



# (AL-101) Apomorphine Licensing

9-1-2021

[WWW.ONCOTELIC.COM](http://WWW.ONCOTELIC.COM)

# Forward-looking Statements

- This document contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this communication regarding strategy, future operations, future financial position, prospects, plans and objectives of management are forward-looking statements related to Oncotelic Therapeutics, Inc. (f/k/a Mateon Therapeutics, Inc.), its wholly owned subsidiaries, Oncotelic Inc. and PointR Data Inc. and its non controlled interest entity EdgePoint AI, Inc. (cumulatively referred to as the “Company”). In addition, when or if used in this communication, the words “will,” “may,” “would,” “approximate,” “expect,” “intend,” and similar expressions and their variants, as they relate to the Company, may identify forward-looking statements. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation, uncertainties as to the timing of financing and the outcome of the clinical program and the outcome of FDA interactions. This review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in the Company’s Annual Report on Form 10-K filed with the SEC on April 15, 2021 as well as other Quarterly Reports and Current Reports filed with the SEC. Forward looking statements are based on information available and assumptions as of the date of this report. Except as required by applicable law, the Company undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

# Approved Apomorphine

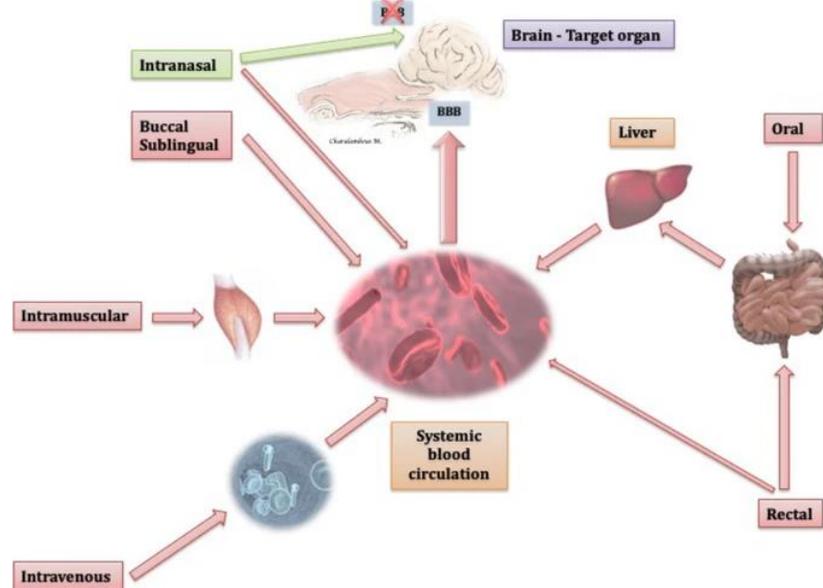
- Uprima (apomorphine). Erectile Dysfunction- EU. **Sublingual**.
- Apokyn (apomorphine HCl injection) / dopamine agonist/ To help restore the balance of dopamine in the brain/ Parkinson OFF cycle. For the acute, intermittent treatment of hypomobility, “off” episodes (“end-of-dose wearing off” and unpredictable “on/off” episodes) associated with advanced Parkinson’s disease. **Subcutaneous** administration only. Approval Date: April 1, 2004. Company Name: Mylan Laboratories.
- KYNMOBI™ (apomorphine HCl) **sublingual film** / To treat the acute, intermittent treatment of OFF episodes in patients with Parkinson’s disease (PD) dissolves under the tongue. Approval Date: May-21-2020/ Company Name: Sunovion Pharmaceuticals
- This allows for the 505(b)2 regulatory pathway which encourages further development of an already approved drug through two major incentives:
  1. **Short Development time.** The 505 (b)(2) pathway provides manufacturers with new dosage, route of administration to acquire FDA approval by completing limited safety and efficacy clinical program referencing the bulk of preclinical and clinical data on file by the initial manufacturers to complete the new drug application (“NDA”).
  2. **Long Market Exclusivity.** The 505(b)2 filer is generally eligible for 3-5 years of market exclusivity. A drug approved via a full NDA is normally granted a 5-year market exclusivity period, while a generic product approved through the abbreviated new drug application, or ANDA, pathway may earn 6 months of market exclusivity.
  3. Orange book patent certification. Method of use and composition of matter patents protect AL-101 from generic competitors out to 2041.

# Example of a successful 505(b)2 Pathway Product - Abraxane

- *"The 505(b)(2) pathway represents an appealing regulatory strategy for some companies, and the only viable strategy for others. This creates an abundance of newfound time, saves money and resources. By utilizing previously completed research as part of an FDA submission, companies can reduce their cost, on an NDA via the 505(b)(2) pathway, from potentially several billions of dollars to just tens of millions. But beyond time and money, this can mean the difference between new, groundbreaking drugs entering the market in the near future versus years down the line. The consequences are enormous both for the pharmaceutical companies and patients".* <https://www.prnewswire.com/il/news-releases/frost--sullivan-major-drug-companies-are-securing-an-edge-by-leveraging-the-505b2-pathway-300951503.html>
- As an example, Abraxane (Paclitaxel), for the treatment of breast cancer by Abraxis and subsequently Celgene, changed the formulation world to move to nanoparticles and led to minimizing adverse effects and enhanced efficacy. The approximate peak annual sales for Abraxane were \$682M for breast cancer alone. Abraxane, since its approval in 2005, has maintained its dominance in solid tumor space with successive approvals for breast, lung, and pancreatic cancers.
- Abraxane contributed FY20 sales of \$1.25bn to Bristol Myers Squibb's revenues who acquired Celgene. <https://seekingalpha.com/article/4416507-bristol-myers-squibbs-floundering-days-behind-full-steam-ahead>
- Abraxane was acquired by Celgene for \$2.9B (<https://www.reuters.com/article/us-abraxis-takeover-celgene/celgene-to-buy-abraxis-bioscience-for-2-9-billion-idUSTRE65T1Z120100630>)
- Cynviloq - the next generation Abraxane - was acquired, initially by Sorrento Therapeutics from Igdrasol Inc., and subsequently by NantPharma for \$1.3B (<https://www.genengnews.com/news/sorrento-sells-cynviloq-for-1-3b/>)
- Vuong Trieu, CEO of the Company, was the CEO of Igdrasol and led the development of Cynviloq. Cynviloq was acquired by Sorrento Therapeutics, and Dr. Trieu became CSO / BOD of Sorrento Therapeutics. Dr. Trieu is also one of the inventors of Abraxane.

# AL-101 (Intranasal Apomorphine)

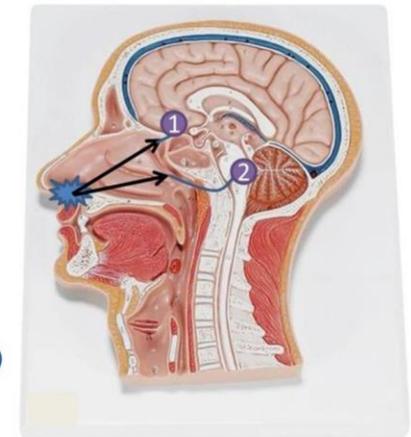
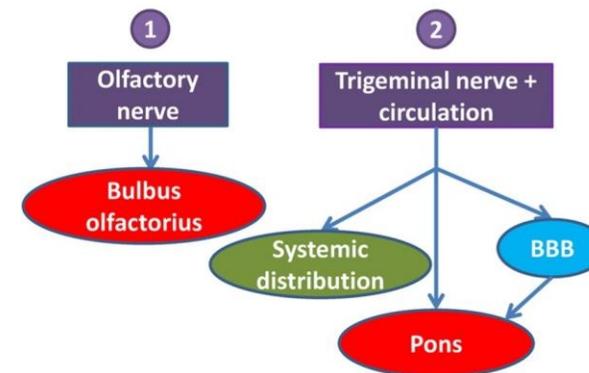
- Unique nasal technology made up of anionic, cationic, & zwitter-ionic compounds capable of stabilizing difficult drug substances and providing rapid systemic absorption at a fraction of the oral dose.
- Intra-nasal (IN) delivery avoids first pass metabolism in the liver.
- IN delivered 10x more drug into central nervous system (“CNS”) versus sublingual and subcutaneous. This preference for the central nervous organ reduces the off-target toxicity of apomorphine ie. hypotension
- Increased efficacy and decreased toxicity



## NASAL DRUG ADMINISTRATION FOR CNS TARGETING

Intranasal drug delivery to the CNS

1. Olfactory pathway (Bulbus olfactorius)
2. Respiratory pathway (Brainstem, pons)



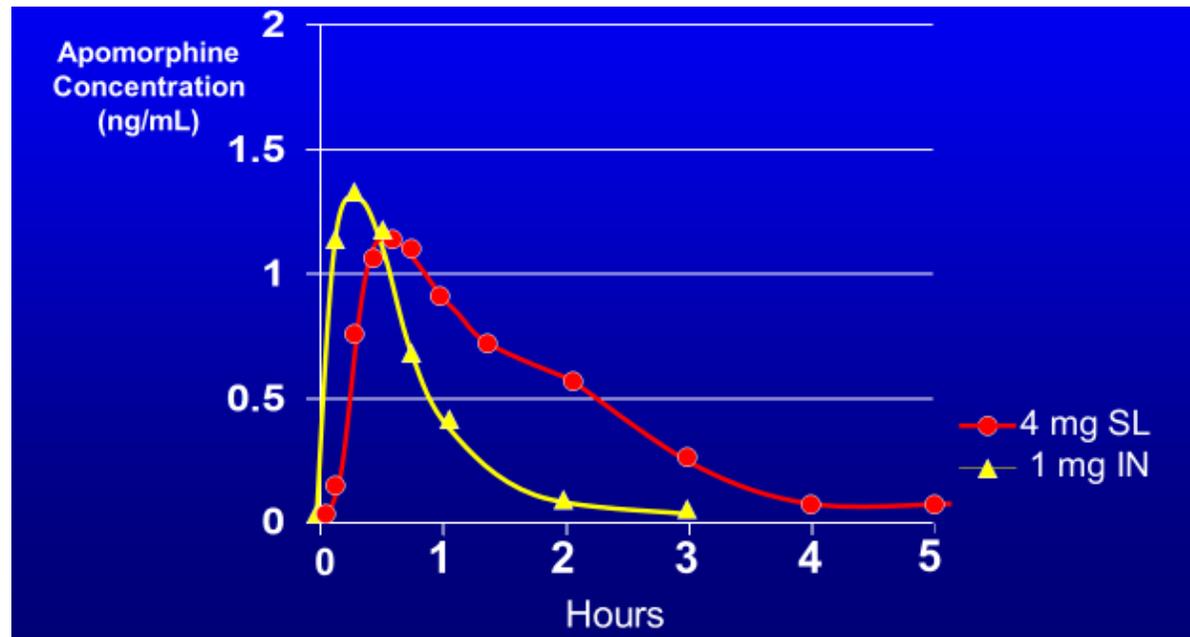
# Overall IN Apomorphine Safety Profile

- Nasal apomorphine has a low adverse event profile
- Over 200 patients (2,200 doses) have participated in our clinical trials for intranasal apomorphine (including geriatric patients up to 78 years old)
- Very low incidence of nausea
- To date *no* incidences of vomiting, syncope or hypotension in patients in our trials

<b>Adverse Event</b>	<b>Apomorphine IN</b>	<b>Viagra</b>	<b>Cialis</b>	<b>Apomorphine SL</b>
<b>Headache</b>	<b>0.8%</b>	16%	13.9%	6.5%
<b>Nausea</b>	<b>0.8%</b>	< 2%	?	22.2%
<b>Dizziness</b>	<b>3.3%</b>	2%	6.2%	14.5%
<b>Flushing</b>	<b>0%</b>	10%	4.2%	6.5%
<b>Dyspepsia</b>	<b>0%</b>	7%	7.7%	?
<b>Vomiting</b>	<b>0%</b>	< 2%; Not 0%	?	4.3%
<b>Hypotension*</b>	<b>0%</b>	< 2%; Not 0%	?	6%
<b>Syncope</b>	<b>0%</b>	0.14%	?	2%

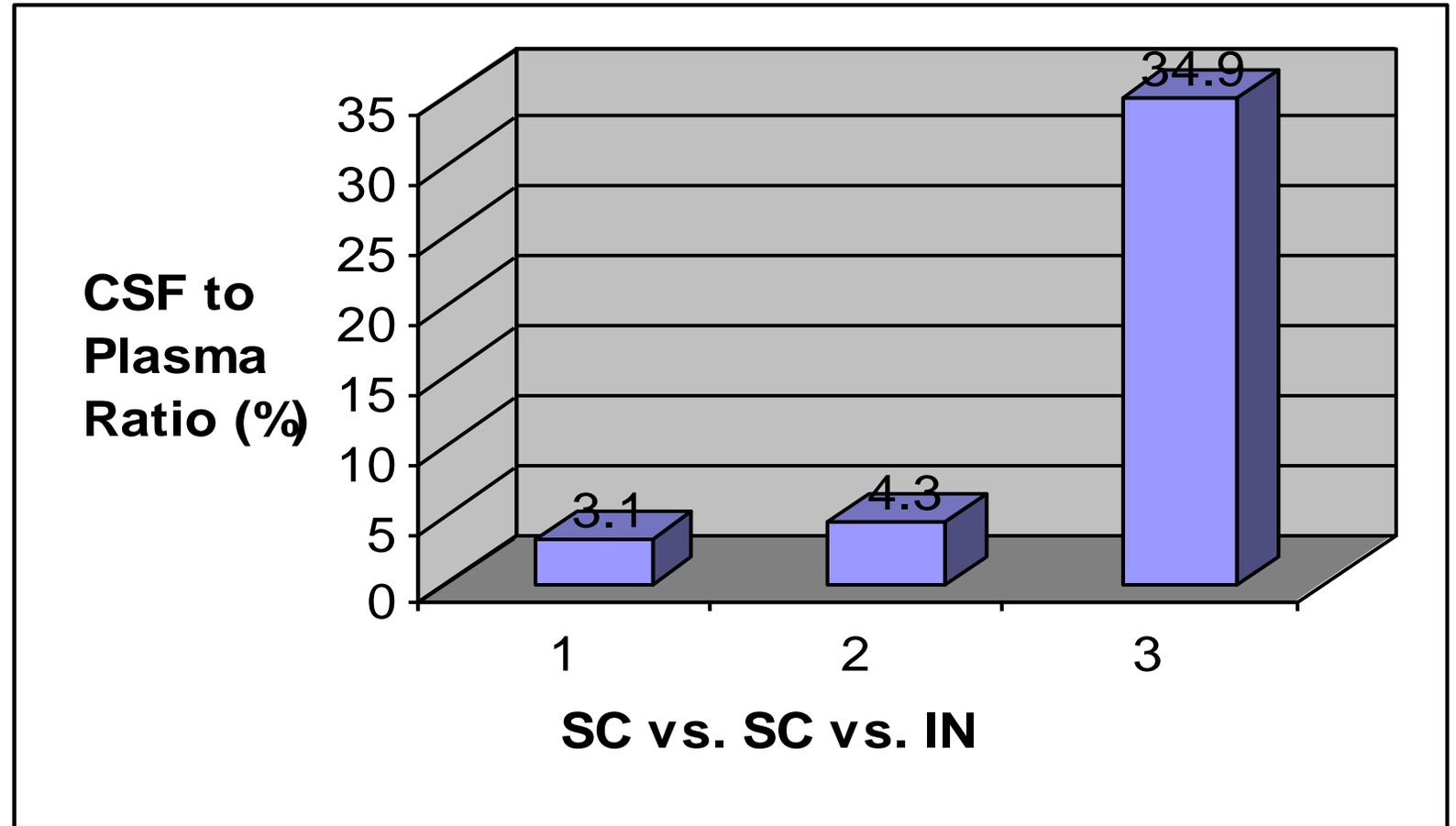
# Pharmacokinetic Comparison

- IN AL-101 is absorbed and delivered faster: sublingual (SL) tablet dissolution itself is time-limiting
- IN AL-101 is more efficient: IN higher  $C_{max}$  is related to rapid uptake and good absorption; IN lower drug exposure defined by AUC is related to total absorption
- IN AL-101 is less variable: "Safety may be difficult to predict (for SL formulation) based on dose due to variability in  $C_{max}$ "
- The bioavailability of apomorphine from sublingual tablets, relative to subcutaneous administration, is approximately 17 – 18 %.



# CSF Uptake Via IN AL-101 versus Subcutaneous

- The subcutaneous formulation produced 2.5-4.3% levels in the CSF compared to plasma
- The IN formulation produces 26.7-44.1% levels in the CSF relative to plasma
- The IN formulation provides CSF levels that are 10X higher than subcutaneous formulation



# Conclusions

- IN Apomorphine has a clear 505(b)2 regulatory pathway to approval.
- SL Apomorphine is safe and effective in Parkinson
  - Global approval – Opens the way for a successful 505(b)2 pathway based on Sunovion
- IN Apomorphine is safe and effective in ED
  - EU- Uprima. Superior to Viagra when combined
- IN Apomorphine shown in phase 2 trial to be effective in FSD
  - NCE- no 505(b)2 pathway. Limited competition. High market potential
- IN Apomorphine is effectiveness at 1/4th the SL dose, without any major side effects
- IM Apomorphine provides CSF levels that are four (4) standard deviations higher than subcutaneous formulation
- No Hypotension observed among over 200 patients treated
- **A strong drug candidate to anchor Oncotelic once the oncology/virology program is fully funded by the JV**
  - **Oncotelic- CNS/Oncotelic. IN AL-101 fast to market strategy via fast to market 505(b)2 pathway**
  - JV - Oncology/Infectious disease/Oncotelic/GMP. OT-101/CA4P/Oxi4503

# ED- market potential

- ED is the most prevalent male sexual disorder globally. The market will continue to grow due to increased vascular disorders followed by the aging population across the world. Furthermore, rising psychological problems, followed by chronic diseases like diabetes, alcohol, and smoking habits are also considered as one of the major driving factors for the growth of the market.
- Oral therapies, especially Viagra, Cialis, and Levitra, dominated the market with around USD **3.8 billion revenue in 2020**. All the three flagship oral ED therapies will lose patent protection during the forecast period, thereby providing space for the entry of low-cost generics.
- AL-101 (Apomorphine) has the potential to capture this market, if shown superior to Viagra in combination therapy. Niche marketplace can be established as drug of choice of failed failure ED treatment.
- The synergistic combination of heighten desire/libido with AL-101 and erection with PDE5 inhibitors was observed in ED patients: patient preference was 88.4% for the combination and 4.6% for sildenafil.
- VALUE IN HEALTH 15 (2012) A1 - A256/ IS SILDENAFIL - APOMORPHINE SUBLINGUAL COMBINATION SIGNIFICANTLY MORE EFFECTIVE THAN SUBLINGUAL SILDENAFIL IN TREATING ERECTILE DYSFUNCTION? Solayman MH, Badary OA, Salem KA, El-Hamamsy M
- RESULTS: Only 43 patients completed the whole schedule and had results evaluable for efficacy. Sildenafil - apomorphine combination had a significantly higher estimate than sildenafil in regard to the mean percent of attempts resulting in erection firm enough for intercourse (77.6% vs. 63.1%, p 0.001) and resulting in successful intercourse (51.1% vs. 34%, p 0.001), as well as erectile function as evaluated by the change in the median IIEF-5 score from baseline (18 vs. 15 with baseline of 7, P0.001). Also, the proportion of affirmative answers regarding the SEP diary was significantly higher after the combination (question 2: 79.1% vs. 55.8% P0.01 and question 3: 65.1% vs. 44.2%, P0.05). **At the end of the study, patient preference was 88.4% for the combination and 4.6% for sildenafil.**
- <https://www.globenewswire.com/en/news-release/2020/10/30/2117803/0/en/Global-Erectile-Dysfunction-Drugs-Market-Will-Reach-USD-2-687-6-Million-by-2026-Facts-Factors.html>

# FSD / HSDD Market Potential

- In 2012, the FDA identified female sexual dysfunction as one of 20 disease areas of high priority and focused attention. In 2016, the FDA published a draft guidance titled “Low Sexual Interest Desire and/or Arousal in Women: Developing Drugs for Treatment,” to assist companies developing drugs for the treatment of these conditions. The FDA is committed to continuing to work with companies to develop safe and effective treatments for female sexual dysfunction.
- June 21, 2019 /The U.S. Food and Drug Administration approved Vyleesi (bremelanotide) to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. The FDA granted approval of Vyleesi to AMAG Pharmaceuticals.
- “There are women who, for no known reason, have reduced sexual desire that causes marked distress, and who can benefit from safe and effective pharmacologic treatment. Today’s approval provides women with another treatment option for this condition,” said Hylton V. Joffe, M.D., M.M.Sc., director of the Center for Drug Evaluation and Research’s Division of Bone, Reproductive and Urologic Products. “As part of the FDA’s commitment to protect and advance the health of women, we’ll continue to support the development of safe and effective treatments for female sexual dysfunction.”
- HSDD is characterized by low sexual desire that causes marked distress or interpersonal difficulty and is not due to a co-existing medical or psychiatric condition, problems within the relationship or the effects of a medication or other drug substance. Acquired HSDD develops in a patient who previously experienced no problems with sexual desire. Generalized HSDD refers to HSDD that occurs regardless of the type of sexual activity, situation or partner.
- Affects 5.8 million U.S. premenopausal women<sup>3</sup> (1 in 10 premenopausal women)<sup>1,2</sup>. 98% (5.7M) of affected premenopausal women not on therapy. One in 10 premenopausal women have low desire with associated distress.
- 1 Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol.* 2008;112(5):970–978.
- 2 Goldstein I, Kim NN, Clayton AH, et al. Hypoactive sexual desire disorder: International Society for the Study of Women’s Sexual Health (ISSWSH) expert consensus panel review. *Mayo Clin Proc.* 2017;92(1):114-128.

# Female Sexual Dysfunction

- 2004. A Double-Blind Randomized Placebo Control Study Comparing the Objective and Subjective Changes in Female Sexual Response Using Sublingual Apomorphine. SL Apomorphine seemed to produce more subjective and objective changes in the sexual arousal phase of women with orgasmic sexual dysfunction than placebo. Future research is needed to evaluate the place of this drug in the treatment of the female sexual dysfunction.
- 2004. PLACEBO-CONTROLLED STUDY ON EFFICACY AND SAFETY OF DAILY APOMORPHINE SL INTAKE IN PREMENOPAUSAL WOMEN AFFECTED BY HYPOACTIVE SEXUAL DESIRE DISORDER AND SEXUAL AROUSAL DISORDER. daily apomorphine SL may improve the sexual life of women affected by sexual difficulties. Additional studies are needed to define the daily use of apomorphine SL in large subgroups of women on the basis of etiology and the severity of sexual dysfunction.

# Parkinson Market Potential

- Parkinson's disease is a chronic neurodegenerative disease in which dopamine producing cells are lost. It is projected that 1.2 million Americans will be living with PD by 2030<sup>10</sup>. Within the first four to six years after diagnosis, regardless of disease severity, up to 60 percent of people with PD experience OFF episodes.<sup>2</sup>
- The market is expected to rise from \$3.5bn in 2019 to \$11.5bn in 2029. The PD market is highly competitive, featuring many levodopa-combination therapies and adjunctive drug classes that aim to alleviate motor symptoms. The current treatment options are primarily symptomatic, off-patent, and not very effective in controlling the motor fluctuations that occur in advanced-stage patients. <sup>4</sup>
- Kynmobi is expected generate revenues of upto \$219M annually. <sup>3</sup>
- 1 Parkinson's Disease Foundation Website: <https://www.parkinson.org/about-us/Press-Room/Press-Releases/New-Study-Shows-Over-1-Million-People-in-the-United-States-Estimated-to-be-Living-with-Parkinsons-Disease-by-2030>. Accessed May 2020.
- 2 Schrag, A. "Dyskinesias and motor fluctuations in Parkinson's disease: A community-based study." Brain. November 2000, Vol. 123, Issue 11. p. 2297-2305. Available online: <https://academic.oup.com/brain/article/123/11/2297/256050>. Accessed May 2020.
- 3 <https://store.globaldata.com/report/gdhc6184ctidb--parkinsons-disease-global-clinical-trials-review-h1-2020/>
- 4. <https://www.globaldata.com/parkinsons-disease-market-reach-11-5bn-2029-7mm-driven-novel-pipeline-agents-says-globaldata/>

# Comparable deals

- Female Sexual Dysfunction/ 2017: AMAG and Palatin Technologies/ Bremelanotide/ \$60 million of total upfront consideration, up to \$80 million contingent upon achieving certain regulatory milestones and up to \$300 million contingent upon meeting certain sales milestones.
- Male Erectile Dysfunction/ 2013 : Auxilium and Vivus/ Avanafil/ Auxilium will pay Vivus a one-time license fee of \$30 million. If the Food and Drug Administration approves a change to the drug's label to reflect an onset of the drug's effecting 15 minutes or less, Auxilium will pay a \$15 million milestone payment, as well as royalties and up to \$255 million in potential milestone payments based on various sales goals.
- Parkinson Disease/ 2021: Ipsen is paying IRLAB an upfront cash payment of \$28 million and up to \$335 million in development, regulatory and commercial milestones. IRLAB will also be eligible for low double-digit royalties on global net sales of the drug.
- AMAG Pharmaceuticals and Palatin Technologies Enter Into Exclusive Licensing Agreement for North American Rights to Rekynda™ (bremelanotide), a Potential Treatment for a Common Female Sexual Disorder January 9, 2017 | AMAG Pharmaceuticals, Inc. (Nasdaq:AMAG) together with Palatin Technologies, Inc. (NYSE MKT:PTN) today announced they have entered into an agreement for exclusive North American rights to develop and commercialize Rekynda™ (bremelanotide), an investigational product designed for on-demand treatment of hypoactive sexual desire disorder (HSDD) in pre-menopausal women, that has successfully completed two Phase 3 trials. The anticipated filing date in the U.S. for a NDA for Rekynda is in early 2018, with an anticipated approval and launch by early 2019. <https://www.amagpharma.com/news/amag-pharmaceuticals-and-palatin-technologies-enter-into-exclusive-licensing-agreement-for-north-american-rights-to-rekynda-bremelanotide-a-potential-treatment-for-a-common-female-sexual-d/>
- 10/11/2013/ Auxilium, Vivus in deal worth up to \$300 million for erectile dysfunction drug. CHESTERBROOK, Pa. — Auxilium Pharmaceuticals will have exclusive rights to market a drug for erectile dysfunction in the United States and Canada, under a new licensing agreement with the drug's manufacturer. Auxilium announced the deal with Vivus for Stendra (avail). <https://drugstorenews.com/pharmacy/auxilium-vivus-deal-worth-300-million-erectile-dysfunction-drug>
- Ipsen Bets \$363 Million on IRLAB's Phase II Parkinson's Drug/ Published: Jul 16, 2021 / Paris-based Ipsen inked a licensing deal with Sweden's IRLAB for mesdopetam, a possible drug for Parkinson's disease. The drug, a novel dopamine D3-receptor antagonist, is being evaluated in Phase IIb trials for people with Parkinson's disease who experience levodopa-induced dyskinesia (LID). The drug is also in early development for Parkinson's Disease Psychosis (PDP).
- The comparable deals above are only for indicative purposes. The Company cannot guarantee that IN Apomorphine would be able to obtain similar deals.

# Deal Structure

- Considering a recent deal for FSD, which has \$28M in upfront in cash and \$335M in milestone payments, the payments proposed below are back-end loaded and highly favorable to Oncotelic.
  - No upfront payments
  - \$1M on \$20M raise or uplisting to a National Stock Exchange.
  - \$9M aggregate on regulatory milestones, assuming the Company will raise further funding to develop each indication
    - \$4M - \$2M each for PD/ED
    - \$5M for FSD
  - \$40M on sales and marketing milestones
    - These milestones assume revenue from the sales and marketing / and or out-licensing, so limited cash burn to the company.
    - \$10M each for PD, ED and FSD marketing approvals
    - \$10M for sales/licensing milestone
    - Royalties of 15%
  - If out-licensed, will generate milestone payments and royalties.