purchase), By Region; Segment Forecast, 2022 – 2030. [PM2189](#). Jan 2022
28. Silverman M, et al., The Risk Factors for Postpartum Depression: A Population Based Study., *Depress Anxiety*, February 2017. Doi: 10.1002/da.22597.
29. Terzic T and Plesnicar BK., Selective Serotonine Reuptake Inhibitors (SSRI) Usage during Pregnancy., *Psychiatria Danubina*., 2021
30. Edinoff AN., et al., Brexanolone, a GABA-A Modulator, in the Treatment of Postpartum Depression in Adults: A Comprehensive Review., *Frontiers in Psyychiatry*., Sept 14, 2021.
31. Armstrong, Annalee. "Marinus Shares Plunge 67% as Postpartum Depression Drug Fails to Best Placebo." *S&P Global*, 23 July 2019, <https://www.spglobal.com/marketintelligence/en/news-insights/trending/ xo14ht2aajlfrau9eevew2>.
32. *Investor Presentation - Investor.sagerx.com*. <https://investor.sagerx.com/static-files/c06a322b-5147-4193-b87d-b5ada4e55dca>.
33. "SEC Filing: Sage Therapeutics, Inc." *SEC Filing | Sage Therapeutics, Inc.*, https://investor.sagerx.com/node/12206/html#ITEM_15_EXHIBITS_FINANCIAL_STATEMENT_SCH.
34. Hackett, Mallory. "Digital Chatbot Woebot Lands FDA Breakthrough Designation to Tackle Postpartum Depression." *MobiHealthNews*, 26 May 2021, <https://www.mobihealthnews.com/news/digital-chatbot-woebot-lands-fda-breakthrough-designation-tackle-postpartum-depression>.
35. "Mobile Application in the Management of Mild to Moderate Postpartum Depression (PPD) - Full Text View." *Full Text View - ClinicalTrials.gov*, <https://clinicaltrials.gov/ct2/show/NCT05077644>.
36. Macritrends. US Birth rate. <https://www.macrotrends.net/countries/USA/united-states/birth-rate>. Accessed 4/10/22

Summary of Assumptions

Market Identification – Appendix 1

- Mechanism of action: BBB-032 if efficacious in males and females
 - Potentially through acting on estrogen or prolactin which are both increased in men/women postpartum (Ref. 9)
- 3.495 M new mothers/fathers in 2020 (Ref. 13, 14)
- 63% of PPD patients use pharmacological treatment (55% combo + 8% mono); except 100% for Post-traumatic Psychosis (PPP) (Ref. 10, 11, 12)
- 11.5% incidence rate of new maternal PPD; 50% diagnosis rate (Ref. 8, 10, 11, 12)
- 1:1000 new mothers have PPP; 100% diagnosis rate (Ref. 16)
- Long-term maternal PPD: Mothers that have given birth in past 2-3 years; 30% of Y1 mothers in Y2; 5% of Y2 mothers in Y3; 50% diagnosis rate (Ref. 8, 9, 18)
- Paternal PPD: Current year of fatherhood; 8% incidence rate; 20% diagnosis rate (Ref. 9)

Market Economics – Appendix 2, 3, 4, 7

- Brand Name SSRIs cost \$5,853 USD/year; Brexanolone cost is \$39,000/treatment (60hr infusion) (Ref.19)
- BBB-032 priced at \$6,000 USD/treatment (9 doses) and treatment lasts 1 year
- COGS for BBB-032 is 40%; 2% annual increase in COGS
- Drug companies' peak sales range \$1-14B USD annually
- 2% increase in the price of therapy annually due to inflation
- Market size decreases by 1% every year due to slight reductions in birth rate and loss of long-term maternal PPD patients
- Starting penetration of 2%, 10% penetrance by year 5

Route to Market – Appendix 5, 6

- Average time for CNS therapeutic process in clinical trials and FDA-approval is 8.2 years, average cost is 53.1 M (USD) (Ref. 4, 20)
- BBB-032 cost for R&D, Trials, FDA-Approval is 61.5 M (USD), with 57.5 M (USD) remaining (Phase II – FDA Approval)
- Clinical trial cost/patient is \$41,413; 1500 patients in Phase III (Ref. 21)
- Patent provides 10-year exclusivity for BBB-032 post-approval

Appendices

- *Appendix 1: Market Size and Segmentation Calculations and Assumptions*
- *Appendix 2: Price & Cost of Sales Analysis*
- *Appendix 3: Proforma Statements*
- *Appendix 4: Pharmaceutical Revenue Potentials*
- *Appendix 5: Research & Development Costs*
- *Appendix 6: R&D Cost Analysis*
- *Appendix 7: Market Opportunity*

Appendix 1: Market Size and Segmentation Calculations/Assumptions

of New Mothers/Fathers in US in 2020: ~3.495 M 3.61M Births in US; Twins 32.1 : 1000 ; Triples+ 79.6 : 100,000 (Ref. 13, 14)

PPD Patient Segments (Annual Patient Numbers)			Adjusted/Reasonable Annual Market	Details and Assumptions
Segment	PPD Incidence	# Diagnosed	Pharmacological Treatment*	
New Maternal PPD	401899	200949	126598	*assuming 63% use pharmacological treatment (55% combo + 8% mono) except for 100% for PPP (Ref. 10, 11, 12) Gave birth in current year (11.5% incidence rate), ~50% diagnosis rate (Ref. 8, 10, 11, 12)
Maternal PP Psychosis	3495	3495	3495	1:1000 new mothers & assume all diagnosed + pharmacotherapy treated, used 100% diagnosis rate (Ref. 16)
Long-term PPD	140665	70332	44309	Gave birth in past 2-3 years; 30% of the Y1 mothers in Y2, 5% into Y3, ~50% diagnosis rate (Ref. 8, 9, 18)
Paternal PPD	279582	55916	35227	Current year of fatherhood (8% incidence rate), diagnosis rate not found, just says 'low' used 20% (Ref. 9)
Female + Male PPD	825640	330693	209630	
Only Female PPD	546058	274776	174402	

Year	Birth Rate	Growth Rate
2022	12.012	0.090%
2021	12.001	0.090%
2020	11.990	0.090%
2019	11.979	0.090%
2018	11.968	-0.950%
2017	12.083	-0.940%
2016	12.198	-0.940%
2015	12.314	-0.930%
2014	12.429	-0.920%
2013	12.544	-1.980%
2012	12.798	-1.940%
2011	13.051	-1.910%
2010	13.305	-1.870%
2009	13.558	-1.840%
2008	13.812	-0.320%
2007	13.856	-0.320%
2006	13.900	-0.320%
2005	13.945	-0.310%
2004	13.989	-0.310%
2003	14.033	-0.360%
2002	14.083	-0.350%
2001	14.133	-0.350%

PPD Disease Mechanism Information: Hormone Levels Compared to Baseline (Ref. 9)

HORMONE	PREPARTUM WOMEN	POSTPARTUM WOMEN	PREPARTUM MEN	POSTPARTUM MEN
Cortisol	Increased	Increased	Decreased	Decreased, then normalizes
Testosterone	Mildly increased	Normalizes	Decreased	Decreased, then normalizes
Estrogen/estradiol	Increased	Increased	Increased	Increased
Prolactin	Increased	Increased	Increased	Increased

(Ref. 36)

Appendix 2: Price & Cost of Sales Analysis

Better Blue Bio price per treatment estimated at ~\$6,000 based on average SSRI annual treatment cost

PPD Pharmacotherapy Treatment	Price	Timeframe	Annual Cost
Avg. SSRI uninsured Generic cost	\$ 63	per month	\$ 750
Avg. SSRI uninsured Brand-Name cost	\$ 488	per month	\$ 5,853
Brexanolone	\$ 38,501	total (60hr infusion)	\$ 38,501
Avg Annual Treatment Cost/Patient			\$ 15,034.67

Reference: 19

Price Assumptions

- *BBB-032 full treatment with 3 doses is comparable to SSRI annual treatment costs for similar efficacy*
- *Brexanolone is not a comparable treatment cost as this is an infusion versus oral treatment*

COGS Assumptions

- *IBIS World Brand Name Pharmaceutical Manufacturing in the US average COGS for mid-size companies ranges from 39% to 59%*
- *Used 40% COGS in financial proforma for BBB*

IBIS Pharmaceutical Industry Report Cost of Sales as Percentage of Sales			
Company Asset Size	3yr	5yr	10yr
10m-25m	56.69%	46.13%	68.81%
25m-50m	42.67%	51.60%	57.68%
50m-100m	46.62%	71.70%	87.03%
100m-250m	11.68%	10.52%	22.54%
Average	39.41%	44.99%	59.02%

Appendix 3: Proforma Statements

Estimates of peak revenues of \$165M by 2032 and \$192M by year 10 post-FDA approvals

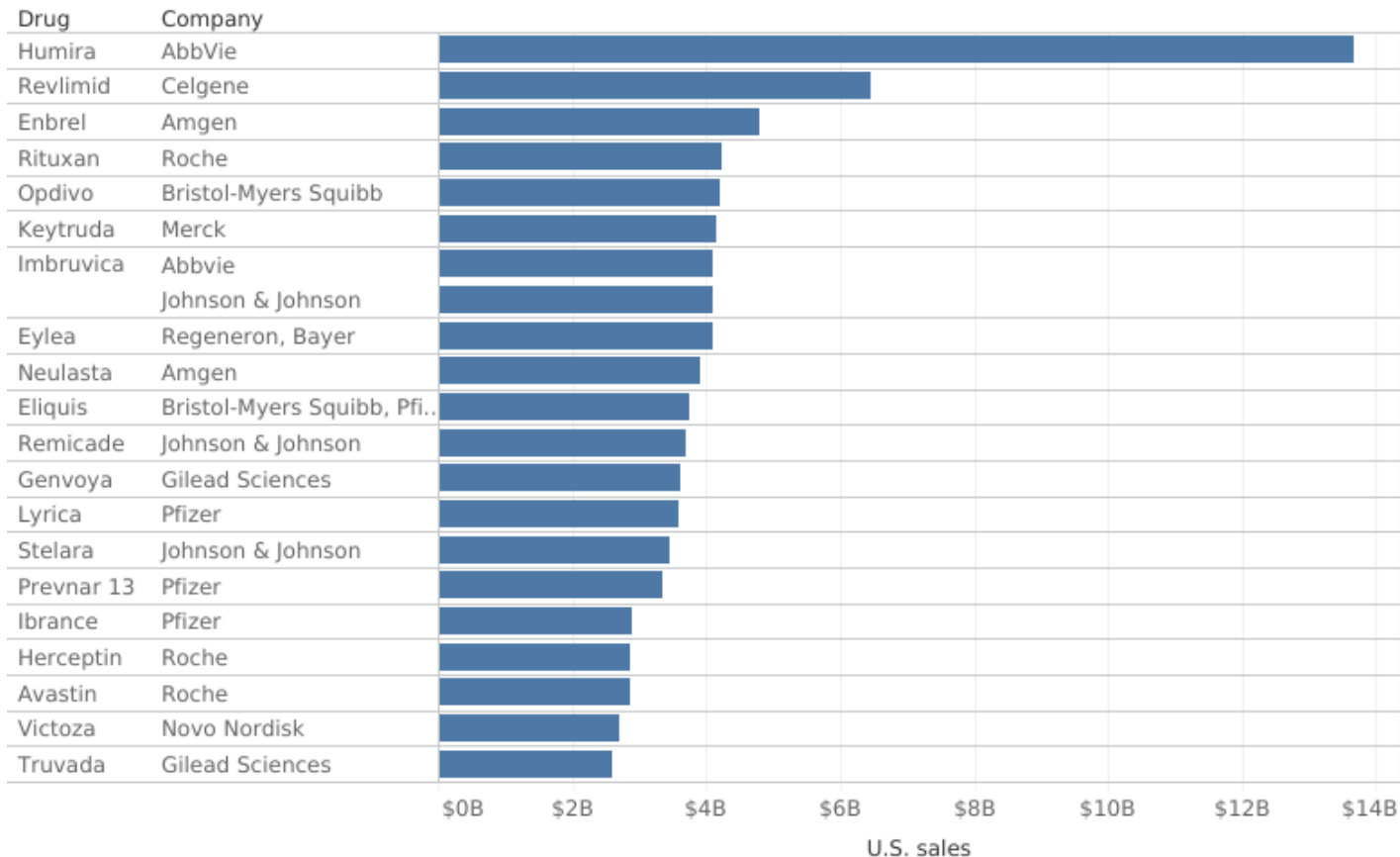
BBB-032 Pro-forma Financial Statements

		Patent - Market Exclusivity									
		1	2	3	4	5	6	7	8	9	10
		MARKET									
		2028	2029	2030	2031	2032	2033	2034	2035	2036	2037
Revenue											
Patient Market Size	1%	245,000	247,450	249,925	252,424	254,948	257,497	260,072	262,673	265,300	267,953
Penetration Rate	2%	2%	4%	6%	8%	10%	10%	10%	10%	10%	10%
Customer Size	2%	4,900	9,898	14,995	20,194	25,495	25,750	26,007	26,267	26,530	26,795
Price per 9dose treatment	2%	\$6,000	\$6,120	\$6,242	\$6,367	\$6,495	\$6,624	\$6,757	\$6,892	\$7,030	\$7,171
Average treatments/yr		1	1	1	1	1	1	1	1	1	1
Total Revenue		\$29,400,000	\$60,575,760	\$93,607,722	\$128,579,567	\$165,578,337	\$170,578,803	\$175,730,283	\$181,037,337	\$186,504,665	\$192,137,106
Expenditures											
R&D Costs		\$61,500,000									
Cost of Sales per treatment	40%	\$2,400	\$2,448	\$2,497	\$2,547	\$2,598	\$2,650	\$2,703	\$2,757	\$2,812	\$2,868
Total Cost of Sales		\$11,760,000	\$24,230,304	\$37,443,089	\$51,431,827	\$66,231,335	\$68,231,521	\$70,292,113	\$72,414,935	\$74,601,866	\$76,854,842
Total Costs		\$73,260,000	\$24,230,304	\$37,443,089	\$51,431,827	\$66,231,335	\$68,231,521	\$70,292,113	\$72,414,935	\$74,601,866	\$76,854,842
Profit (Loss)		(\$43,860,000)	\$36,345,456	\$56,164,633	\$77,147,740	\$99,347,002	\$102,347,282	\$105,438,170	\$108,622,402	\$111,902,799	\$115,282,264

Appendix 4: Pharmaceutical Revenue Potentials

Drug companies' peak sales range from \$1B to \$14B.
Postpartum market is within the median range

Top drug sales of 2018



New Drugs Approved in 2018 With Largest Peak Sales Potential

Drug (Company)	Peak Sales Potential \$ billion	Indication
Biktarvy (Gilead Sciences)	6.6	HIV
Ultomiris (Alexion)	2.3	Paroxysmal nocturnal hemoglobinuria (PNH)
Symdeko (Vertex Pharmaceuticals)	2.3	Cystic fibrosis
Orilissa (AbbVie)	1.9	Endometriosis
Crysvita (Ultragenyx)	1.8	X-linked hypophosphatemia (XLH)
Erleada (Johnson & Johnson)	1.7	Non-metastatic prostate cancer
TakzYRO (Shire)	1.7	Hereditary angioedema
Olumiant (Eli Lilly)	1.5	Moderate to severe rheumatoid arthritis
Epidiolex (GW Pharmaceuticals)	1.3	Dravet & Lennox-Gastau syndrome
Aimovig (Amgen)	1.3	Migraine
Libtayo (Regeneron Pharmaceuticals)	1.2	Metastatic cutaneous squamous cell carcinoma
Onpatro (AInylam Pharmaceuticals)	1.1	Familial Amyloid Neuropathies
Lokelma (AstraZeneca)	1.0	Hyperkalemia

Appendix 5: Research & Development Costs

Better Blue Bio estimates total R&D costs of \$61.5M, with \$57.5M remaining for market ready product



	Phase I Complete	Phase II 2022	Phase II 2023	Phase III 2024	Phase III 2025	Phase III 2026	FDA & Phase IV 2027	Total R&D
Expenditures								
Subject Size	50	150	150	1500	1500	1500		
Cost per subject	\$80,000	\$43,333	\$43,333	\$4,444	\$4,444	\$4,444		
R&D Costs	\$4,000,000	\$6,500,000	\$6,500,000	\$6,666,667	\$6,666,667	\$6,666,667	\$24,500,000	\$61,500,000
Cost of Sales per treatment								
Total Costs	\$4,000,000	\$6,500,000	\$6,500,000	\$6,666,667	\$6,666,667	\$6,666,667	\$24,500,000	\$61,500,000
		\$13M		\$20M				

When breaking down the estimated total **trial cost per patient**, the average total came in at \$41,413 (IQR of \$29,894 to \$75,047)

Appendix 6: R&D Cost Analysis

Total R&D costs ranges from \$44M to \$115M, with an average of \$67M. Better Blue Bio estimated at \$61.5M

Financial proforma model assumes Rule of Thumb cost per phase:

- Phase 1: ~\$4M
- Phase 2: \$13.6M
- Phase 3: \$20M
- FDA Review Phase: \$2M

Phase 4 ranges from \$6.8M to \$72.9M, with the average of \$26M and median of \$25M. Used \$22.5M for financial proforma.

Therapeutic Area	Phase 1	Phase 2	Phase 3	Phase 1, 2, & 3 Subtotal [d]	FDA NDA/BLA Review Phase [c]	Phase 4	Total [d]
Anti-Infective	\$4.2 (5)	\$14.2 (6)	\$22.8 (5)	\$41.2 (3)	\$2.0	\$11.0 (12)	\$54.2 (10)
Cardiovascular	\$2.2 (9)	\$7.0 (13)	\$25.2 (3)	\$34.4 (10)	\$2.0	\$27.8 (4)	\$64.1 (6)
Central Nervous System	\$3.9 (6)	\$13.9 (7)	\$19.2 (7)	\$37.0 (6)	\$2.0	\$14.1 (11)	\$53.1 (11)
Dermatology	\$1.8 (10)	\$8.9 (12)	\$11.5 (13)	\$22.2 (13)	\$2.0	\$25.2 (7)	\$49.3 (12)
Endocrine	\$1.4 (12)	\$12.1 (10)	\$17.0 (9)	\$30.5 (12)	\$2.0	\$26.7 (6)	\$59.1 (7)
Gastrointestinal	\$2.4 (8)	\$15.8 (4)	\$14.5 (11)	\$32.7 (11)	\$2.0	\$21.8 (8)	\$56.4 (8)
Genitourinary System	\$3.1 (7)	\$14.6 (5)	\$17.5 (8)	\$35.2 (8)	\$2.0	\$6.8 (13)	\$44.0 (13)
Hematology	\$1.7 (11)	\$19.6 (1)	\$15.0 (10)	\$36.3 (7)	\$2.0	\$27.0 (5)	\$65.2 (5)
Immunomodulation	\$6.6 (1)	\$16.0 (3)	\$11.9 (12)	\$34.5 (9)	\$2.0	\$19.8 (9)	\$56.2 (9)
Oncology	\$4.5 (4)	\$11.2 (11)	\$22.1 (6)	\$37.8 (5)	\$2.0	\$38.9 (2)	\$78.6 (3)
Ophthalmology	\$5.3 (2)	\$13.8 (8)	\$30.7 (2)	\$49.8 (2)	\$2.0	\$17.6 (10)	\$69.4 (4)
Pain and Anesthesia	\$1.4 (13)	\$17.0 (2)	\$52.9 (1)	\$71.3 (1)	\$2.0	\$32.1 (3)	\$105.4 (2)
Respiratory System	\$5.2 (3)	\$12.2 (9)	\$23.1 (4)	\$40.5 (4)	\$2.0	\$72.9 (1)	\$115.3 (1)
Average	\$3.4	\$13.6	\$21.8	\$38.7	\$2.0	\$26.3	\$67.0
Per article	\$4.0	\$13.0	\$20.0	\$37.0	\$2.0	\$22.5	\$61.5
Median	\$3.1	\$13.9	\$19.2	\$36.2	\$2.0	\$25.2	\$63.4

Reference: 4

Average Cost for CNS Therapeutic Process in Clinical Trials + FDA Approval
Average Time for CNS Therapeutic Process in Clinical Trials + FDA Approval

53.1 M Total Cost
8.2 Years

Reference: 20

Appendix 7: Market Opportunity

Better Blue Bio estimates peak revenues of \$165M by 2032 and \$192M by year 10 post-FDA approvals

Assumptions

- FDA Approval by 2027
- Market Launch by 2028
- 10-year exclusivity period
- Revenues
 - ✓ 2% initial penetration
 - ✓ \$6k per treatment based on annual SSRI current treatments
 - ✓ 2% annual increases
- Costs
 - ✓ Total R&D of \$61.5M
 - ✓ COGS averages 40% for the U.S. Rx manufacturing industry (small to mid-sized companies)
 - ✓ 2% annual increase

