

ONCOTELIC  
MATEON THERAPEUTICS

A TGF-beta Company

July 14, 2021

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# 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.

# Management Team

- Vuong Trieu, PhD (CEO). Dr. Trieu, an expert in pharmaceutical development, currently serves as CEO/Chairman of Oncotelic Inc.. Previously he was President and CEO of Igdrasol- developer of 2nd generation Abraxane. When Igdrasol merged with Sorrento Therapeutics, he became CSO and Board Director.
- Seymour Fein, MD (CMO). Dr. Fein has been extensively involved in the successful development of numerous drugs, biologics and medical devices over this time leading to FDA approvals for over 20 drugs (NDAs, sNDAs, BLAs) and devices (PMAs).
- Amit Shah (CFO). Mr. Shaha has served as a senior financial officer for a number of life science companies, including Chief Financial Officer at Marina Biotech, Inc., a publicly traded biotechnology company (2017 to 2018)
- Saran Saund (CBO). Mr. Saund is has been founder, CEO and GM at startups and public companies. His track record includes senior leadership roles at companies that were acquired by leaders such as Marvell (MRVL) and Qualcomm (QCOM). His startup Cybercash (CYCH) had a successful IPO on NASDAQ.
- Anthony E. Maida III, PhD (CCO). Dr. Maida, an expert in immuno-oncology, currently serves as Senior Vice President – Clinical Research at Northwest Biotherapeutics, Inc. Prior to joining Northwest Dr. Maida served as Vice President, Clinical Research and General Manager, Oncology, World-wide at PharmaNet, Inc.

# Overview of Oncotelic Therapeutics

JV:

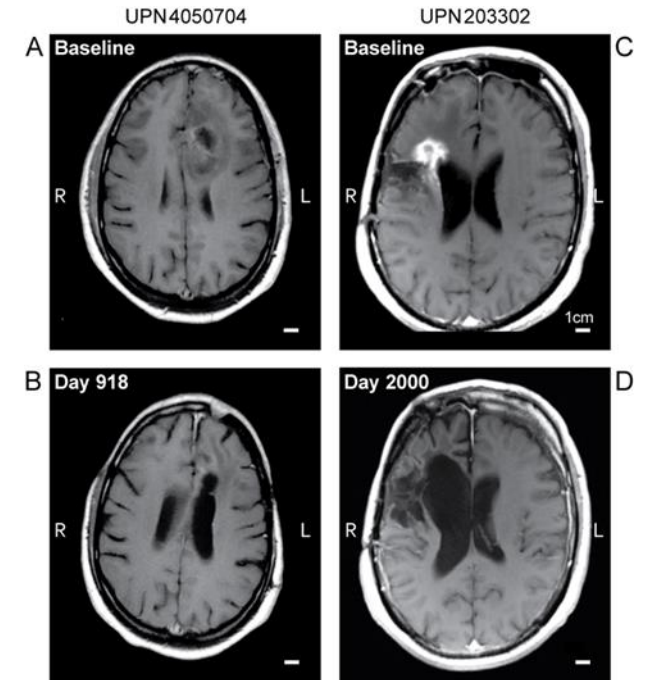
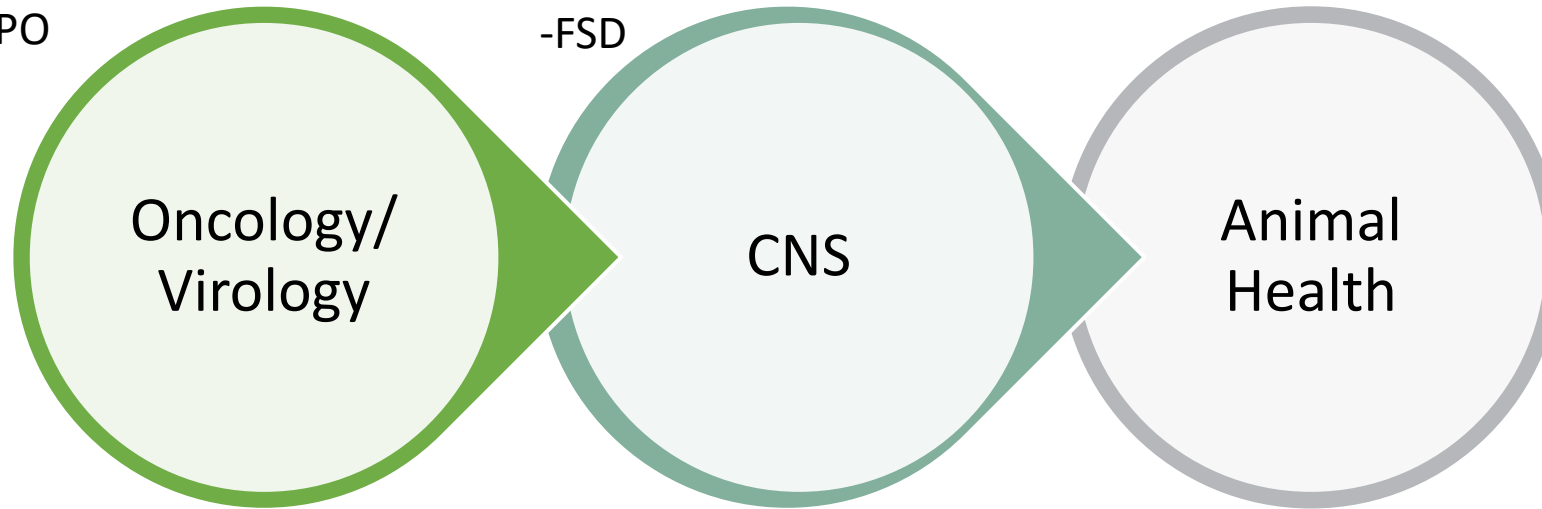
- TGF-beta inhibitors (OT-101 and Artemisinin)
- Oncology & Virology
- HK IPO

Apomorphine

- 505(b)2 Fast to market
- Parkinson Disease
- ED
- FSD

Animal Health

- Oncology
- CA4P
- Artemisinin



**ONCOLOGY**  
**& COVID-19**



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OT-101/ Trabectedin

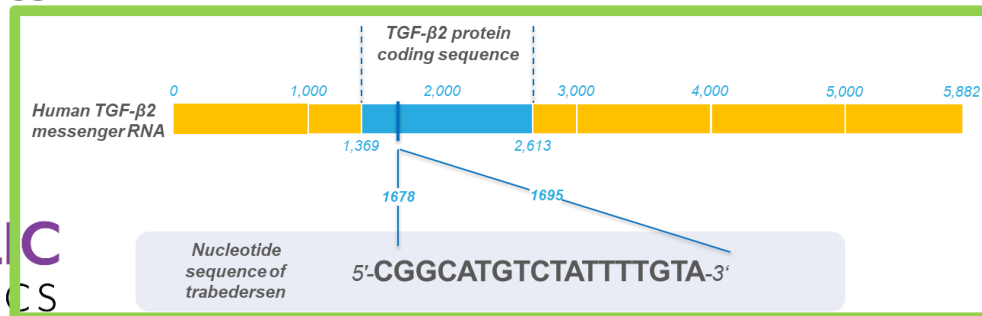
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# Antisense as Next Generation Drugs

Attributes	Small Molecules	mAb	Antisense
Inception	1850s to present	1920s to present	<b>1990s to present</b>
Size	200-500	>150,000	<b>5,000 to 7,000</b>
Drug Discovery	Random screening	Focused screening	<b>Rationally designed</b>
Success Rate	Low-~5%	Moderate-~50%	<b>High-~90%</b>
Predictable PK	No	Yes	<b>Yes</b>
On Target Safety	Target Specific	Target Specific	<b>Target Specific</b>
Off Target Safety	Nonspecific Targets	Cross Reactivities	<b>Sequence Homology</b>
Risk Profile	High >50%	Moderate =< 40%	<b>Low ~1%</b>
Speed of Development	15-20 years	10-15 years	<b>1-5 yrs</b>
Manufacturing Cost	Low	High	<b>Low</b>
Amenable to Individual Therapy	No	No	<b>Yes</b>

# OT-101: Drug Product- TGF- $\beta$ 2 Antisense.

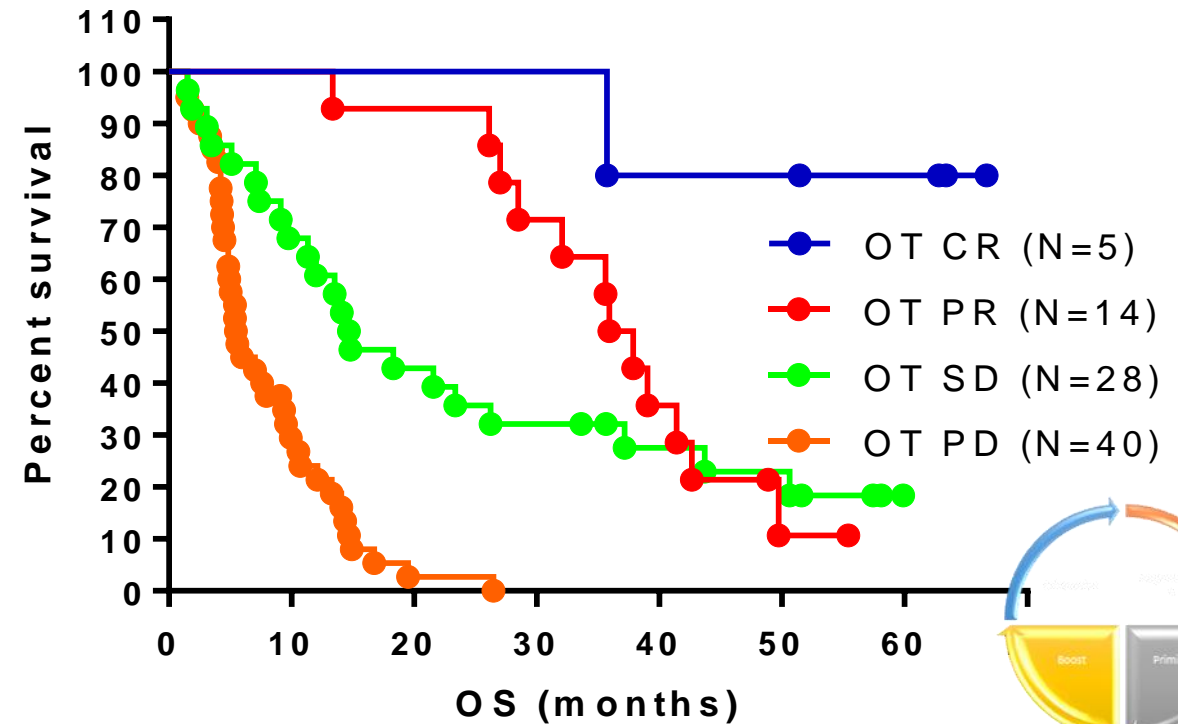
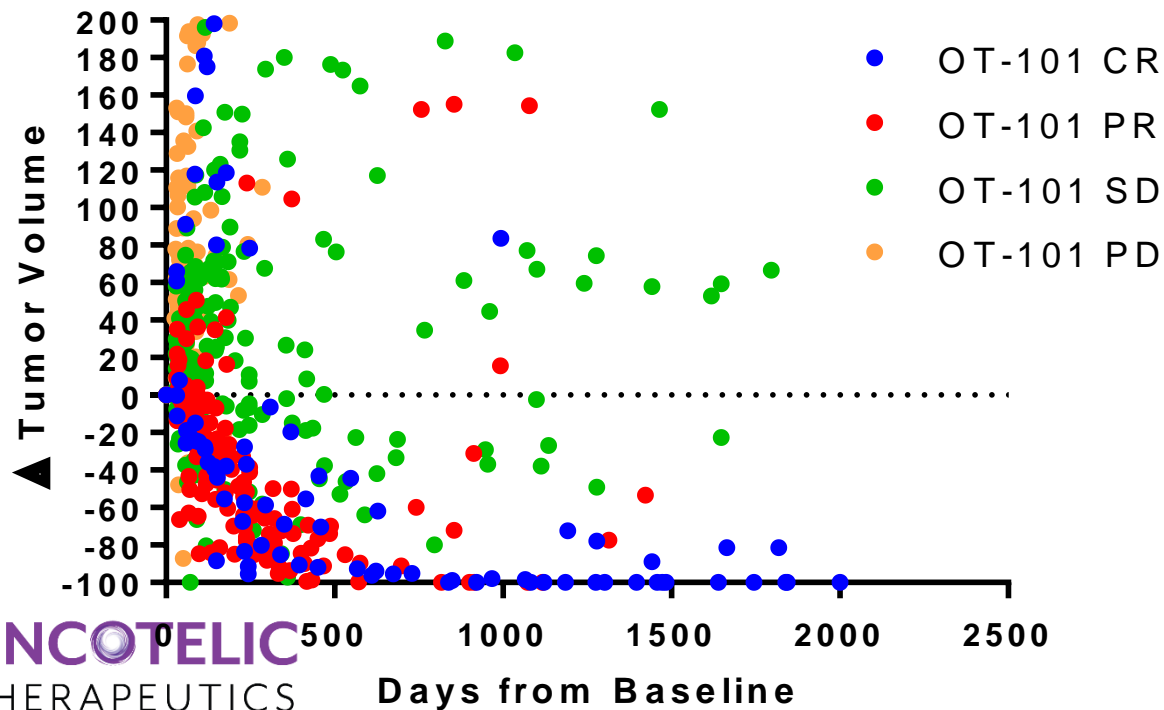
- Trabedersen (OT-101) is a single-stranded phosphorothioate antisense oligodeoxynucleotide (18-mer) targeting the human TGF- $\beta$ 2 messenger RNA
- Ready for registration trials--Over 200 patients treated across 6 clinical trials
- Strong Patent protection until 2037
- Orphan designation granted for three tumor indications in US & EU/ Rare Pediatric Designation in the US.
- Manufacturing process optimized and scaled up sufficient drug to treat over >5,000 patients
- **Clinical efficacy demonstrated in treatment failure patients- glioblastoma, pancreatic, melanoma**
- **Expected to improve tumor response to Keytruda and revenue to match that of Keytruda**
- The widespread interest in TGF-beta reflects the commercial opportunity for drugs that enable more people to respond to checkpoint inhibitors and evidence that the protein may be the key to unlocking those sales. In 2017, Roche shared bladder cancer data showing non-responders to its checkpoint inhibitor, Tecentriq, had high levels of TGF-beta. Roche followed up on that finding by linking the inhibition of TGF-beta in mice to increased Tecentriq efficacy. Since then data have been consistent that inhibition of TGF-beta would enhance immune checkpoint therapies



# Clinical Efficacy: Glioblastoma

Treatment failure patients (recalcitrant to radiation, surgery, and chemo)

- Objective responses were observed among the 87 evaluable patients treated with OT-101:
- Best Objective Responses were: 5 CR (5.9%), 14 PR (16.5%), 28 SD (31.8%), and 40 PD (45.9%)
- Confirmed Best Objective Responses were: 4 CR (4.7%), 12 PR (12.9%), 31 SD (36.5%), and 40 PD (45.9%)
- Best Objective Responses were confirmed with deeper tumor reduction.
- Best Objective Responses were confirmed with improved OS: CR: >66mos, PR: 36.9 mos, SD: 14.7 mos, and PD: 5.5mos.





# Clinical Efficacy: Pancreatic Cancer

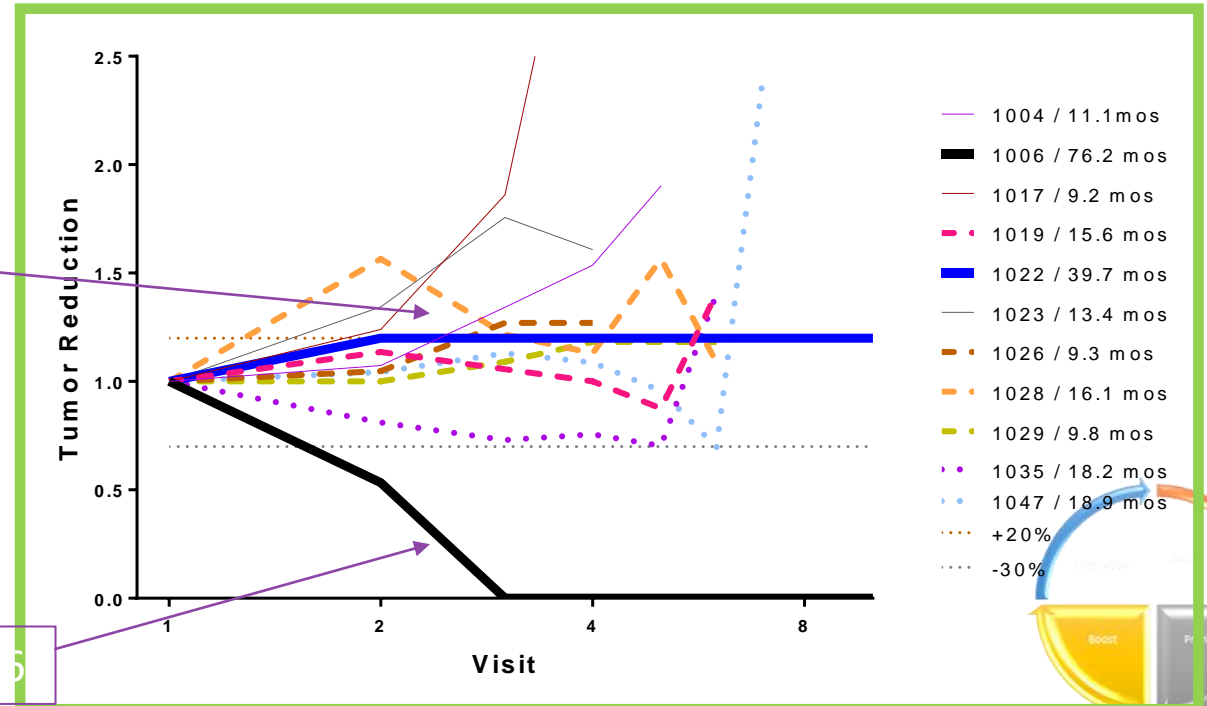
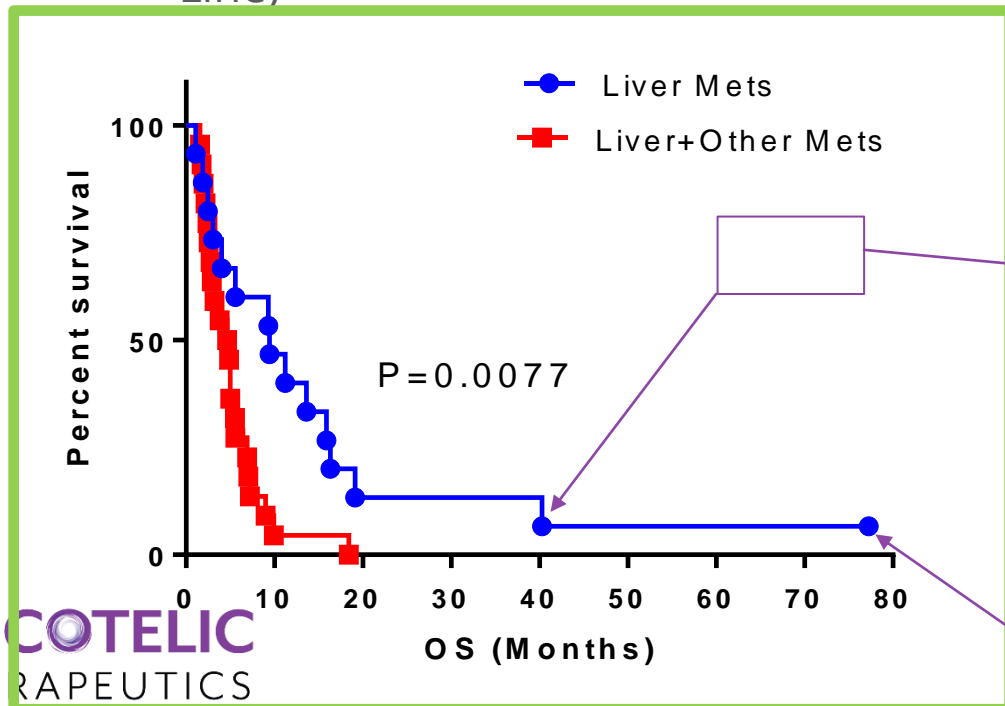
Phase 2- treatment failure pts/ recalcitrant to Whipple and chemo

- **Patient 1006: CR as far out as 77 mos**

- Surgery: Whipple's procedure
- 1<sup>st</sup> line: 5-FU/LV, Dose 425 mg/m<sup>2</sup>
- 2<sup>nd</sup> line: 5-FU/LV, Dose 2600 mg/m<sup>2</sup>/24hr
- 3<sup>rd</sup> line: Gemcitabine, Dose 1000 mg/m<sup>2</sup>/week
- OT-101- Liver mets/ Complete Response (Black Line)

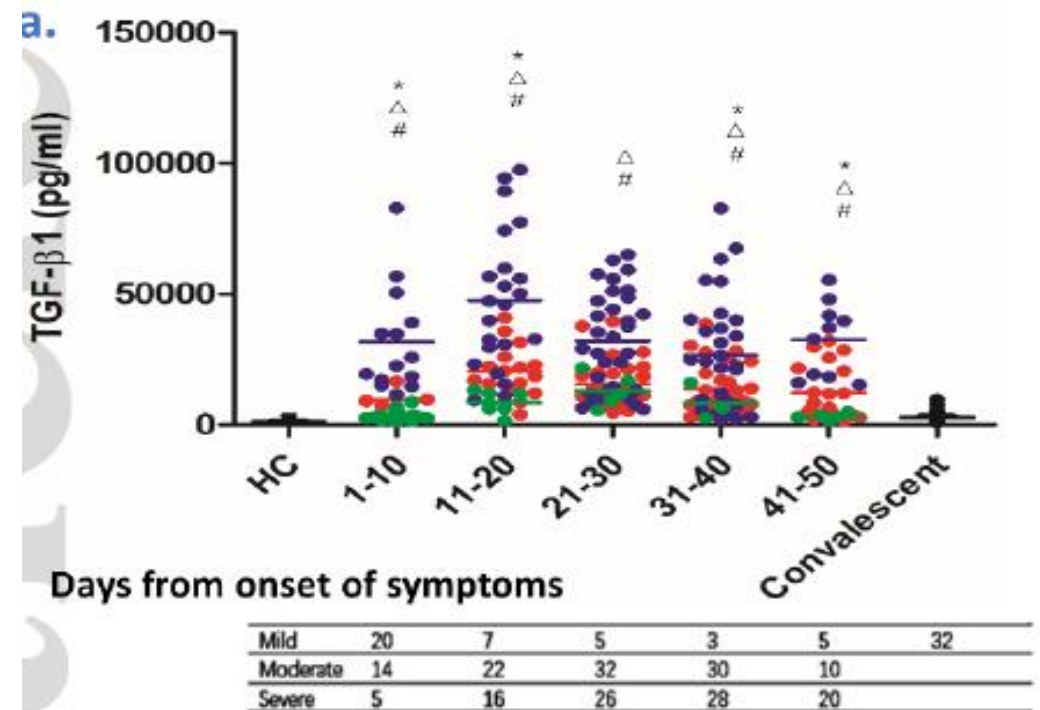
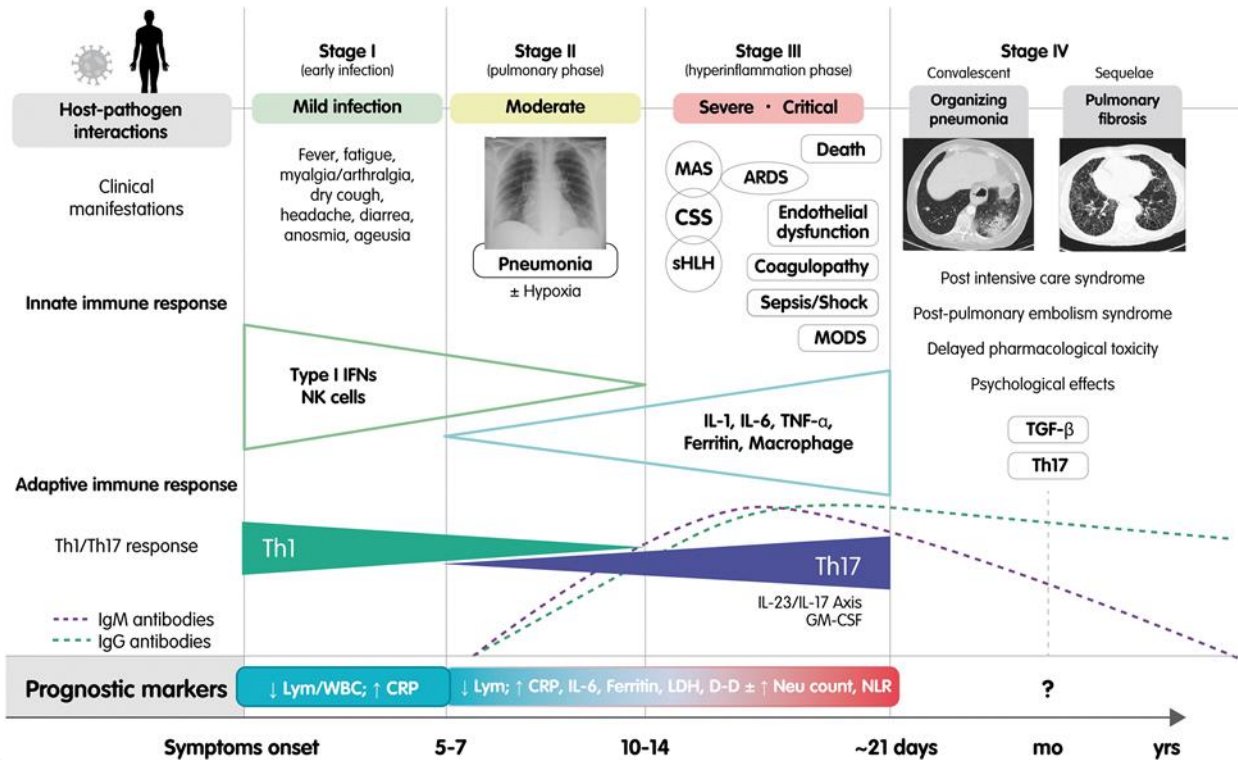
- **Patient 1022: OS of 40 months**

- Surgery: Whipple's procedure
- 1<sup>st</sup> line: Radiation therapy (50 Gy)
- 2<sup>nd</sup> line: 5FU
- OT-101- Liver Mets/ Stable Disease (Blue Line)



# Clinical Efficacy: COVID

- Large surge in TGF-beta during active COVID infection
- An established role of TGF-beta in scarring and late stage post-COVID symptoms
- Strong in vitro activity against SARS-COV-2 on Vero cells
- OT-101 is in phase 2 clinical trial against COVID



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# Vascular Disruptor Agent (VDA)

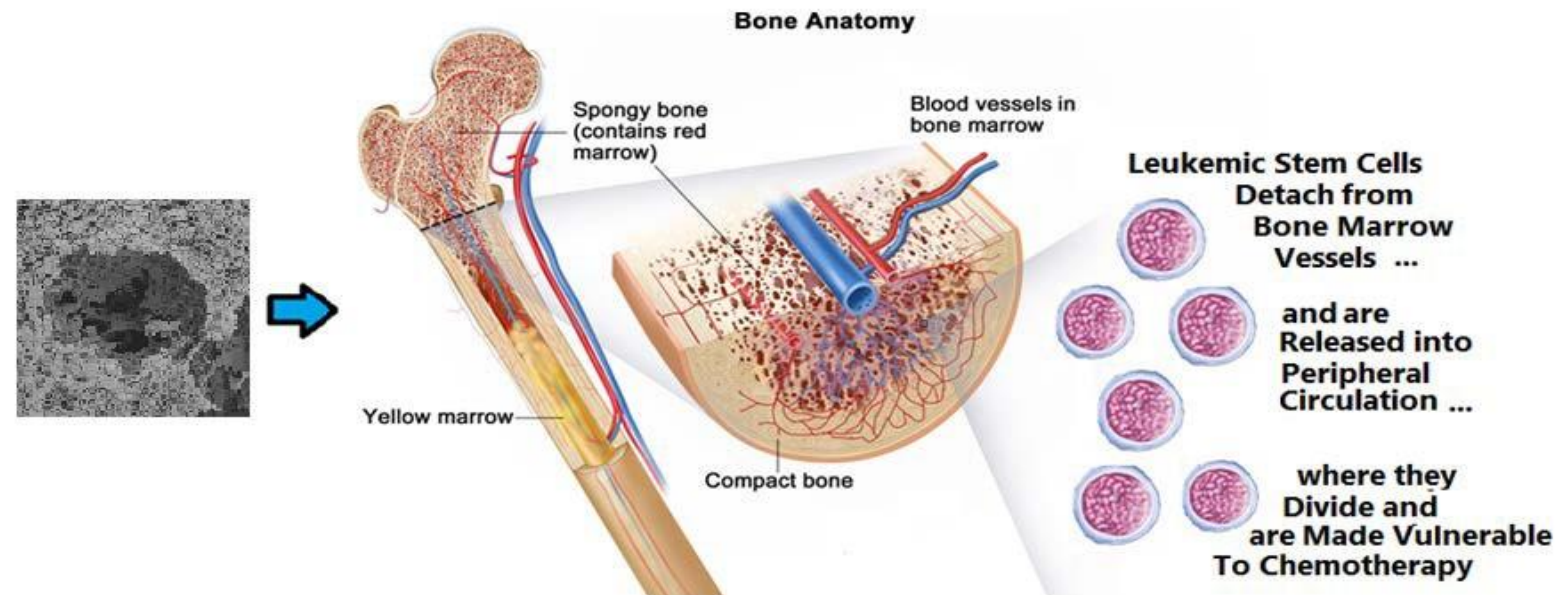
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# OXi4503: Mechanism-of-Action in AML

- Phase 1B study was to define the maximum tolerated dose and safety profile of OXi4503 and cytarabine administered in combination (OXA) in patients with relapsed/refractory AML.
- The study was completed in August 2019 and met its primary endpoint.
- The study showed that adding OXi4503 to the standard chemotherapy drug cytarabine was generally well tolerated by AML patients and a maximum tolerated dose level of OXi4503 was identified
- In 26 evaluable AML patients, there were 4 complete remissions (CR/CRi) and one partial remission (PR). The CR responses were associated with >1-year overall survival times.
- Rare Pediatric Disease designation for AML

**Rapid tumor necrosis releases dividing and chemotherapy-vulnerable leukemic stem cells into the periphery**

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# OX4503: Completed Cohort Results to Date

## Complete Remissions and Dose Response

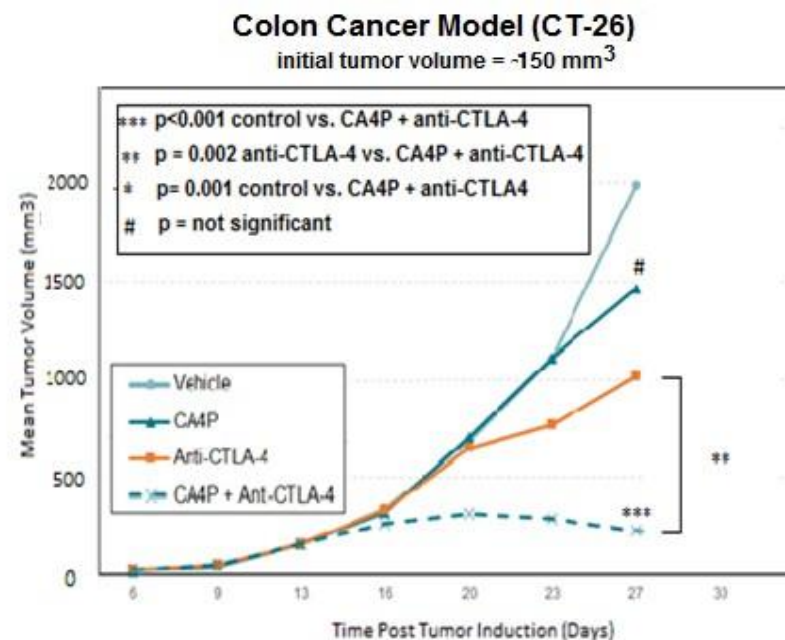
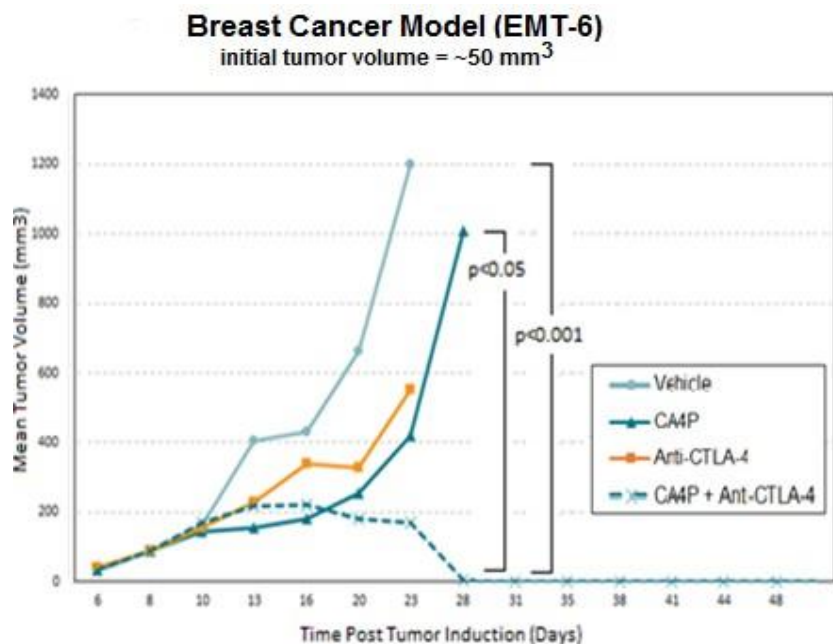
Clinical trial has shown initial evidence of efficacy

Completed Cohort (Dose)	n	CR%	PR Rate	ORR
Cohort 1 (3.75 mg/m <sup>2</sup> )	6	17%	0%	17%
Cohort 2 (4.68 mg/m <sup>2</sup> )	4	25%	0%	25%
Cohort 3 (6.25 mg/m <sup>2</sup> )	4	25%	25%	50%
Cohort 4 (7.81 mg/m <sup>2</sup> )	3	0%	33%	33%
Cohort 5 (9.76 mg/m <sup>2</sup> )	4	50%	0%	50%



# CA4P: Significant Tumor Regressions and Improved Overall Survival

- Stable Disease (SD) of 5 melanoma pts treated with CA4P Single Agent Phase 1 studies
- Partial Response (PR) was observed of 6 melanoma patients treated follow progressing during first-line trial therapy with dacarbazine and sorafenib
- Durable tumor regression in animal models when used in combination with checkpoint inhibitors
- Rare Pediatric Disease application for melanoma been submitted with favorable responses from FDA



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# OT-101 and Artemisinin/ COVID

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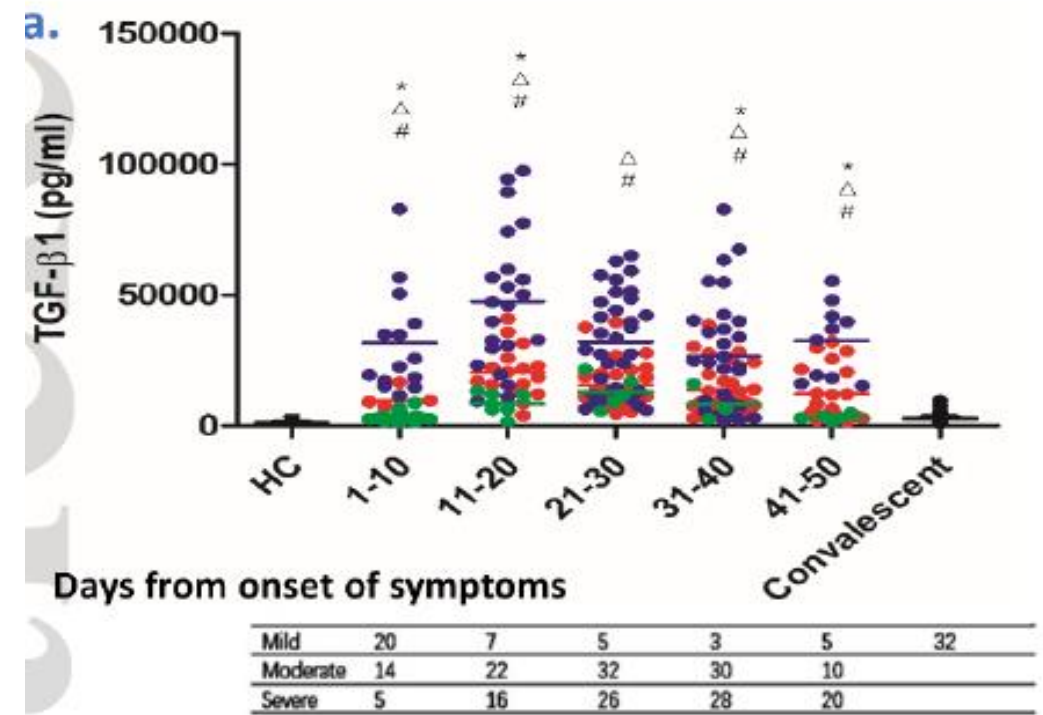
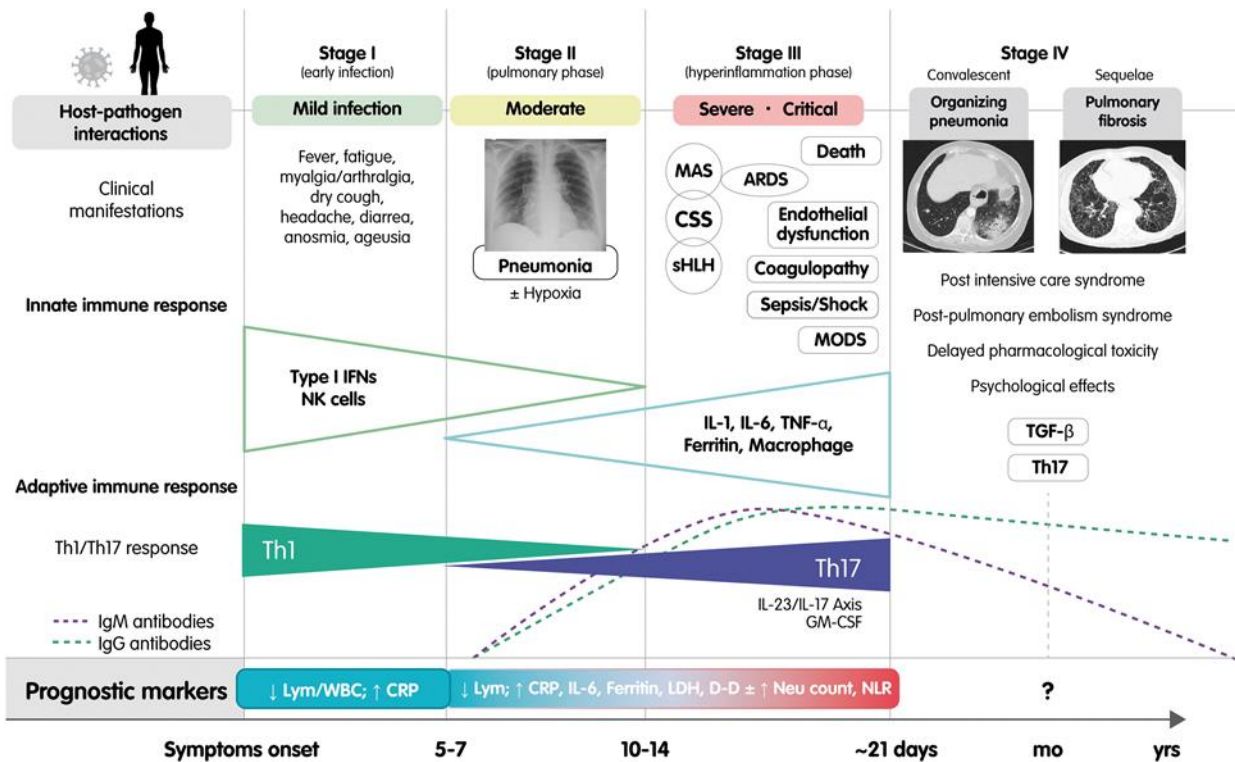
# Conventional COVID-19 Therapeutics

Drug Name	Mechanism/ Target	Outcome	Trial Name/N
Lopinavir	Antiviral/ Protease Inhibitor	Fail	WHO SOLIDARITY/ 1411 UK RECOVERY/ 1616
Hydroxychloroquine	Antiviral/ Antimalarial/ TRL	Fail	WHO SOLIDARITY/ 954 UK RECOVERY/ 790
Remdesivir	Antiviral/ RNA Polymerase	Fail	WHO SOLIDARITY/ 2750
Interferon	Antiviral/ Immune Activation	Fail	WHO SOLIDARITY/ 2063
Kevzara® (sarilumab)	mAb against IL-6 receptor	Fail	Sanofi Phase 3/ 420 Total
Actemra (tocilizumab)	mAb against IL-6 receptor	Fail	COVACTA/ 450 Total
laris® (canakinumab)	mAb against IL-1 $\beta$	Fail	CAN-COVID/ 454 Total
Jakavi® (ruxolitinib)	oral inhibitor of the JAK 1 and JAK 2	Fail	RUXCOVID/432 Total
Bamlanivimab/ LY-CoV555	anti-SARS-CoV-2 mAb (Spike Protein)	Fail	BLAZE-2/ 350 Total
Convalescent plasma	Anti-SARS-CoV-2 antibodies	Fail	India PLACID/ 464 Total
Azithromycin	Antibiotics	Fail	RECOVERY/2582 COALITION II/447 Total
Ivermectin	Anti-Viral/ Viral translocation to nucleus	Fail	JAMA 2021/ 400 Total
Artemisinin/ ARTIVeda/PulmoHeal	Anti- TGF-beta	Success	ARTI-19/ 120 Total
<b><u>Dexamethasone</u></b>	<b><u>Anti-Inflammatory</u></b>	<b><u>Success</u></b>	<b><u>RECOVERY/ 2104</u></b>

**Large WHO SOLIDARITY Trial and UK RECOVERY Trial – only DEXAMETHASONE was effective – but only for severe COVID**

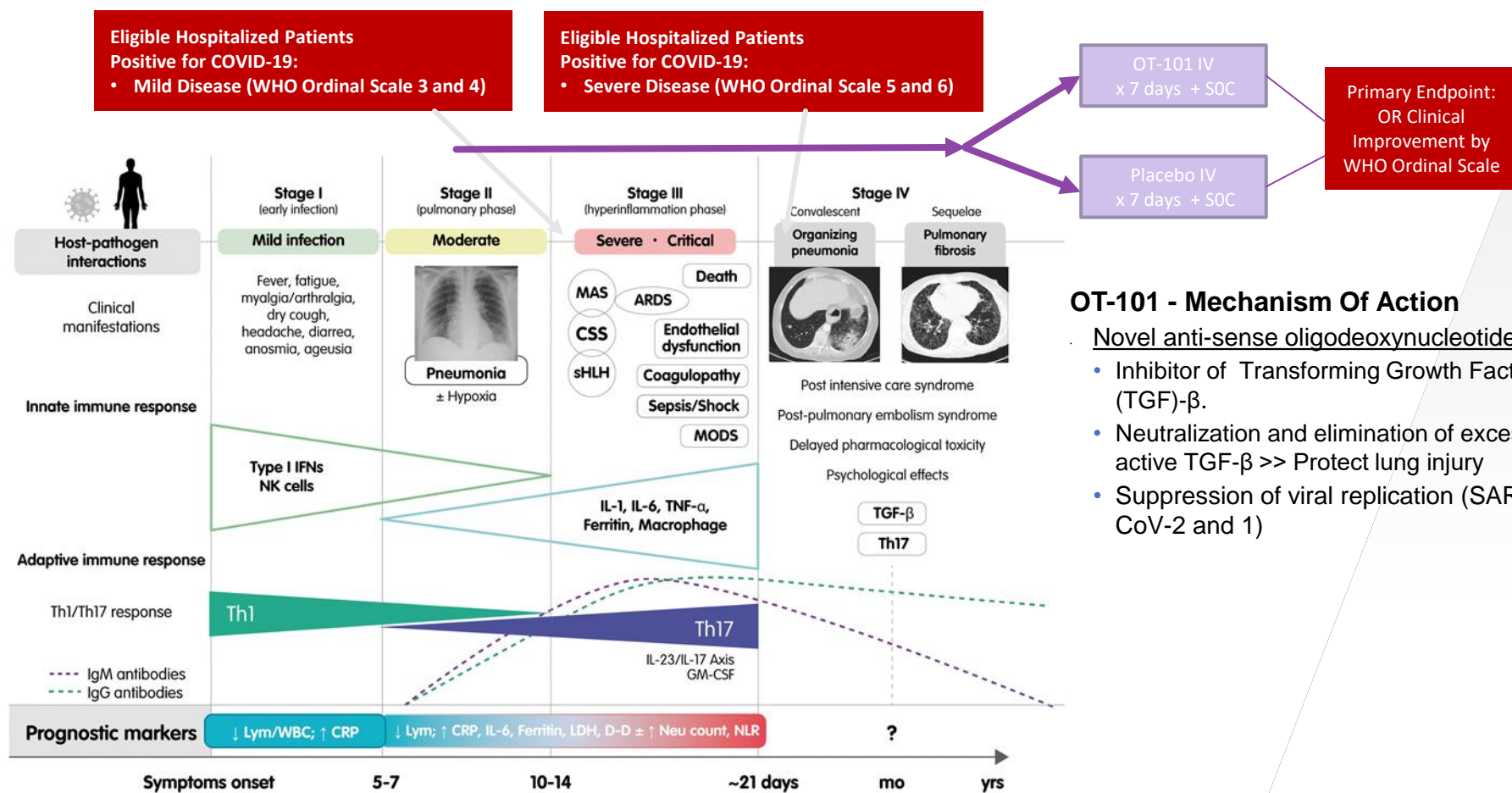
# TGF-beta is the right target for COVID-19

- Large surge in TGF-beta during active COVID infection
- An established role of TGF-beta in scarring and late stage post-COVID symptoms





# COVID-19 CLINICAL COURSE AFTER SARS-COV-2 INFECTION AND THE OT-101 TRIAL



## OT-101 - Mechanism Of Action

### Novel anti-sense oligodeoxynucleotide

- Inhibitor of Transforming Growth Factor (TGF)-β.
- Neutralization and elimination of excess active TGF-β >> Protect lung injury
- Suppression of viral replication (SARS-CoV-2 and 1)



# India ARTI-19 Protocol

- **Patients with mild/ moderate COVID without oxygen support**
- **Compatible with: Seven Star Hospital COVID protocol:** Remdesivir/Sompraz D/Zifi CV/Zac D/CCM/Broclear/Budamate/Rapitus/Montek LC/ lower molecular weight heparin/**prednisolone/Doxycycline**
- **Compatible with Raje Hospital COVID Protocol: Paracetamol/B.complex/Vitamin-C/Pantoprazole/Doxycycline/Ivermectin/Zinc/Foracort - Rotacaps inhalation**
- **Compatible with Government General Hospital COVID Protocol:** Inj. Ceftriaxone/**Tab Paracetamol**/Inj. Fragmi/Tab Covifor/Azithromycin/**pantoprazole/Inj. Dexamethasone**/Inj. Odndansetron/Tab Multivitamin /**Tab Ascorbic Acid**/Tab Calcium Carbonate/**Tab Zinc Sulfate**
- Prashant V. Rahate- Seven Star Hospital, Nagpur, Maharashtra, India
- Viljay B. Barge- Government Medical College and Chhatrapati Pramila Raje Hospital, Chowk, Kolhapur, Maharashtra, India
- K. Sunil Nalk- Government Medical College and Government General Hospital, Srikakulam, Andhra Pradesh, India

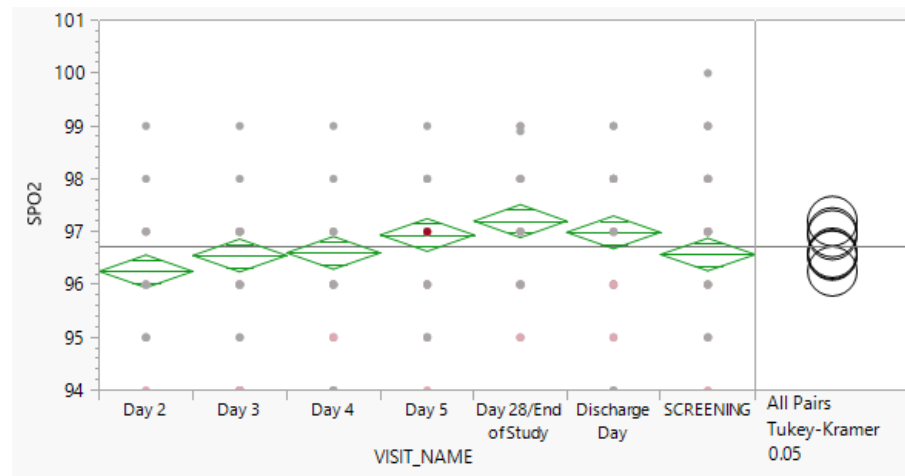
# India Heart Care Foundation Protocol

- According to Dr K K Aggarwal (Heart care foundation)
- COVID treatment
- Code 1 – CONTACT : Ivermectin 12 mg and doxycycline 100 mg daily x 3 days, Betadine or neem gargles, Vitamins and minerals, Colchine 0.5 mg one daily for 21 days if CRP > 1. High protein diet, adequate fluids and sleep.
- Quarantine children's < 12 no treatment. Precautions first 5 days and shift to code 2 if symptoms appear.
- Code 2 – MILD COVID: (Loss / altered smell, taste, fever <101 , no falling spo2, no breathing problem, no pneumonia) clinical or confirmed : code 1 + Colchicine + Meftal 500 mg three times daily (10 days) + famotidine 40 mg daily. Add seroflo or budesonide inhaler for three months if cough is present. Shift to code 3 if falls in the category.
- HRCT if cough starts day 3 or it's persistent.
- Code 3 – Severe illness or comorbid or high risk: (Day 1-5 most important: Fever > 101 F , or CRP >10 or rising , or Pneumonia , or falling oxygen on exercise, or breathlessness) : Add to code 1 + 2 : oxygen at home , start steroids prednisolone 1 mg per kg daily or equivalent (methyl prednisolone) dose or dexamethasone 12 mg for 10 days(if not contraindicated) PLUS warf 5 mg daily (or dabigatran 150 mg or rivaroxaban 15 mg or apixaban 5 mg twice daily) for 21 days. **Add pulmoheal one daily (08800893315) if pneumonia.** Persistent breathless or rising CRP inspite of treatment consider admission and repeat HRCT scan for advanced treatment. If initial CT score is > 8/25, fever > 104, breathless, SPO2 <90 better to get admitted, Remdesivir in first 10 days, plasma in 0-7 days and tocilizumab in steroid failure may be considered.
- SOS : vomiting DOM DT/ Loose motion ORS/ constipation lose 30 ml/ Hiccups mucaine gel/ cough zedex, Wet cough pro zedex, low heart rate ignore, high heart rate ivabred 5 mg , High BP 5 mg amlodipine, streaks of blood in sputum ignore. After food sugar may increase, add replaginide 2 mg below tongue before meals.



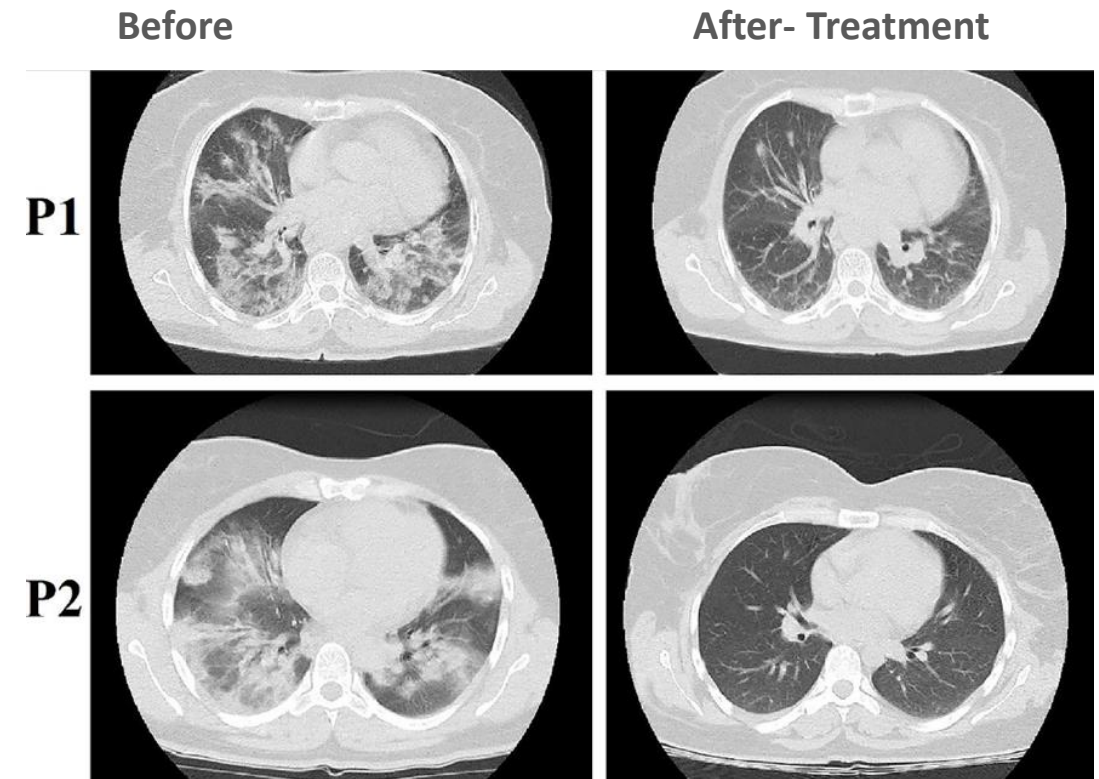
# Outcomes (Primary/ Secondary) of the Study – top line data of 120 pts

- ▶ 500 mg daily for 5 days use cough app to monitor clinical and cough severity. Consult with physician if symptoms persist or if tested positive for COVID. Treatment under physician care = 5 day on / 5 day off for evaluation. Continue up to three cycles.
- ▶ PulmoHeal showed a very favorable safety profile, and the only PulmoHeal-related adverse events were transient mild rash and mild hypertension.
- ▶ PulmoHeal, when added to the SOC, accelerated the recovery of patients with mild-moderate COVID-19 across all COVID-19 symptoms examined including fever, sore throat, dry cough, and ache.
  - ▶ **Almost all of WHO-4 pts achieved a reduction WHO-3 on the first few doses of PulmoHeal,  $p = 0.0043$  ( $n = 56$  /PulmoHeal+SOC vs  $n=25$ /SOC).**
- ▶ All vitals were normalized by the end of the 28 day monitoring period.
  - ▶ **Most importantly,  $O_2$  sat fully recovered by day 28 with PulmoHeal+SOC ( $p < 0.0001$ ) but not with SOC alone ( $p = ns$ ).**
  - ▶ **Similarly, respiratory rate fully recovered by day 28 with PulmoHeal +SOC ( $p < 0.0001$ ) but not with SOC alone ( $ns$ ).**
- ▶ These data provide clinical proof of concept that PulmoHeal restores lung functions due to viral infection. Consistent with its TGF- $\beta$  activity.

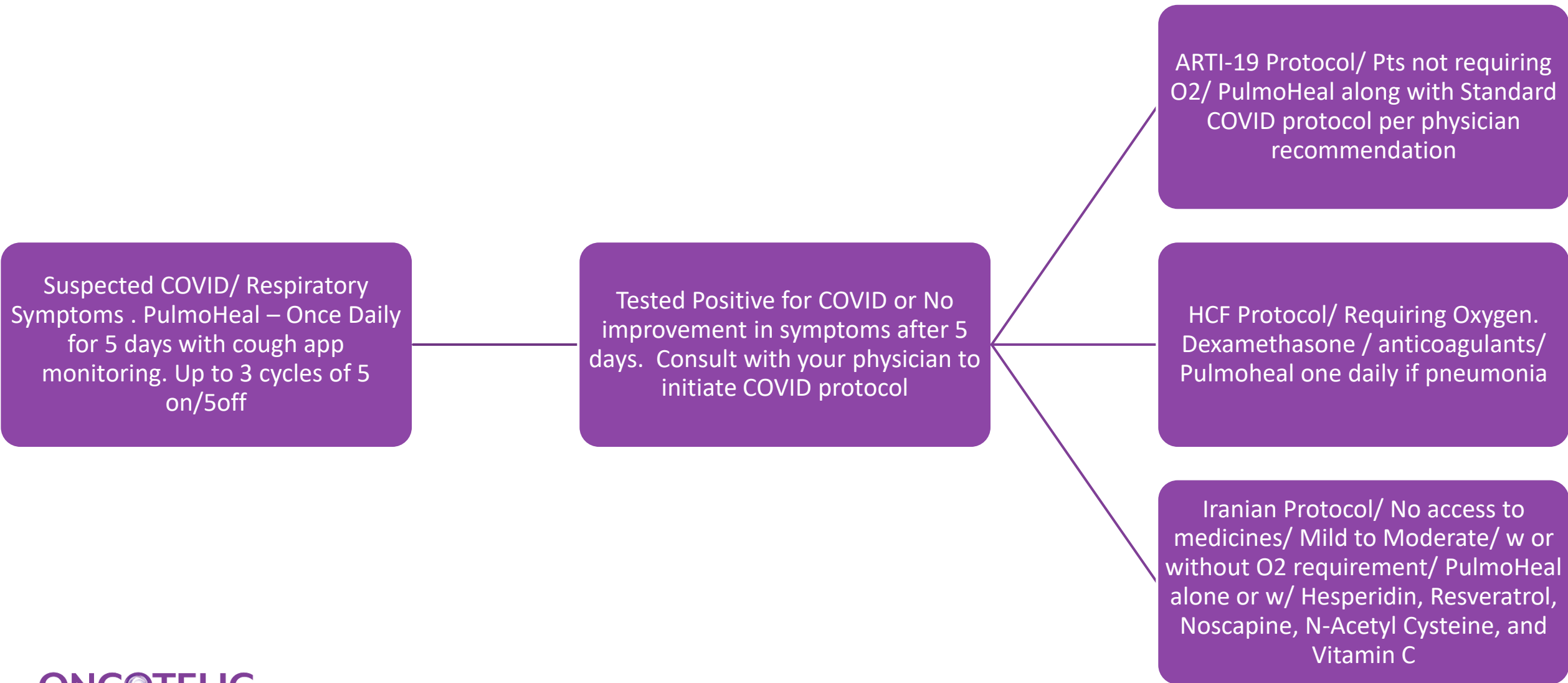


# Iran Iman Reza Hospital Protocol

- Imam Reza Hospital, Sirjan Faculty of Medical Sciences, Iran with the reference number: IR.SIRUMS.REC.1399.033; IRCT registration number: IRCT20181030041504N1
- Intervention: **Artemisinin**, Hesperidin, Resveratrol, Noscipine, N-Acetyl Cysteine, and Vitamin C.
- SOC Arm: Lopinavir/Ritonavir, Azithromycin, Hydroxychloroquine sulfate, and Naproxen;
- Mild: mild clinical symptoms with no pneumonia manifestation on CT (X-ray Computed Tomography) scan imaging;
- Moderate: fever, cough, respiratory symptoms, and pneumonia manifestation on CT imaging. O2
- O2 sat fully recovered with Artemisinin arm but not with SOC arm ( $96.56 \pm 0.82$  vs.  $95.17 \pm 1.20$ ,  $p=0.002$ )
- Treatment Protocol is approved for COVID by Iranian FDA. Over 5000 pts already successfully treated.



# Recommend Treatment Schema







505(b)2/ PD/ED/FSD

9-6-2021

# 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.

# Apomorphine as the anchor for Oncotelic pipeline

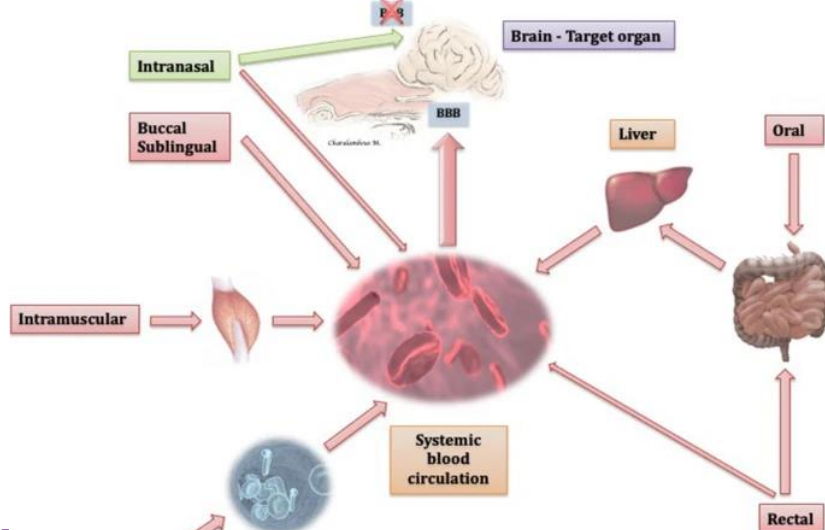
- AL-101- Apomorphine has a clear 505(b)2 regulatory pathway to approval.
- SL Apomorphine is safe and effective in Parkinson
  - Global approval – Opens the way for a successful 505(b)2 pathway based on Sunovion
- AL-101 Apomorphine is safe and effective in ED
  - EU- Uprima. Superior to Viagra when combined
- AL-101 Apomorphine shown in phase 2 trial to be effective in FSD
  - NCE- no 505(b)2 pathway. Limited competition. High market potential
- AL-101 Apomorphine is effectiveness at 1/4th the SL dose, without any major side effects
- AL-101 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

# 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)

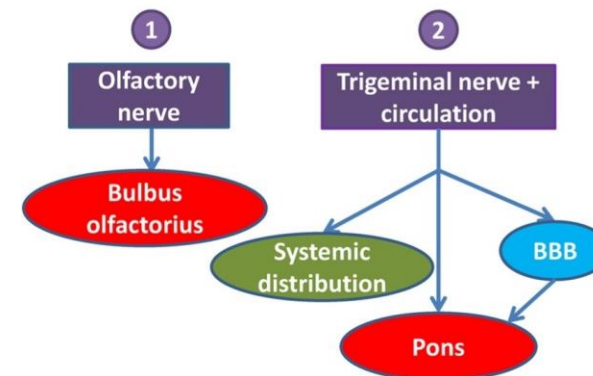
- Unique nasal technology made up of anionic, cationic, & zwitter-ionic compounds capable of stabilizing difficult drug substances and providing rapid systemic absorption at a fraction of the oral dose.
- Intra-nasal (IN) delivery avoids first pass metabolism in the liver.
- IN delivered 10x more drug 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)





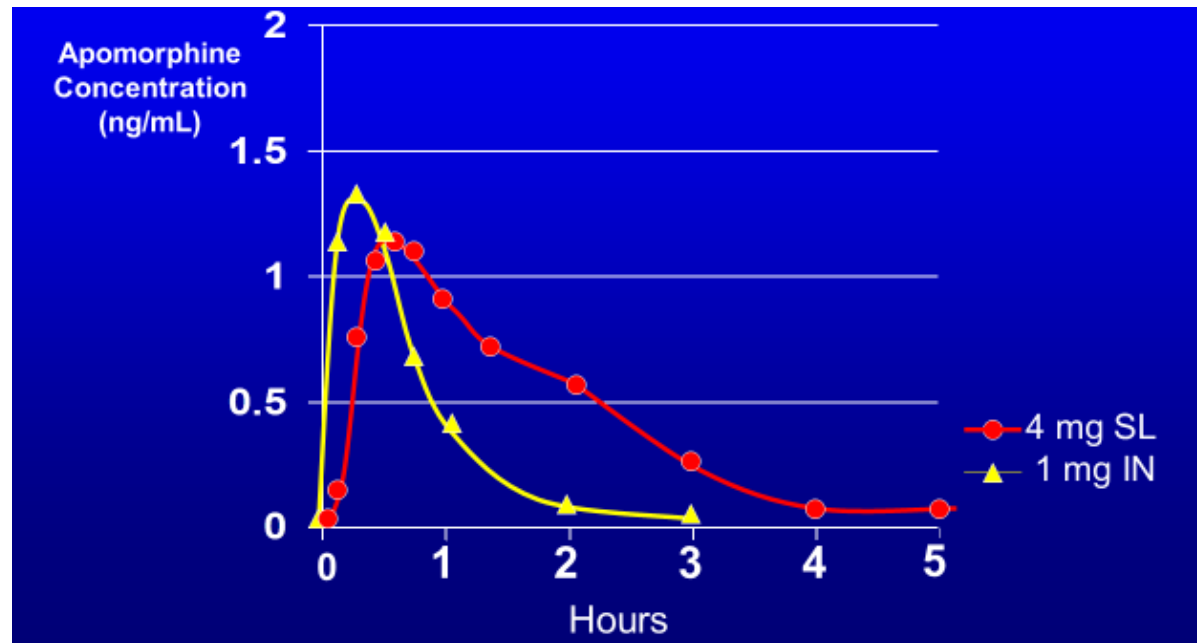
# Overall IN Apomorphine Safety Profile

- 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

- AL-101 is absorbed and delivered faster: sublingual (SL) tablet dissolution itself is time-limiting
- 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
- 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

